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BRACHYTHERAPY AND RADIOISOTOPES

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ABSTRACT

Brachytherapy (brak-e-THER-uh-pee) is a procedure that involves placing radioactive material inside your body. Brachytherapy is a type of radiation therapy that's used to treat cancer. Brachytherapy is sometimes also called internal radiation therapy. In this type of radiation therapy, the radioactive source delivered through seeds, ribbons, catheters or wires is placed within or just next to a tumor and may be left in place permanently or temporarily, depending on the cancer type and location. That allows eliminations of cancer cells from inside the tumor mass as opposed to a radiation beam going through healthy tissue to reach tumor cells (in case of external beam radiotherapy).

INTRODUCTION

Brachytherapy is a type of cancer treatment that uses radiation to eradicate cancer cells and shrink tumor mass. In this type of radiation therapy, the radioactive source delivered through seeds, ribbons, catheters or wires is placed within or just next to a tumor and may be left in place permanently or temporarily, depending on the cancer type and location. That allows eliminations of cancer cells from inside the tumor mass as opposed to a radiation beam going through healthy tissue to reach tumor cells (in case of external beam radiotherapy).Brachytherapy (brak-e-THER-uh-pee) is a procedure that involves placing radioactive material inside your body .Brachytherapy is one type of radiation therapy that's used to treat cancer. Brachytherapy is sometimes called internal radiation. Brachytherapy allows doctors to deliver higher doses of radiation to more-specific areas of the body, compared with the conventional form of radiation therapy (external beam radiation) that projects radiation from a machine outside of your radiation, and the overall treatment time is usually shorter with brachytherapy. Brachytherapy is used to treat several types of cancer, including:Bile duct cancer, Brain cancer, Breast cancer Cervical cancer, Endometrial cancer Esophageal cancer, Eye cancer, Head and neck cancers ,Lung cancePancreaticcancer,Prostate cancer, Rectal cancer Skin cancer, Soft tissue cancers,Vaginal cancer. Brachytherapy can be used alone or in conjunction with other cancer treatments. For instance, brachytherapy is sometimes used after surgery to destroy any cancer cells that may remain. Brachytherapy can also be used along with external beam radiation.

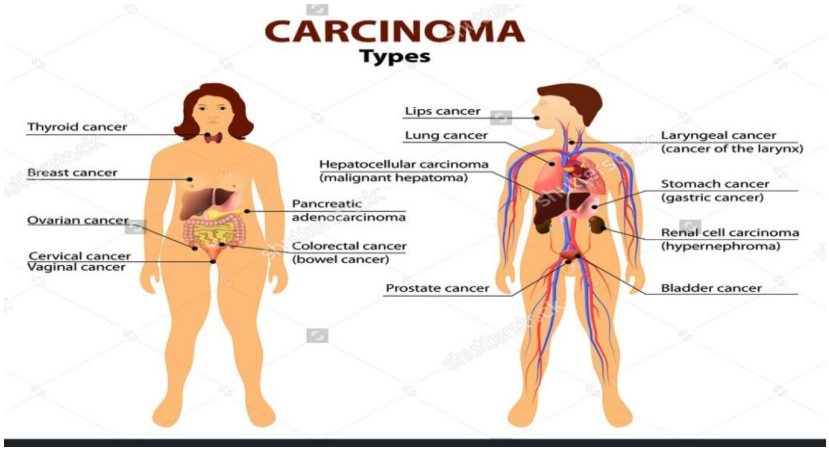


Figure 1: Types of carcinoma.

