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Radiation Therapy and Radiation Therapy Techniques in Cancer Treatment

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ABSTRACT

Radiation therapy (RT) is an effective modality to treat cancer. RT is applicable in a wide range of tumors and can be used alone or in conjunction with surgery and/or systemic therapy. RT works by causing double-stranded breaks in DNA, which are repaired more slowly in tumor compared with normal tissues.

A variety of radiation techniques have been developed. The most widely used of these include: External beam radiation therapy (EBRT), which now primarily uses three-dimensional conformal radiation therapy (3D-CRT) techniques to maximize the dose of radiation to the tumor and minimize exposure of normal tissue to radiation. Important variants on three-dimensional techniques include intensity-modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT). Stereotactic techniques (stereotactic radiosurgery [SRS] and stereotactic body radiation therapy [SBRT]), which use a single fraction or a limited number of fractions of radiation to ablate tumors. Stereotactic techniques rely upon very accurate tumor localization, using magnetic resonance imaging or computed tomography, combined with precise patient immobilization. Brachytherapy, in which a radiation source is placed inside or next to the area requiring treatment. Brachytherapy has a particularly important role in the management of men with prostate cancer and of women with gynecologic malignancies.

1. Introduction

Radiation therapy or radiotherapy, is a therapy using ionizing radiation, as a part of cancer treatment to control or kill malignant cells and normally delivered by a linear accelerator. Radiation therapy may be curative in a number of types of cancer if they are localized to one area of the body. It may also be used as part of adjuvant therapy, to prevent tumor recurrence after surgery to remove a primary malignant tumor. The optimal treatment intent (curative, adjuvant, neoadjuvant therapeutic, or palliative) will depend on the tumor type, location, and stage, as well as the general health of the patient.

Increasingly, RT has been used with surgery and systemic therapies in combined modality approaches for a wide range of malignancies to maximize tumor control and quality of life while minimizing toxicity and preserving the organs. The best outcomes are achieved when each patient is evaluated in a multidisciplinary setting and the team of clinicians, including surgeons, medical oncologists, radiation oncologists, and other specialists, jointly determine the best treatment. In various settings, RT may be the sole treatment, can be given concurrently with systemic agents, or may precede or follow surgery to minimize the chance of microscopic disease left after treatment. In addition, RT may be used palliatively when disease is incurable. The duration of treatment can vary from a single treatment up to eight weeks of daily irradiation. In each clinical scenario, the technique, dose, expected outcomes, and related toxicities change depending upon the diagnosis and treatment site.

Mechanism of Action

Radiation therapy is commonly applied to the cancerous tumor because of its ability to control cell growth. Ionizing radiation works by damaging the DNA of cancerous tissue leading to cellular death. RT primarily damages the DNA of cancer cells by ionizing the atoms that make up the DNA chain. Ionizations result in broken atomic and molecular bonds; the generation of double-strand breaks in DNA is considered the dominant factor that causes cellular lethality (1). Both malignant and normal cells in the treatment field are subject to the ionizing effects of radiation. Normal cells generally are better able to repair damage caused by radiation at the cellular level, using molecular machinery that detects DNA breaks and mutations and repairs them. In contrast, many malignant cells lack these molecular mechanisms and, therefore, are preferentially damaged by radiation. However, normal tissues have limits on the dose of radiation that they can safely withstand; these limits determine the maximum dose that can be safely administered during a course of treatment.

Types

Historically, the two main divisions of radiation therapy are as following ;external beam radiation therapy (EBRT or XRT) or teletherapy, brachytherapy or sealed source radiation therapy.

The differences relate to the position of the radiation source; external is outside the body, brachytherapy uses sealed radioactive sources placed precisely in the area under treatment, and systemic radioisotopes are given by infusion or oral ingestion. Brachytherapy can use temporary or permanent placement of radioactive sources. The temporary sources are usually placed by a technique called afterloading. In afterloading a hollow tube or applicator is placed surgically in the organ to be treated, and the sources are loaded into the applicator after the applicator is implanted. This minimizes radiation exposure to health care personel.

Particle therapy is a special case of external beam radiation therapy where the particles are protons or heavier ions.

External Beam Radiation Therapy

The most common RT approach is to deliver the radiation from a source outside the patient ("external beam radiation therapy" [EBRT]). EBRT machines produce ionizing radiation either by radioactive decay of a nuclide such as cobalt-60 or electronically by the acceleration of electrons or other charged particles, such as protons.

