REVIEW ARTICLE

Neutron Therapy-A Novel Approach To Radiotherapeutics: A Review

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ABSTRACT

The oncogenic cells require ionizing radiation for radio-therapeutics because it forms electrically charged particles or ions. These ions remove electrons from the atom and molecules which in turn either causes cell death or genetic changes that curbs cell growth. For deeper penetration into the tissues greater energy in needed. A neutron mostly has no charge. Neutron beam radiation can sometimes help when other forms of radiation therapy don't work. Neutrons have high biological effectiveness so it requires about one third dose as compare to photons, electrons and proton. Neutron beams are produced by a large and expensive particle accelerator that is known as cyclotron. Cyclotron accelerator produces the protons. The powerful magnets bend and aim the beam to strike a beryllium target, this interaction produces neutrons. The neutron beam radiotherapy is powerful, specialized and highly effective form of external beam radiotherapy that can control the large tumours because unlike low Linear Energy Transfer (LET) radiation, it does not depend upon the presence of oxygen to kill the malignant cells. This review highlights the principle mechanism of action of neutron beam therapy (NBT), advantages, limitations and it's amazing application in the management of malignancies.

Keywords - Cancer, Neutron beam, Radiotherapy

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INTRODUCTION

In economically developed countries cancer is the major cause of mortality which claims about 350,000 lives annually, and is a leading factor of death in developing countries. Head and neck cancer ranks sixth amongst all types and is considered as the most prevalent cancer throughout the world. Global statistics show the fact that there are about 640,000 cases of head and neck cancer per year, resulting in nearly 350,000 deaths per year.[1]

Cancer has multi-factorial etiology and is a disease which affects multiple genetic and cellular organization and can affect all cell types. Hanahan and Weinberg have identified six cancer cell phenotypes or hallmarks of cancer:

- Cells with unlimited proliferative potential. Environmental independence for growth.
- Evasion of apoptosis.
- Angiogenesis.
- Invasion.
- Metastasis to different parts of body.
- If uncontrolled cell growth or metastatic spread occurs it will result in death of the individual.[2,3]

Soon after Roentgen discovered x-rays in 1895, in the late 19th century, cancer radiotherapy has its advent and it went through series of developments since then.[4] Marie Curie won the second Nobel Prize for her research into radium,

establishing her position as a pioneer in the field of radiation therapy.[5]

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.

High-energy radiation damages genetic material (deoxyribonucleic acid, DNA) of cells and thus blocking their ability to divide and proliferate further.[6]

Radiation therapy uses high-energy x-rays to kill cancer cells, thereby shrinking the cancer growth. The objective of radiation therapy is to maximize the probability of cure with a minimum of side effects. Radiation therapy is considered a local treatment because only the cancer cells in the area of the body where the radiation is delivered are killed. If cancer exists outside the radiation field, those cancer cells are not affected by the radiation.[7]

Radiation therapy can be delivered by following three ways:

1. **Teletherapy or External beam radiation therapy (EBRT):** It involves the delivery of electromagnetic radiation (X-rays, gamma rays) or particulate radiation (electrons, protons) via linear accelerator or radionuclide source that aims x-rays at the body.
2. **Brachytherapy or Interstitial implantation:** Is a method of radiation therapy in which encapsulated source or a group of such sources is utilized to deliver gamma or beta radiation at a distance of up to a few centimetres either by surface, intracavitary or interstitial application. Source suitable for brachytherapy usage consists of small amounts of radionuclide which are totally encapsulated by a non toxic and inert material such as stainless steel or platinum. Radioactive sources come in the form of small needles, wires, rods and spheres.
3. **Radioactive Isotopes:** Radioisotopes are either injected or taken as a drink to treat tumours. Commonly used isotopes are Iodine 131, Phosphorous -32, Yittrium-90.

Most patients receive one or the other kind of radiation and some patients receive both. Most radiation therapies utilize photons - lightweight particles that damage cancerous cells. Neutron beam therapy or fast neutron therapy is a specialized form of external beam therapy that uses neutrons which are much heavier than photons. Neutron beam therapy (NBT) uses neutrons, which appear to be more effective in destroying very dense tumors.[4,7]