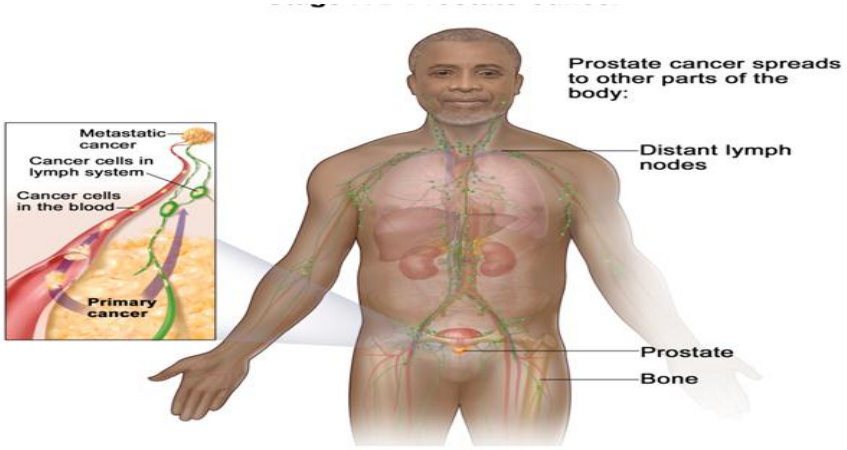
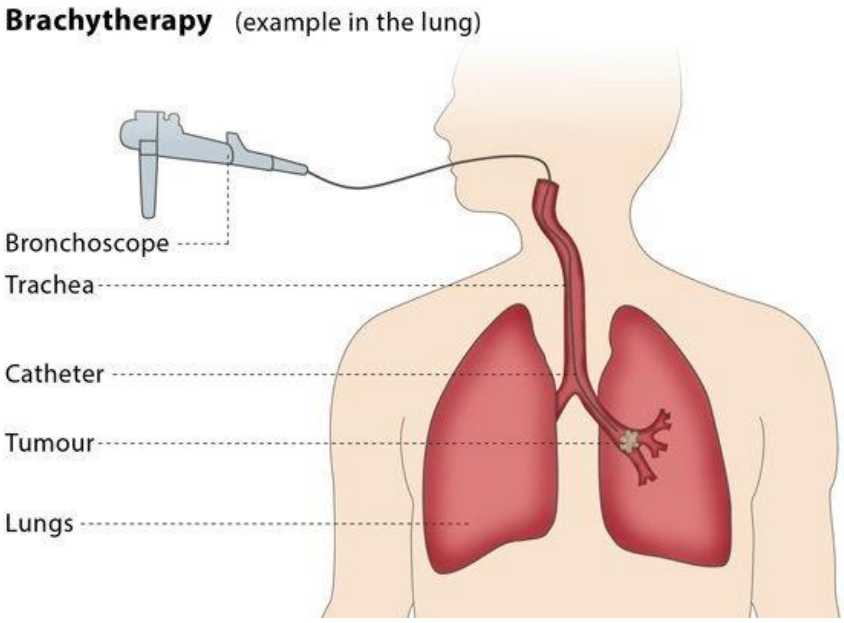


Figure 2: Prostrate cancer.



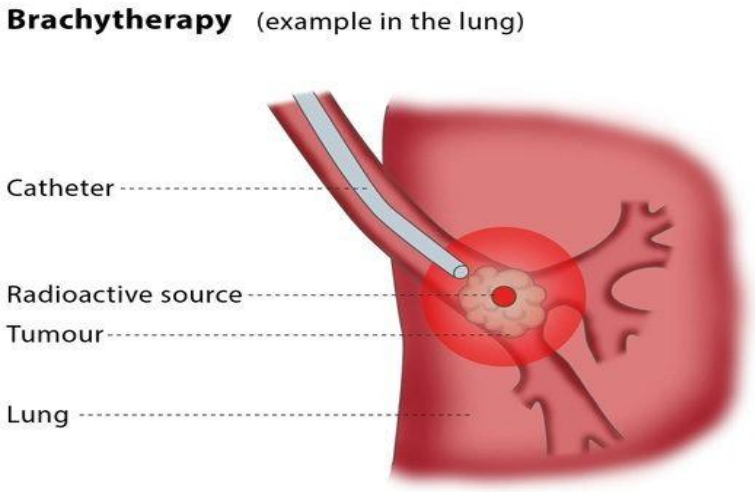


Fig. 3: Procedure of Brachytherapy.

How to use radiation

Placement may be inside a body cavity or in body tissue

Radiation placed inside a body cavity. During intracavity brachytherapy, a device containing radioactive material is placed in a body opening, such as the windpipe or the vagina. The device may be a tube or cylinder made to fit the specific body opening. Your radiation therapy team may place the brachytherapy device by hand or may use a computerized machine to help place the device.

Imaging equipment, such as a CT scanner or ultrasound machine, may be used to ensure the device is placed in the most effective location.

Radiation inserted into body tissue. During interstitial brachytherapy, devices containing radioactive material are placed within body tissue, such as within the breast or prostate.

Devices that deliver interstitial radiation into the treatment area include wires, balloons and tiny seeds the size of grains of rice. High-dose-rate vs. low-dose-rate brachytherapy

