ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 03, pp.48532-48534, March, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

CASE STUDY

RADIOTHERAPY: AN UPDATE AND REVIEW

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ARTICLE INFO

Article History:
Received 18th December, 2016
Received in revised form
02nd January, 2017
Accepted 24th February, 2017
Published online 31st March, 2017

Key words:
Radiation, Radiotherapy, Interventional, Brachytherapy, Isotopes.

ABSTRACT

In the past 20 years, the technological advances in radiotherapy have been immense which have improved effectiveness, decreased complications and expanded implications of radiation therapy; but some of the technology has not been rigorously evaluated. Although, the promise of new imaging modalities is great, it is not without its hurdles. Importantly, there are large financial and educational barriers in the initial setup and implementation of these new modalities. The present article is a review about the existing modalities of radiotherapy in practice and update on current researches.

Citation: Dr. Asmita Jain, Dr. Anindya Bhalla and Dr. Sankalp Verma, 2017. "Radiotherapy: An update and review", *International Journal of Current Research*, 9, (03), 48532-48534.

INTRODUCTION

Ionizing radiation is used for both diagnostic and therapeutic purposes. The use of ionizing radiation for the treatment of cancer dates back to the late 19th century, remarkably soon after Roentgen discovered X-rays in 1895. (Chou *et al*., 2010) The field of radiotherapy has undergone an amazing series of developments since its inception over a century ago. Several recent advances have been made in radiation techniques, planning and delivery process like (Chou *et al*., 2010; Gerber and Chan, 2008):

i. Refinements in altered fractionation
ii. Three-dimensional conformal radiotherapy
iii. Intensity-modulated radiotherapy
iv. Charged-particle radiotherapy (protons, helium or neon)
v. Neutron-beam radiotherapy
vi. Radioimmunotherapy
vii. Intraoperative radiotherapy
viii. Stereotactic radiosurgery.

Principles of radiation therapy

Radiation is a physical agent, which is used to destroy cancer cells. The radiation used is called ionizing radiation because it forms ions (electrically charged particles) and deposits energy in the cells of the tissues it passes through. This deposited energy can kill cancer cells or cause genetic changes resulting in cancer cell death. (Gerber and Chan, 2008; Ramadas *et al*., 2005; Hazel Colyer, 2003) High-energy radiation damages genetic material (deoxyribonucleic acid, DNA) of cells and thus blocking their ability to divide and proliferate further (Jackson and Bartek, 2009). Although radiation damages both normal cells as well as cancer cells, the goal of radiation therapy is to maximize the radiation dose to abnormal cancer cells while minimizing exposure to normal cells, which is adjacent to cancer cells or in the path of radiation. Normal cells usually can repair themselves at a faster rate and retain its normal function status than the cancer cells. Cancer cells in general are not as efficient as normal cells in repairing the damage caused by radiation treatment resulting in differential cancer cell killing (Samantha Morris, 2001; Begg *et al*., 2011). Radiation can be given with the intent of cure as well as being used as a very effective modality of palliative treatment to relieve patients from symptoms caused by the cancer. Further indications of radiation therapy include combination strategies with other treatment modalities such as surgery, chemotherapy or immunotherapy. If used before surgery (neoadjuvant therapy), radiation will aim to shrink the tumor. If used after surgery (adjuvant therapy), radiation will destroy microscopic tumor cells that may have been left behind. It is well known that tumors differ in their sensitivity to radiation treatment.

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Radiation therapy works through in various ways to remove the cancer cells

The biological target of radiation in the cell is DNA

1. Direct effects of radiation: Radiation can directly interact with cellular DNA and cause damage
2. Indirect effects of radiation: The indirect DNA damage caused by the free radicals is derived from the ionization or excitation of the water component of the cells

Modalities of radiotherapy

There are two ways to deliver radiation to the location of the cancer. External beam radiation is delivered from outside the body by aiming high-energy rays (photons, protons or particle radiation) to the location of the tumor. Internal radiation or brachytherapy is delivered from inside the body by radioactive sources, sealed in catheters or seeds directly into the tumor site. (Gerber and Chan, 2008; Begg *et al*., 2011; Case, 1953)

Teletherapy/external beam radiation

This is the most common modality accounting for 90% of radiation therapy. It involves the delivery of electromagnetic radiation (e.g. X-rays, gamma rays) or particulate radiation (e.g. electrons, protons) from a linear accelerator or radionuclide source, such as 60cobalt kept at a distance away from the patient. It is of two types depending on energy of rays, which are used for this purpose.

- Kilovoltage Therapy

  (i) Superficial X-rays (50-150 kV)
  (ii) Orthovoltage X-rays (150-300 kV).

- Megavoltage Therapy

  (i) Cobalt gamma rays (1.17-1.33 mV)
  (ii) Linear accelerators (4-25 mV) (1 mV = 1000 kV).