NEUTRON BEAM THERAPY

Neutron was discovered by Sir James Chadwick in 1932. In 1938, clinical trials for treating cancers by neutrons started but had to face premature obstruction as the cyclotron was needed for the World War II. In 1965, Dr. Mary Catterall began irradiation of cancer patients with neutron beam and in the next four years it was found that for certain tumors better local control can be achieved using neutron irradiation. Encouraged by these results, the M.D. Anderson Hospital and Tumor Institute in Houston, the Naval Research Laboratory in Washington, D.C., and the University of Washington in Seattle began neutron therapy research. They started treating patients in the early 1970s. During the mid-1970s Chicago-area radiation oncologists, Lionel Cohen, M.D. and Frank Hendrickson, M.D., worked with Dr. Robert R. Wilson (Fermilab Director from 1968 until July 1978) to build the Neutron Therapy Facility (NTF) at Fermilab. Measurements of neutron beam characteristics and dose distributions were completed in 1976; patient treatments begun in September 7, 1976.

The National Cancer Institute funded the operation of the facility from June 30, 1975, until October 1, 1985. During that period NTF conducted clinical trials to determine the appropriateness of using neutrons to treat various types of cancers. Initial research included using different doses in order to determine the optimum, safe therapeutic dose with minimum treatment-related late side effects. Some of the trials involved random assigning of eligible

patients to receive either the best conventional treatment for their cancer, or neutrons, which at the time were considered to be experimental. Neutrons are an entirely different type of radiation which has different radiobiological properties than conventional radiation. A neutron is a constituent of the atomic nucleus and interacts directly with the atomic nuclei in tissue. Neutron beam therapy entails the use of a particle accelerator; protons from the accelerator are deflected by a magnet to a target which creates the neutron beam.[4,8,9]

WHY NEUTRON BEAM THERAPY???

Certain tumors are radioresistant, meaning that they are very difficult to kill using conventional X-ray radiation therapy hence neutrons (neutron beam therapy) are used because they have greater biologic impact on cells than any other type of radiation.[10]

Extensive research leading to an understanding of the radiobiology of neutrons was conducted in England during the 1970's. There are following most important findings in relation to neutron therapy:

1. Neutrons are more effective per unit dose than x-rays.
2. Cell survival curves for neutrons are more nearly exponential than those of x-rays
3. The modifying effect of hypoxia is smaller for neutrons than for photons
4. Cell sensitivity to neutrons is much less dependent on cell growth stage than cell sensitivity to photons.[11]

The primary reason supporting the use of neutrons for therapy is their relative biological effectiveness (RBE). For the neutron energies supplied by the Neutron Therapy Facility (NTF) beam, one-third lesser dose is required to achieve the same clinical effect with neutrons as is required with conventional photons. Certain tumours are classified as being radio resistant. The resistance of tumors to conventional radiation therapy has been attributed to:

A - Ischemic (hypoxic) zones, in which tumor cells are protected from the oxidizing free radicals produced by ionizing radiation in well-oxygenated tissues.

B - Repair enzymes that confer an unusually high capacity to sustain and recover from radiation injury.

C - Variation in the response of cells in different phases of the cell cycle, this means that, slow-growing tumors with a large proportion of noncycling, relatively insensitive cells can survive doses of radiation that would be lethal in more rapidly cycling tumors.

D - Intracellular reducing substances (such as melanin) that can intercept oxidizing free radicals before they can react irreversibly with chromosomal DNA.

These mechanisms can lead to development of relative resistance to low linear energy transfer (LET) radiation. High – LET particles irradiation i.e neutron beam induces irreversible chromosomal disruption (double-strand breaks), which kills cells with less dependence on the cell-cycle status, biochemical environment, or treatment schedule. So tumours that respond very poorly to conventional photon therapy, neutrons are more effective, beyond just the factor of three in relative biological effectiveness (RBE).[12,13]

BIOLOGICAL EFFECTIVENESS OF NEUTRON THERAPY

Factors leading to cell destruction or biological effectiveness of radiation include linear energy transfer, total dose, fractionation rate and radio-sensitivity of the cells or tissues. Higher linear energy transfer deposits higher energy on the targeted areas.[14-16]

The basic effect of ionizing radiation is to destroy the ability of cells to divide by damaging their DNA strands. One measure of this destructive ability is called linear energy transfer (LET). Fast neutrons are high LET radiation and the damage is done primarily by nuclear interactions. Photons, electrons and protons are low LET radiation and their damage is done by activated radicals produced from atomic interactions. If a cancer cell is damaged by low LET radiation it may repair itself and continue to grow. With high LET radiation, the chance for a damaged cancer cell to repair itself is very low.[8]