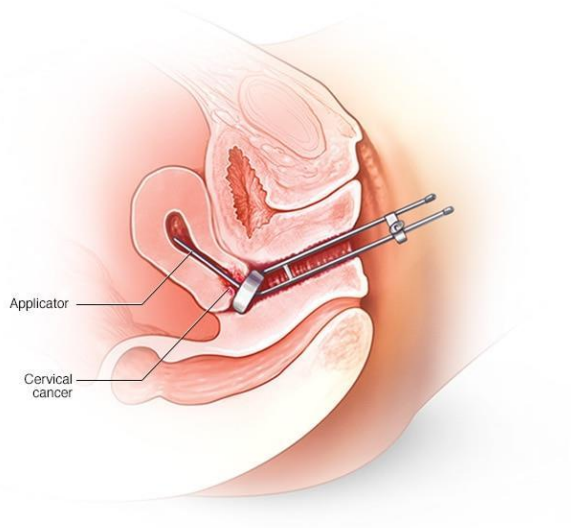


Fig. 5: Intracavity brachytherapy

High-dose-rate brachytherapy

During high-dose-rate brachytherapy, radioactive material is placed in your body for a short period — from a few minutes up to 20 minutes. You may undergo one or two sessions a day over a number of days or weeks.You'll lie in a comfortable position during high-dose-rate brachytherapy. This may be a simple tube or tubes placed inside a body cavity or small needles inserted into the tumor.The radioactive material is inserted into the brachytherapy device with the help of a computerized machine.You shouldn't feel any pain during brachytherapy, Once the radioactive material is removed from your body, you won't give off radiation or be radioactive. You aren't a danger to other people, and you can go on with your usual activities.

Low-dose rate-brachytherapy. During low-dose-rate brachytherapy, a continuous low dose of radiation is released over time — from several hours to several days. You'll typically stay in the hospital while the radiation is in place. Radioactive material is placed in your body by hand or by machine.

Permanent brachytherapy. In some cases, such as with prostate cancer brachytherapy, radioactive material is placed in your body permanently.

The radioactive material is typically placed by hand with the guidance of an imaging test, such as ultrasound or CT.

- Intracavitary brachytherapy for gynecologic, lung and esophagealtumors
- Interstitial brachytherapy for head and neck, extremity soft tissue sarcoma, breast, prostate and gynecologictumors
- Yttrium 90 radioembolization for select liver tumors

What Happens Before Your First Brachytherapy Treatment

You will have a 1- to 2-hour meeting with your doctor or nurse to plan your treatment before you begin brachytherapy. At this time, you will have a physical exam, talk about your medical history, and maybe have imaging tests. Your doctor will discuss the type of brachytherapy that is best for you, its benefits and side effects, and ways you can care for yourself during and after treatment. You can then decide whether to have brachytherapy.

How Brachytherapy Is Put in Place

Most brachytherapy is put in place through a catheter, which is a small, stretchy tube. Sometimes, brachytherapy is put in place through a larger device called an applicator. The way the brachytherapy is put in place depends on your type of cancer. Your doctor will place the catheter or applicator into your body before you begin treatment.

Techniques for placing brachytherapy include

- **Interstitial brachytherapy**, in which the radiation source is placed within the tumor. This technique is used for prostate cancer, for instance.
- **Intracavity brachytherapy**, in which the radiation source is placed within a body cavity or a cavity created by surgery. For example, radiation can be placed in the vagina to treat cervical or endometrial cancer.
- **Episcleral brachytherapy**, in which the radiation source is attached to the eye. This technique is used to treat melanoma of the eye.

Once the catheter or applicator is in place, the radiation source is placed inside it. The radiation source may be kept in place for a few minutes, for many days, or for the rest of your life. How long it remains in place depends on the type of radiation source, your type of cancer,

where the cancer is in your body, your health, and other cancer treatments you have had.

Types of Brachytherapy
There are three types of brachytherapy:

Low-dose rate (LDR) implants: In this type of brachytherapy, the radiation source stays in place for 1 to 7 days. You are likely to be in the hospital during this time. Once your treatment is finished, your doctor will remove the radiation source and the catheter or applicator.

High-dose rate (HDR) implants: In this type of brachytherapy, the radiation source is left in place for just 10 to 20 minutes at a time and then taken out. You may have treatment twice a day for 2 to 5 days or once a week for 2 to 5 weeks. The schedule depends on your type of cancer. During the course of treatment, your catheter or applicator may stay in place, or it may be put in place before each treatment. You may be in the hospital during this time, or you may make daily trips to the hospital to have the radiation source put in place. As with LDR implants, your doctor will remove the catheter or applicator once you have finished treatment.

Permanent implants: After the radiation source is put in place, the catheter is removed. The implants remain in your body for the rest of your life, but the radiation gets weaker each day. As time goes on, almost all the radiation will go away. When the radiation is first put in place, you may need to limit your time around other people and take other safety measures. Be extra careful not to spend time with children or pregenencytional Institutes of Health.

Radio isotopes for Brachytherapy
Pd-103 Seeds For Prostate Cancers
In order to treat prostate cancer, radioactive Palladium-103 or Iodine-125 seeds are placed directly into the prostate gland, using either after loading needles with a special "gun" or preloaded needles.