Radiation therapy techniques

Fractionation

Radiation therapy delivered in a fractionated regime is based on the differing radiobiological proper-ties of cancer and various normal tissues. These regimes in general amplify the survival advantage of normal tissues over cancer cells, largely based on better sublethal damage repair of radiation damage in normal cells as compared to cancer cells. Normal cells proliferate relatively more slowly compared to the rapidly proliferating cancer cells and therefore have time to repair damage before replication. Initial observations of the effects of fractionated radiation therapy in the 1920s eventually led to the development of regimes comparing different treatment schedules based on total dose, number of fractions and overall treatment time (Jackson and Bartek, 2009; Samantha Morris, 2001; Samantha Morris, 2001). Current regimes are based on the more refined linear-quadratic formula which addresses the time-dose factors for individual tumor types and normal tissues (Samantha Morris, 2001). A typical radiation therapy regime now consists of daily fractions of 1.5 to 3Gy given over several weeks.

3D Conformal radiotherapy (3DCRT)

2D radiation therapy using rectangular fields based on plain X-ray imaging has largely been re-placed by 3D radiation therapy based on CT imaging which allows accurate localization of the tumour and critical normal organ structures for optimal beam placement and shielding. The aim is to deliver radiation to the gross tumour volume (GTV), with a margin for microscopic tumour extension called the clinical target volume (CTV), and a further margin uncertainties from organ motion and setup variations called the planning target volume (PTV) (Bernier *et al*., 2004).

Intensity modulated radiation therapy (IMRT)

IMRT allows the oncologist to create irregular-shaped radiation doses that conform to the tumour whilst simultaneously avoiding critical organs. IMRT is made possible through: a) inverse planning soft-ware and b) computer-controlled intensity-modulation of multiple radiation beams during treatment. This has allowed improve-ments in the therapeutic ratio for several tumor sites, such as head and neck cancers, prostate cancers and gynecological cancers (Jackson and Bartek, 2009).

Image-guided radiotherapy (IGRT)

As treatment margins become tighter and more conformal, the potential to miss tumour due to organ motion and patient setup variations become greater. When critical structures are close to the tumour, a slight positional error may also lead to inadvertent radiation of the normal organs. IGRT allows the detection of such errors by information acquired through pre-radiotherapy imaging which allows for correction. The improved accuracy has made dose escalation feasible, and this has allowed an improvement in the therapeutic ratio for several tumor sites, such as head and neck cancers and prostate cancers (Gerber and Chan, 2008; Hazel Colyer, 2003; Jackson and Bartek, 2009; Case, 1953; Samantha Morris, 2001).

Stereotactic body radiation therapy (SBRT)

Due to the high radiation dose, any tissue immediately adjacent to the tumour is likely to be damaged. However as the amount of normal tissue in the high dose region is small and non-eloquent, clinically significant toxicity is low. SBRT has shown excellent results in the treatment of early stage non-small cell lung cancer in patients unfit for surgery. Other tumours include in the prostate, head and neck, hepatic, renal, oligometastases, spinal and pan-creatic (Case, 1953; Samantha Morris, 2001; Bernier and Hall, 2004).

Types of radiation used to treat cancer

Photon beams carry a low radiation charge and have a much lower mass. X-rays and gamma rays are routinely used photons in radiation therapy to treat various cancers. X- rays and gamma rays are sparsely ionizing radiations, considered low LET (linear energy transfer) electromagnetic rays and further com-posed of massless particles of energy are called pho-tons. X-rays are generated by a device that excite electrons (e.g. cathode ray tubes and linear accelerators), while gamma rays originate from the decay of radioactive substances (e.g.cobalt-60, radium and cesium). (Samantha Morris, 2001; Begg *et al*., 2011) Electron beams are commonly used in everyday radiation therapy treatment and are particularly useful to treat tumours close to a body surface since they do not penetrate deeply into tissues. External beam radiation therapy is also carried out with heavier particles such as: neutrons produced by neutron generators and cyclotrons; protons produced by cyclotrons and synchrotrons; and heavy ions (helium, carbon, nitrogen, argon, neon) produced by synchrocyclotrons and synchrotrons. Proton beams are a newer form of particle beam radiation used to treat cancer. It can offer better dose distribution due to its unique absorption profile in tissues, known as the Bragg's peak, allowing deposition of maximum destructive energy at the tumor site while minimizing the damage to healthy tissues along their path. These have particular clinical use in pediatric tumors and in adults tumors located near critical structures such as spinal cord and skull base tumors, where maximal normal tissue sparing is crucial (Chou *et al*., 2010; Ramadas *et al*., 2005). Neutron beams are generated inside neutron generators after proton beams are deflected to a target. They have high LET and can cause more DNA damage than photons.

Conclusion

Radiation remains an important modality for cancer treatment with ongoing efforts towards de-signing new radiation treatment modalities and tech-niques which continue to improve the survival and quality of life of cancer patients. With the improved clinical outcomes of cancer treatment, minimizing radiation therapy related toxicities has also become a priority.

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