Linear accelerators — Linear accelerators have replaced most cobalt-60 machines in recent decades. In a linear accelerator, electrons are accelerated to high energy and are allowed to either exit the machine as an electron beam or to strike a target that produces X-rays (also known as photons), which are directed at the tumor. Linear accelerators are relatively small devices, they can generate either photon or electron beams of various energies, and their output is managed with sophisticated computer controls. Photons are the most widely used radiation mode due to their ability to penetrate deeply and reach internal organs. Electrons are often used for superficial targets such as the skin and breast, where the goal is to minimize radiation to deeper tissues and organs. Better organ sparing can be achieved with this treatment modality. Often photons and electrons can be carefully mixed to deliver the best possible tumor and normal tissue dose distribution.

Conformal therapy — Conformal therapy is a term that describes a strategy for matching ("conforming") the high-dose radiation region to the target volume while minimizing the radiation dose to normal tissues. This term is typically used when the target volumes are defined on a CT or other high-definition imaging study used during the treatment planning. Therefore, three-dimensional conformal radiation therapy (3D-CRT) usually implies a CT- or MRI-based treatment plan. These plans allow radiation oncologists to calculate and optimize the radiation dose received by the tumor, as well as the adjacent normal tissues. Refinements of 3D-CRT include intensity-modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT). Conformal therapy has not been demonstrated to improve survival for the majority of clinical situations. However, conformal therapy is generally accepted as a way to reduce toxicity (2-4). With reduced toxicity, dose escalation trials have become possible in an effort to improve long-term tumor control. Furthermore, use of 3D-CRT has made retreatment of a previously irradiated area feasible in more situations than were previously possible

Intensity-modulated radiation therapy — IMRT is an advanced form of 3D-CRT that changes the intensity of radiation in different parts of a single radiation beam while the treatment is delivered. IMRT results in a larger volume of normal tissue receiving lower doses of radiation compared with older techniques13-15 IMRT was developed in late 1980s and the first commercial system was introduced in 1992 (5).

Image-guided radiation therapy — Uncertainty about patient positioning requires that clinicians add extra margins to the target volumes beyond that based upon the original imaging of the tumor. Real-time imaging of the treatment target and normal organs during each treatment allows for minimization of such additional margins and the reduction of irradiated volumes, as it decreases the chance of missing a target. This technology is collectively referred to as IGRT, and it employs various methods for real-time imaging and treatment adjustment.

Particle therapy — Particle therapy is a special form of EBRT, with protons being the most widely used (6). Special equipment is used to generate high-energy particles, and these devices are large and costly to build and operate.

Proton beam — Proton radiation reduces the dose to normal tissues by allowing for more precise dose delivery because of the unique physical properties of heavy particles. Protons penetrate tissue to a variable depth, depending upon their energy, and then deposit that energy in the tissue in a sharp peak. This rapid dose falloff at a depth that can be controlled by the initial energy of the protons allows for decreased radiation to adjoining normal tissue by a factor of 2 to 3 (7). At the present time, the clinical superiority of protons compared with photons is clearly established in some pediatric populations and in rare situations when normal structures in close proximity to the treatment target limit the ability to deliver conventional photon beam therapy, such as uveal melanoma and sarcomas of the skull base and spine (8-15). Additional trials are underway to determine the role of protons

Other heavy particles — Other heavy particles have also been used for RT. Neutrons have a very limited clinical application, and experience with carbon ions is limited to only a few countries, such as Japan and Germany. Neutron RT is believed to have an advantage in the treatment of certain tumors that exhibit a resistance to conventional photon beam RT, such as inoperable or recurrent salivary gland malignancies or incompletely resected sarcomas of bone, cartilage, and soft tissue (16-18). Increased risk of secondary malignancy with neutron exposure remains a major concern (19).

Stereotactic radiation therapy techniques — Stereotactic RT techniques administer the full calculated dose of radiation in one or a very limited number of treatment fractions. Stereotactic techniques typically utilize photons that are generated by a linear accelerator or by a cobalt-60 source. There are two types of stereotactic radiation. Stereotactic radiosurgery (SRS) is when doctors use a single or several stereotactic radiation treatments of the brain or spine. Stereotactic body radiation therapy (SBRT) refers to one or several stereotactic radiation treatments with the body, such as the lungs.

Brachytherapy

Brachytherapy is a form of RT in which a radiation source is placed inside or next to the area requiring treatment. Radiation sources are precisely placed directly at the site of the cancerous tumour. This means that the irradiation only affects a very localized area –exposure to radiation of healthy tissues further away from the sources is reduced. These characteristics of brachytherapy provide advantages over external beam radiation therapy – the tumour can be treated with very high doses of localized radiation, whilst reducing the probability of unnecessary damage to surrounding healthy tissues (20,21). A course of brachytherapy can often be completed in less time than other radiation therapy techniques. This can help reduce the chance of surviving cancer cells dividing and growing in the intervals between each radiation therapy dose (21).