Both of these seeds give off low-energy x-rays, and the majority of the radioactivity is released within a short period of time. Only each seed irradiates a small volume of prostate tissue, and therefore many seeds have to be placed throughout the prostate to cover the entire gland and the cancer site. Because of the low x-ray radiation energy released, radiation exposure to adjacent normal organs is reduced.

The radioactive seeds treat the entire prostate gland because the microscopic cancer cells may be present at different sites within the gland, even though the biopsy in the general area was negative. The number of seeds implanted into the prostate for treatment depends on the size and shape of the prostate gland. On average, the number, of seeds implanted is approximately 100.

In performing brachytherapy, the doctor places a biplaner ultrasound probe in the rectum to image the prostate. The biplaner ultrasound, along with fluoroscopy, gives a multidimensional view of the prostate on several TV screens. These images are then used to accurately place the needles and to space the seeds in the prostate gland. No surgical incision is required.

Needles are advanced through an area of skin (behind the scrotum and in front of the rectum) into the prostate with the aid of:
1. A template attached to the ultrasound probe and,
2. A computer plan designed specifically for the size of the patient's prostate.

Radioactive seeds are then deposited through the needle into the prostate gland. The seeds are permanently placed in the prostate gland. Depending on the radioactive seeds that are selected, they give off radiation for 3 months to a year. Both the probe and needles are removed when the procedure is completed. Cystoscope is done to evaluate the urethra and the bladder and to retrieve any seeds found in the bladder.

About radioactive seed implantation for prostate cancer
Internal radiation therapy, also called Interstitial Radiotherapy or Brachytherapy involves implanting radioactive seeds into the prostate gland to treat cancer.

In selected men, this option offers quick, minimally invasive treatment with good cancer control. Small radioactive rice-sized pellets or "seeds" (Palladium 103 or Iodine 125) are placed directly into the prostate gland and give off a known amount of radioactivity into the surrounding prostate tissue. In this way, radiation is placed as close as possible to the cancerous cells so that the pelvic organs are exposed to less radiation than with external beam radiation.

Seeds are implanted without a surgical incision. They are inserted through the skin of the perineum (just behind the scrotum and in front of the anus) using small pre-loaded needles. General or spinal anesthesia is used. Each seed is carefully placed in a predetermined location and depth. Placement is guided by a template attached to an ultrasound probe and a computer plan is designed specifically for the size of the patient's prostate. Placement is monitored in real time with ultrasound and fluoroscopy.

The permanent seeds give off radiation continually for an extended period of time. The amount of time that the seeds remain radioactive depends on the dose and what type of radioactive material is used. For example, the half-life of Palladium-103 is 17 days. That means that the prostate receives half of the dose in the first 17 days; then one quarter in the next 17 days. The useful dose will have been delivered in three to four half-lives.

The entire gland gets treated because microscopic cancer cells may be present at different sites in the prostate even though the biopsy in the general area was negative. The seeds irradiate a small volume of tissue so several seeds have to be placed to cover the entire gland. The number of seeds used can range from 40 to 150, depending on the size of the prostate gland.

Potential side effects

Any medical treatment may cause side effects or put you at risk for a more serious and/or permanent complication. You may experience a few, none, or **(very rarely)** all of these side effects. Most will disappear or lessen with time. Also, if other types of treatment are given in conjunction with radiation therapy, side effects may be more frequent and/or more severe than if radiation therapy alone had been given.

Probable side effects

- Fatigue
- Pelvic discomfort
- Urinary frequency (feeling the need to urinate frequently Urinary urgency, or feeling the need to urinate right away)

Possible side effects

- Burning during urination
- Urinary retention (passing urine, but unable to fully empty the bladder)
- Urinary obstruction (unable to pass urine)
- Rectal bleeding
- Sexual dysfunction
- Urinary incontinence (unable to control bladder)
- Bowel incontinence (unable to control bowels)

Diarrhea

Hospitals and medical facilities are among the largest users of radioactive sources, typically for teletherapy and brachytherapy applications. Until the 1950s, the only significant radioactive sources produced were the radium-226 sources that were used for brachytherapy. Most of the old radium sources used in brachytherapy have been replaced by cobalt-60, cesium-137 and iridium192

Iridium Ir 192 is a radioactive isotope of iridium. Iridium-192 emits gamma rays and has a half-life of 74 days. A high dose rate of this radioisotope can be used in brachytherapy to treat tumors by selectively delivering a cytotoxic dose of radiation to the tumor site.

The average intake of ^{137}Cs from fallout in 1964 reached 9 Bq per day in Central Europe (Figure 2), or 3280 Bq in the whole year. For adult individuals, this meant an effective dose of 46 μSv. The daily intake of 1.1 Bq of ^{90}Sr (Figure 3), or 400 Bq per year, added 14 μSv. In all, the intake of fallout radioactivity up to 1985 in adults living in Central Europe resulted in a lifetime dose of 240 μSv from ^{137}Cs and 160 μSv from ^{90}Sr.