Neutrons interact primarily via (n,p) or spallation interactions, depositing a large amount of energy, (high LET), and often transforming the atom in

the DNA strand into a completely different atom. A tumor cell whose DNA is damaged to this extent cannot repair itself and will ultimately die. This inability for the tumor to repair is one factor accounting for the higher relative biological effectiveness (RBE) of neutron therapy and for the differences in the shapes of cell-survival curves. Many of the studies hypothesized that the number of double-strand breaks in DNA was greater for high LET neutrons than for low LET radiation. It was believed that the greater number of double strand breaks was responsible for the smaller amount of repair observed with high LET radiation. The smaller incidence of repair with high LET radiation is due to the more extensive nature of the damage at an interaction site rather than a larger number of interaction sites. The high RBE associated with high LET radiation has also been attributed to the fact that for high LET radiation, cell killing is relatively independent of cell growth-cycle stage.[11]

PROCEDURE

Before a patient receives neutron therapy, proper diagnostic procedures such as computed tomography (CT) scan, magnetic resonance imaging (MRI) and positron emission tomography (PET) scan should be performed to establish the exact location of the tumor and to decide exactly which spots to target with the neutron beam. Then the patient visits the neutron therapy facility for a treatment planning session. During this visit, a radiation oncology physician simulates the treatment, determining the best positions for the patient and the equipment and the appropriate dose of neutrons. This process is computerized.

It may take up to a week to develop an optimal treatment plan and actually begin treatment. For treatment, the patient lays on a padded table, also referred to as a couch. A pillar supports the table from underneath. The radiation therapist can move the table up and down, sideways and lengthwise, and can swing and rotate it to get the patient in exactly the right position for the neutron beam.(Figure:1) Most patients receive beams from different angles, usually two to four. The neutron beam comes out of a large arm called agantry. The gantry can rotate 360 degrees to deliver the beam from above or below the patient or from the side. To accommodate the large gantry arm, the floor can open as the gantry turns below the patient. At the end of the gantry near the patient is a section called the treatment head, the part from which the beam emerges. Attached to the head is a leaf collimator. The "leaves" are narrow rectangular pieces of steel. There are 40 leaves inside the collimator. According to the radiation treatment plan computer controls the position of each leaf which leads to exposure of the area with precise size, shape and location for patient's tumor. This area is called a field and each field is examined by a radiation oncologist. The leaves block the areas of the beam that may damage healthy tissue and opening formed by the leaves allows the beam to penetrate the malignant tissue. The whole rotating assembly, including the gantry, treatment head, collimator, and gantry counter weighs about 39 tons. An actual treatment session takes about 30 to 60 minutes, depending on how complicated the treatment delivery scheme is. Most of this time is spent getting the patient and equipment into the right positions. The time when the neutron beam is on lasts only about 1 to 2 minutes from each treatment angle. Typically patients get 16 to 18 treatments over a period of 4 to 5 weeks. Sometimes patients find it tiring or uncomfortable to lie still for their treatment; otherwise there's no discomfort during the treatment when the beam is hitting the target area.[17]

Figure-1: Patient treating room for neutron radiation therapy

NEUTRON THERAPY CENTRES AND EQUIPMENT

Several centers around the world have used fast neutrons for treating cancer. Due to lack of funding and support, at present only three are active in the USA. The University of Washington and the Gershenson Radiation Oncology Center operate fast neutron therapy beams and both are equipped with a Multi-Leaf Collimator (MLC) to shape the neutron beam.(Figure:2)

UNIVERSITY OF WASHINGTON

The Radiation Oncology Department operates a proton cyclotron that produces fast neutrons from directing 50.5MeV protons onto a beryllium target.

The UW Cyclotron is equipped with a gantry mounted delivery system an MLC to produce shaped fields. The UW Neutron system is referred to as the Clinical Neutron Therapy System (CNTS).

The CNTS is typical of most neutron therapy systems. A large, well shielded building is required to cut down on radiation exposure to the general public and to house the necessary equipment.