Brachytherapy has defined roles in a number of malignancies. The potential role of brachytherapy is illustrated by its use in prostate cancer, gynecologic malignancies, and breast cancer:

Intraoperative Radiation Therapy

Intraoperative radiation therapy (IORT) is the delivery of radiation at the time of surgery. Whereas the dose delivered by external beam radiation therapy (EBRT) is limited by the tolerance of surrounding normal tissues, IORT allows exclusion of part or all of the dose-limiting sensitive structures by operative mobilization and/or direct shielding of these structures. A single-fraction treatment is used, and dose is limited by structures (nerves, fixed organs) that cannot be displaced. The decision to deliver IORT is often made intraoperatively, based upon clinical and frozen-section pathology evaluation. Areas at high risk of local recurrence (positive margins, incompletely resected tumors) can be visualized and targeted while the patient is under anesthesia (22).

The use of IORT was initiated in the 1960s in Japan and currently, a linear accelerator-based electron treatment approach is used in approximately 90 centers in at least 16 countries worldwide (23).

IORT is most useful for pelvic and abdominal malignancies where normal bowel limits the dose that can be delivered with EBRT. However, the dose delivered in a single fraction with IORT is rarely sufficient for tumor control, and therefore, IORT is usually preceded or followed by additional EBRT.

Author contributions:

Eda Bengi Yılmaz: Conceptualization, Methodology, Software, Data curation, Writing-Original draft preparation, Software, Validation, Visualization, Investigation, Writing-Reviewing and Editing.

REFERENCES

Abe M, Fukuda M, Yamano K, et al (1971) Intra-operative irradiation in abdominal and cerebral tumours. Acta Radiol Ther Phys Biol 10:408.

Carol M. Integrated 3D conformal multivane intensity modulation delivery system for radiotherapy. In: Proceedings of the XIth International Conference on the Use of Computers in Radiation Therapy, Hounsell A (Ed), Manckester, UK 1991. p.172.

Delaney TF, Kooey HM. Protons and Charge Particle Radiotherapy, 1st, Lippincott Williams & Wilkins, Philadelphia 2008.

Douglas JG, Koh WJ, Austin-Seymour M, Laramore GE (2003) Treatment of salivary gland neoplasms with fast neutron radiotherapy. Arch Otolaryngol Head Neck Surg 129:944.

Durante M, Orecchia R, Loeffler JS. Charged-particle therapy in cancer: clinical uses and future perspectives (2017) Nat Rev Clin Oncol 14:483.

Dutta SW, Showalter SL, Showalter TN, Libby B, Trifiletti DM (2017) Intraoperative radiation therapy for breast cancer patients: current perspectives. Breast Cancer: Targets and Therapy. 9: 257–263.

Garden AS, Morrison WH, Wong PF, et al (2007) Disease-control rates following intensity-modulated radiation therapy for small primary oropharyngeal carcinoma. Int J Radiat Oncol Biol Phys 67:438.

Gerbaulet A, et al. (2005). "General aspects". In Gerbaulet A, Pötter R, Mazeron J, Limbergen EV (eds.). The GEC ESTRO handbook of brachytherapy. Belgium: ACCO.

Guerrero Urbano MT, Nutting CM (2004) Clinical use of intensity-modulated radiotherapy: part I. Br J Radiol 77:88.

Laramore GE, Krall JM, Griffin TW, et al (1993) Neutron versus photon irradiation for unresectable salivary gland tumors: final report of an RTOG-MRC randomized clinical trial. Radiation Therapy Oncology Group. Medical Research Council. Int J Radiat Oncol Biol Phys 27:235.

MacDougall RH, Kerr GR, Duncan W (2006) Incidence of sarcoma in patients treated with fast neutrons. Int J Radiat Oncol Biol Phys 66:842.

Miralbell R, Lomax A, Cella L, Schneider U (2002) Potential reduction of the incidence of radiation-induced second cancers by using proton beams in the treatment of pediatric tumors. Int J Radiat Oncol Biol Phys 4:824.

Pow EH, Kwong DL, McMillan AS, et al (2006) Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: initial report on a randomized controlled clinical trial. Int J Radiat Oncol Biol Phys 66:981

Revell SH. Relationship between chromosome damage and cell death, Liss A (Ed), New York City 1983. p.113.

Schwartz DL, Einck J, Bellon J, Laramore GE (2001) Fast neutron radiotherapy for soft tissue and cartilaginous sarcomas at high risk for local recurrence. Int J Radiat Oncol Biol Phys 50:449.

St Clair WH, Adams JA, Bues M, et al (2004) Advantage of protons compared to conventional X-ray or IMRT in the treatment of a pediatric patient with medulloblastoma. Int J Radiat Oncol Biol Phys 58:727.

Stewart AJ; et al. (2007). "Radiobiological concepts for brachytherapy". In Devlin P (ed.). Brachytherapy. Applications and Techniques. Philadelphia: LWW.