The most common radioisotope of cesium is cesium-137. It emits beta and gamma radiation, decaying to stable barium-137. Cesium-137 is widely used in gamma sources. It occurs in these sources as cesium chloride pellets. Cesium chloride is a soluble salt. The contamination from a sealed-source leak absorbs water, becomes damp, and creeps. Contamination from a sealed cesium source is best decontaminated by wet procedures unless the contamination is on a porous surface, in which case, vacuuming should precede wet procedures. Cesium is known to adsorb from a solution onto glass surfaces. Decontaminating a liquid cesium–contaminated surface is best accomplished by wetting the surface, absorbing the solution with a rag or other absorbent material, and rinsing the area several times with water. If the contamination persists, use a detergent solution.

Cobalt-60 (60Co) and caesium-137 (^{137}Cs) are the most widely used sources of gamma radiation. ^{60}Co produces gamma rays with energies of 1.173 and 1.332 MeV and has a half-life of 5.27 years, whereas ^{137}Cs produces gamma rays with energy of 0.662 MeV and has a longer half-life of 30.1 years. For both isotopes, the gamma rays energies are not high enough to induce radioactivity in the irradiated products, which would otherwise be a serious disadvantage to a sterilisation process. In industrial practice, the use of ^{137}Cs has been limited to small self-contained, dry storage irradiators used primarily for the irradiation of blood and for insect sterilisation.

In principle, X-rays may also be used for sterilisation. For example, high- energy electrons produced by an accelerator could be used to produce high- energy photons (e.g., X-rays produced by bombarding a tungsten target). In practice, however, the costs of establishing and running such a facility are relatively high with only low conversion of electron beam power to X-ray beam power (I-Ax Technologies Inc., 2008). The use of high-energy electron sources to produce high-energy X-rays is also limited by the potential for producing radioactivity in the irradiated product. This can occur via a number of processes, including photo-disintegration, neutron activation and photo-activation. However, extensive research has shown that below certain energy thresholds, any induced radioactivity is insignificant compared with that which is naturally present.

RBCs are commonly irradiated by using a cesium 137 source.

The purpose of irradiation of cellular blood products in transfusion medicine is to inactivate immunocompetent lymphocytes. Irradiated RBCs are indicated for the prevention of transfusion-associated graft-versus-host disease in immunocompromised patients, a frequently fatal complication. Neonates, patients with hematologic malignancies, patients with aplastic anemia, bone-marrow transplant recipients,

and patients with congenital immune deficiency are susceptible to transfusion-associated graft-versus-host disease.

Brachytherapy

Metallic needles containing ^{226}Ra, ^{60}Co, or ^{137}Cs or after loading metallic guides or Teflon catheters for insertion of ^{192}Ir wires or seeds have been implanted in the parametrium or cervix, using a transvaginal or transperineal approach (sometimes in lieu of intracavitary insertions when the cervical canal cannot be identified) and frequently with the aid of templates.[137] The procedure is similar to that followed for intracavitary insertions. The cervix should always be held firmly with a tenaculum. For implants in the cervix itself, the needles or nylon catheters with metallic guides (5 to 6 cm long) are inserted straight, about 1.2 cm apart, following the position of the uterus (which can be verified with a finger in the rectum).

Insertion of needles into vital structures, including the bladder and rectum, must be avoided, unless it is necessary to cover the tumor volume. The operator should keep in mind the expected anatomic location of the major pelvic vessels, especially veins.

Scientists have popularized the use of interstitial implants, using perineal templates with introduction of metallic needles through the perineum into the parametrial tissues. Iridium 192 seeds are inserted in an afterloading fashion. Doctors modified their technique by deleting three anteriorly and three posteriorly placed needles in the central row; the central tandem was also omitted in an effort to decrease an initial high incidence of vesicovaginal or rectovaginal fistula. The investigators reported about 75% pelvic tumor control in 118 patients with stages IIB and III carcinoma of the uterine cervix. The major complication rate was 6% with less than 4500 mg/h, 16% with 4500 to 4999 mg/h, 28% with 5500 mg/h, and 87% with higher intracavitary doses (combined with 45 to 50 Gy to the whole pelvis).

Martinez and coworkers described results in 104 patients with locally advanced or recurrent pelvic tumor using a universal perineal template (32 to 35 Gy at a dose rate of 2.75 cGy/h) combined with EBRT (36 Gy to the whole pelvis and 14 Gy to the pelvic side wall with midline block using four-field techniques, 4- or 10-MV photons). Local tumor control was obtained in 82% of 63 patients with gynecologic lesions. The major complication rate requiring surgical intervention was 3.2%.