A beamline transports the proton beam from the cyclotron to a gantry system. The gantry system contains magnets for deflecting and focusing the proton beam onto the beryllium target. The end of the gantry system is referred to as the head, and contains dosimetry systems to measure the dose, along with the MLC and other beam shaping devices. The advantage of having a beam transport and gantry are that the cyclotron can remain stationary, and the radiation source can be rotated around the patient. Along with varying the orientation of the treatment couch which the patient is positioned on, variation of the gantry position allows radiation to be directed from virtually any angle, allowing sparing of normal tissue and maximum radiation dose to the tumor. During treatment, only the patient remains inside the treatment room (called a vault) and the therapists will remotely control the treatment, viewing the patient via video cameras. Each delivery of a set of neutron beam geometry is referred to as a treatment field or beam. The

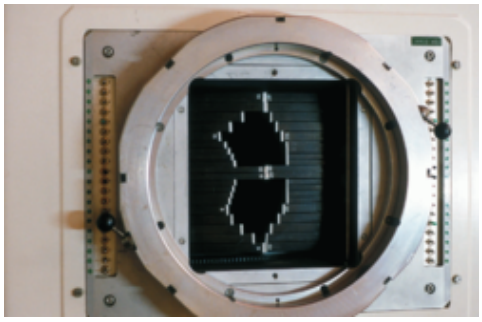

Figure-2: Multi-Leaf Collimator (MLC) used to shape the neutron beam

radiation as effectively as possible, and usually results in fields that conform to the shape of the gross target, with any extension to cover microscopic disease.[17]

NEUTRON CAPTURE THERAPY & BORON NEUTRON CAPTURE THERAPY

Neutron capture therapy (NCT) is a technique that was designed to selectively target high LET heavy charged particle radiation to tumours at the cellular level. There is a difference between neutron capture therapy (NCT) and neutron-based therapy. In NCT, a neutron capture agent like ^{10}B (Boron NCT) with the help of suitable delivery agent is impregnated into malignant tissue, following this, the area is exposed to thermal neutrons by external neutron beam generated by a miniature nuclear reactor or a suitable accelerator-based system. The thermal neutrons interact with the ^{10}B, which has a very high thermal-neutron capture cross section and which, ideally, is present only in the malignant cells. Each boron-neutron interaction produces an alpha particle and a lithium ion. These highly-energetic charged particles deposit their energy within a volume that is comparable to the size of the malignant cell, leading to a high probability of cell inactivation by direct DNA damage. This process offers the possibility of highly selective destruction of malignant tissue, with cellular-level sparing of neighbouring normal tissue. In a sense, BNCT can be viewed as a targeted radionuclide therapy with a mechanism for switching the emissions of the radionuclide on at a selected location in the body and nowhere else.

Another form of neutron therapy that combines the features of fast-neutron therapy and BNCT has also attracted research interest but has yet to be subjected to formal clinical trials. In this modality, a boron neutron capture agent is introduced preferentially into the malignant tissue prior to the administration of standard fast-neutron therapy. Because a small fraction of the neutrons in fast-neutron therapy will be thermalized within the irradiation volume, it should be possible to selectively obtain a small incremental absorbed dose in the target volume from neutron capture. In some cases this small incremental dose may be sufficient to produce a significant improvement in tumor control probability.

BNCT incorporates the targeting principles of chemotherapy and the anatomical localization principles of conventional radiotherapy but with three distinct advantages:

1. Current boron compounds at the required concentrations are non-toxic.
2. The time interval between drug administration and neutron irradiation can be chosen to maximize the concentration differential between tumour and normal tissue.
3. Only the tissues located around the tumour volume are exposed to significant neutron activated boron damage.[19-22]

NEUTRON THERAPY VS REGULAR RADIATION THERAPY

Regular radiation therapy for cancer uses beams of electrons or photons (also called x-rays) to bombard cancer cells. Neutron therapy uses beams of neutrons to attack cancer cells. There are following advantages to using neutrons instead of electrons or photons:

1. Neutron beams are much more powerful.
2. Neutron beams deposit about 20 to 100 times as much energy into the target tissue as regular radiation therapy does.
3. Neutron beams have a higher probability to damage both strands of a cell's DNA, whereas regular radiation in general damages only one strand. So in this way neutron therapy is a good choice in some cases when tumors are resistant to regular radiation.
4. A full course of treatment consists of 12 treatments, three times a week for four weeks, compared to 30-40 treatments, five times a week for six weeks with photons, electrons, or protons.[8,17]

INDICATIONS OF NEUTRON THERAPY

NBT is proposed for the treatment of various forms of cancers including, but limited to:

- Salivary gland tumors
- Locally advanced head and neck tumors
- Locally advanced prostate cancer
- Soft tissue sarcomas
- Small-cell lung cancer
- Breast cancer

Neutron therapy is broadly accepted therapy for the treatment of locally extended, inoperable salivary gland tumours.

Better results were obtained with the neutron beam therapy for soft tissue sarcomas, melanomas and brain tumors as compared with photons, because these tumors are resistant to photon irradiation.