Leborgue and colleagues reported their experience with MDR brachytherapy (1 to 12 Gy/h). In carcinoma of the cervix, EBRT with a central block was given to the pelvis (40 Gy at 2 Gy/fraction), and patients with stage IIB disease received an additional 20 Gy to the whole pelvis without central shielding. A control group of 102 patients was treated with LDR brachytherapy (average dose rate was 0.44 Gy/h, two 32.5-Gy fractions to point A in 74 hours each, 2 weeks apart). The MDR group was treated at 1.6 to 1.7 Gy/h to point A. Dose fractionation schedules for MDR were derived using the linear-quadratic equation to arrive at a biologically equivalent dose. Grade 2 and 3 sequelae were noted in 1 of 102 patients treated with LDR brachytherapy, in 25 (83%) of 30 patients treated with MDR brachytherapy with a 5% dose reduction compared with LDR therapy (61.75 Gy), and in 4 (40%) of 10 and 0 of 38 patients treated with 3 or 6 MDR fractions for a total of 58 or 55.5 Gy to point A, respectively. The average nominal biologically effective dose for the various groups ranged from 78 to 124 Gy. The incidence of the late rectal complications was zero for patients receiving rectal biologically effective doses of less than 50 Gy, 24% to 36% for 50 Gy to 199 Gy, and 67% for 200 Gy or greater. The investigators concluded that the safest schedule was to deliver 18 Gy to the whole pelvis with EBRT, plus brachytherapy delivering a dose rate to point A of 1.6 Gy/h, in six fractions of 8 Gy, two in each treatment day, 10 days apart. Two fractions are given on a single day, 6 hours apart, to reduce the number of insertions to three. This study emphasizes the importance of conducting prospective dose fractionation studies based on sound biologic data.

Gold-198 was the first material used for the purpose. This had a particle size of 5 nm. Although this material has greater and faster uptake than any other subsequently developed radioisotopes, the high dose of radiation thwarted its broader clinical use.Iodine-131 and ^{99m}Tc were later introduced for lymphoscintigraphy. The ^{99m}Tc attached to sulfur colloid is now the most widely used for lymphoscintigraphy. The advantages of ^{99m}Tc sulfur colloids are that they emit only gamma rays and have low radiation exposure, the half-life of ^{99m}Tc is only 6 hours, and it has a peak energy emission peak of 140 keV. This is within the detection range of most gamma camera and handheld gamma probes. The particle size and the attached molecules are the primary factors that determine the rate of uptake into the lymphatics and the filtration within the sentinel node. The optimal particle size of radioisotopes is between 5 and 10 nm. A particle smaller than 5 nm may be taken up by the vascular system. The radioisotopes may be used as either filtered or unfiltered forms. Filtration allows control of particle size to a specific range (15-50 nm). Unfiltered nanocolloids have a particle size ranging from 5 to 1000 nm. The dose of radioisotope used also varies from 0.5 to 0.8 mCi. Using a ^{99m}Tc sulfur colloid in cutaneous lesions, the transit time to the lymph node is less than 1 hour. The radioactivity may be retained in the lymph node for an additional 3 to 6 hours. However, for mucosal head and neck tumors, the transit time is less than 30 minutes. The radioactivity can be detected for 3 to 6 hours after the injection. Ideally, the injection, dynamic scintigraphy, and intraoperative gamma probe localization should be done on the same day.

Tilmanocept is a new agent. It is a ^{99m}Tc-labeled non-particulate radiotracer that contains multiple mannose moieties with high affinity for the CD206 receptor found on macrophages and dendritic cells, enhancing targeting to these cells within the SLN. Studies in breast cancer and melanoma have shown that tilmanocept may have improved clearance from the site of the primary tumor and enhanced retention within the sentinel node when compared to sulfur colloid. Because of the rapid clearance and prolonged retention within the sentinel nodes, patients could be injected preoperatively from immediately prior to surgery up to 30 hours preceding surgery. A single institution reported their experience as part of this larger multicenter trial in their initial report of 20 clinically node-negative patients.[95] The NPV was 100% for five patients with floor-of-mouth tumors.

Interstitial Brachytherapy

Radon gas (^{222}Rn) in beads and radioactive gold (^{198}Au) pellets that emit γ-rays have been used for interstitial brachytherapy. Radioactive sources are inserted permanently and slowly deliver the radiation dose to the surrounding tissue, until complete decay occurs. To minimize personnel exposure, the implantation procedure is done in two steps: first, the insertion of unloaded needles in tissues according to specific radiation planning rules; and second, the loading of the needles with radioactive sources using a special implantation instrument. Achieving consistently satisfactory implants requires a good deal of practice. Treatment is expensive, because radioactive sources can be used only once. This technique is now used rarely and is not allowed in most areas of the United States (the reader may inquire at the local department of social and health services for state regulations, or with the appropriate government agency in other countries). The major drawback is the potential radiation hazard, because the implant is still radioactive when the horse is discharged from the hospital.

Intraperitoneal instillation of radioisotopes, such as gold (^{198}Au) and chromic phosphate (^{32}P), have been studied in patients with ovarian cancer. It is now rarely used. Although the initial studies were performed using ^{198}Au, ^{32}P became the preferred isotope because of ease of handling, lack of gamma radiation, and a relatively low complication rate.^{32}P is a high-energy pure beta-particle emitter with a maximum energy of 1.71 MeV, a maximum penetration of 8 mm (average, 1 mm to 4 mm), and a half-life of 14.3 days. It can be used for intracavitary instillation at a dose of 10 mCi to 20 mCi. The majority of the ^{32}P is absorbed by the peritoneal surface via macrophages and then excreted through the lymphatic channels of the abdomen, that is, the thoracic lymphatics, and from there into the systemic vasculature where it is cleared by the liver. The retroperitoneal pelvic and paraaortic lymph nodes receive low doses of radiation. Because the main pattern of spread of ovarian cancer is transcoelomic, the IP instillation of radiocolloids, which deliver high doses of radiation to the peritoneal surfaces while minimizing systemic effect, would seem theoretically ideal. Gamma camera imaging of the abdomen has shown that the administration procedure including mobilization of the patients in the first 6 hours is critical for homogeneous dispersion of the radiocolloids on the serosal surfaces.[108] Dose calculations gave an estimated tissue surface dose of 30 Gy per 370 MBq of ^{32}P administered. The amount of ^{32}P in peripheral blood increased for 7 days after administration and was then followed by a continuous decrease. The estimated peripheral blood dose is 0.012 Gy, and the maximum bone marrow dose is 0.06 Gy.

Several randomized studies evaluating the efficacy of ^{32}P in early-stage ovarian cancer have been published . The earliest of the randomized trials was published in 1988 by the National Cancer Institute of Canada (NCIC). Two hundred fifty-seven women with stages I to IIA high-risk ovarian cancer or with stage II disease were randomized to one of three trial arms: arm A, WAI (22.5 Gy in 20 fractions); arm B, melphalan; or arm C, ^{32}P. Surgical staging was not mandatory, and most patients' disease was not thoroughly staged. All patients were initially treated with pelvic RT (arm A: 22.5 Gy in 10 fractions; arms B and C: 45 Gy in 20 fractions). The ^{32}P trial arm was discontinued early because of increased bowel toxicity. No significant difference in survival was found.

In 1990 the Gynecologic Oncology Group (GOG) published a randomized controlled trial including 141 patients with stage I, grade-3 or stage II epithelial ovarian cancer randomly assigned to melphalan or a single dose of ^{32}P at the time of surgery. With a median follow-up of more than 6 years the outcomes for the two treatment groups were similar with respect to 5-year disease-free survival (DFS) (80% in both groups) and 5-year OS (81% with melphalan versus 78% with ^{32}P; $p = 0.48$). They concluded that either treatment was a reasonable option.

In 1992, Vergote et al published a randomized trial of 347 patients, stages I to III (no gross residual tumor), who were allocated to cisplatin (50 mg/m^2) every 3 weeks for six cycles or ^{32}P. Patients with intraabdominal adhesions allocated to IP administration of ^{32}P were treated with WAI (22 Gy to the whole abdomen in 20 fractions) followed by 22 Gy in 11 fractions to the pelvis. Patients did not undergo comprehensive staging because lymph node sampling was not performed. The estimated 5-year OS of patients with stage I disease were 82% for the ^{32}P arm, 94% for the WAI arm, and 79% for the cisplatin arm ($p = 0.79$, $p = 0.44$ compared with the cisplatin arm, respectively). Bowel obstruction occurred more frequently in those treated with ^{32}P (9%, $p = 0.02$) or WAI (21%, $p = 0.001$) in comparison with the cisplatin arm (2%). Because no survival benefit was shown, cisplatin was recommended as the standard treatment.

The Italian GruppoInterregionaleCollaborativo in GinecologiaOncologica (GICOG) performed a randomized trial of 152 women with stage IA grade 2, IB grade 2, and IC disease, comparing treatment with cisplatin with that with ^{32}P. Patients underwent a surgical procedure that did not include lymph node sampling. In 15 patients randomized to treatment with ^{32}P, the radioisotope was not delivered, owing to the development of abdominal adhesions. An improved 5-year PFS was reported for the cisplatin group in comparison with the ^{32}P group (85% versus 65%, p = 0.008) but without an OS difference (81% versus 79%, p = 0.35).

The latest randomized study was published by the GOG in 2003. Two hundred twenty-nine women with early-stage ovarian cancer at high risk for relapse (defined as stage IA or IB grade 3, stage IC, or stage II, no macroscopic residual) were assigned to treatment with ^{32}P or with cyclophosphamide and cisplatin.[109] The cumulative incidence of relapse at 10 years was 35% for the ^{32}P arm and 28% for the cyclophosphamide-cisplatin arm. Patients receiving cyclophosphamide-cisplatin had a relapse rate 29% lower than those in the RT arm (p = 0.15) and a death rate 17% lower than those in the RT arm (p = 0.43). The toxicity profiles of both regimens were reasonably well tolerated, although 3% of the patients receiving ^{32}P suffered perforation of the small bowel during the insertion of the IP catheter and 7% had problems with inadequate distribution. Grade-3 or grade-4 gastrointestinal toxicity was seen in 12% of patients treated with cyclophosphamide and cisplatin. The authors concluded that, although there were no statistically significant differences, the lower relapse rate seen in the chemo arm together with ^{32}P complications make platinum-based chemo the preferred adjuvant therapy.

The group at MSKCC has published several reports on the use of I seeds and Au grains for permanent perioperative brachytherapy in patients with persistent or recurrent bronchogenic carcinoma after EBRT or for residual disease after surgical resection. The radioactive seeds or grains are directly implanted in the tumor at the time of thoracotomy under general anesthesia.

Temporary removable implants of the mediastinum with or without resection followed by a moderate dose of postoperative EBRT (35 to 40 Gy) have been used alone or combined with ^{125}I implantation of the known primary tumor. The MSKCC report described local tumor control in 78% of patients with stage I and II tumors and 67% of those with stage III lesions. Furthermore, patients with microscopic residual tumor have significantly better tumor control and survival than those with gross residual disease.

Although lobectomy is the standard for lung cancer because a wedge resection has a three to five times greater incidence of local recurrence, poor pulmonary function may preclude lobectomy. Segmentectomy or wedge resection along with brachytherapy delivered via a vicryl mesh implant imbedded with ^{125}I is a novel therapeutic modality to treat early-stage lung cancer. This modality is being evaluated in a large national prospective randomized trial .However, there are concerns with exposure of operating room personnel and patient contacts to unnecessary radioactivity risks. Accordingly, HDR brachytherapy with afterloader catheters placed at the time of wedge resection has been recently reported. The radiation dose was 24.5 Gy (3.5 Gy per fraction over seven fractions twice daily for 4 days), prescribed to 1 cm deep to the stapled line.

Radiation therapy with beta radiation (strontium-90) and brachytherapy with cesium-137, gold-198, radon-222, cobalt-60, and iridium-192 have been reported for equine lid SCC. Beta radiation has limited penetration (and is primarily used for corneoconjunctival SCC), but the brachytherapy agents are generally placed directly within the eyelid mass. The iridium-192 isotope, contained in stainless steel rods at 1 cm intervals in a plastic coating or within needles, is placed in the SCC mass in parallel rows about 1 cm apart The usual dose is 6000–7000 cGy and requires about 7–10 days of implantation.

Unfortunately, availability, transportation and material costs, radiation exposure to personnel, isolation of the patient, and state radiation safety guidelines are important limitations. Brachyradiation yields the highest success rate for lid SC in the horse, and has well over 95% non-recurrence. Complications of brachytherapy include hair loss, hair and skin depigmentation, necrosis, fibrosis, keratitis, cataract formation, and corneal ulceration.

Cobalt-60 in HDR BrachytherapyHDR Brachytherapy Started with Cobalt-60sIn 1962, Walstam introduced the first concept of a remote afterloader equipped with Co-60. Since its introduction, Co-60 has achieved tremendous success and has continued to evolve to support modern HDR brachytherapy needs. In 2003, Eckert & Ziegler BEBIG successfully designed and introduced the first miniaturized Co-60 source. This design, modern even by today‘s standards, enables treatment with applicators of the smallest diameters and narrow curvatures. To date, more than 270 Eckert & Ziegler BEBIG afterloaders equipped with Co-60 have been installed worldwide and continue to prove their outstanding reliability.

Result:Since brachytherapy is localized, the radiation is delivered specifically to the tumor mass, protecting the surrounding healthy tissue and limiting exposure. Brachytherapy may cause fewer side effects than does external beam radiation, and the overall treatment time is usually shorter. Most patients feel little pain during brachytherapy other than slight discomfort from the applicator that contains the radiation,

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