The National Cancer Institute (NCI) states that "fast neutron-beam radiation improves disease-free and overall survival in patients with unresectable tumors or for patients with recurrent neoplasms." They also state that fast neutron beams have been reported to improve disease-free and overall survival in some types of salivary gland tumors. They further state the following are indications for neutron beam therapy:

Stage I tumors with poor prognosis

Stage II tumors that have spread to lymph nodes

high grade tumors that are inoperable, unresectable, or recurrent

Stage III major salivary gland tumors that have spread to local lymph nodes.[23,24]

SIDE EFFECTS

Acute side effects for fast neutron therapy are similar to those of low LET therapy. The severity depends on the total dose delivered and the general health of the patient. Careful, computerized treatment planning minimizes effects on normal tissues. Side effects depend upon the area of the body that is being treated and may include:

- Fatigue.
- Skin irritation, redness, dryness or swelling in the treated area.
- Hair loss in the treated area.
- With radiation to the head: changes in taste, difficulty swallowing, mouth sores, dry mouth, or jaw tightness.[17]

DISADVANTAGES

- More normal tissue damage as compared to photon therapy.
- Generation of neutron particles is difficult clinically.[4]

The equipment used to deliver neutron beam therapy is approved as a Class II, 510(k) device by the U.S. Food and Drug Administration (FDA). Examples of these devices include Isocentric Neutron Therapy Systems (The Cyclotron Corp., Berkeley, CA), Model 4100 14 MEV Neutron Gen. Therapy (The Cyclotron Corp., Berkeley, CA), and Medcyc Superconduct Isocen Neutron Therapy System (Medcyc Corporation, East Lansing, MI).[23]

CLINICAL EFFECTIVENESS

Liu H et al conducted a study to retrospectively observe and analyze the long-term treatment outcomes for a total of 952 oesophageal cancer patients who were treated with (252)Cf neutron brachytherapy (NBT) in combination with external beam radiotherapy (EBRT). From November 2001 to March 2012, 952 patients with oesophageal cancer underwent NBT in combination with EBRT. The patient numbers distributed over various cancer Stages I, IIA, IIB, III, and IVA were 9, 290, 51, 579, and 23, respectively. The total radiation dose to the reference point via NBT was 8-25 Gy-eq in three to five fractions with one fraction/week. The total dose via EBRT was 40-60 Gy delivered over a period of 5-6 weeks with normal fractionation. considered as initial primary treatment for this population and in patients who were high-risk surgical candidates.[28]

Huber et al conducted a comparative study of patients with advanced adenoid cystic carcinoma of the head and neck who had received radiotherapy (i.e., neutron, photon and mixed Results showed that NBT in combination with EBRT produced favourable local control and long-term survival rates for patients with oesophageal cancer and that the side effects are tolerable.[25]

Hassen-Khodja and Lance stated that the efficacy of neutron therapy is well established only for the treatment of inoperable or unresectable salivary gland tumors, regardless of their degree of malignancy or stage of progression, and for the treatment of large residual tumors after surgical resection. In the former case, neutron therapy alone is the treatment of choice, mainly for unresectable cystic adenoid carcinoma of the main or accessory salivary glands. Naturally, in the case of advanced-stage tumors, the therapeutic aim is palliative. As for large-volume residual diseases, neutron therapy is one of the available postoperative radiotherapy options for improving the chances of tumor control. It may be preferred in a context where little or no use is made of conformal radiation therapy.[26]

Prott et al studied the effectiveness of neutron radiation to Adenoid cystic carcinomas (ACC).Between 1986 and 1995, 72 patients with ACC of the salivary glands were treated with fast neutrons. The median age was 54 years. All the patients had either recurrent or macroscopic rest tumor prior to neutron therapy. The median total dose was 15.03 Gy. with median follow-up of 50 months. The Neutron beam therapy stated as an effective treatment in these selected patients by authors.[27]

Douglas et al reported the treatment of 84 patients with adenoid cystic carcinoma of minor salivary glands that were treated with fast neutron beam therapy. All patients had unresectable or gross disease, and 17 had received conventional radiotherapy. The five-year actuarial local-regional tumor control rate was 47% for all patients treated with curative intent. It was stated that fast NBT should be

beam therapy). Between the time interval of 1983 and 1995 - seventy five patients were treated. All cancers were inoperable, recurrent, or incompletely resected. Neutron therapy was given to 29 patients, 21 patients received mixed beam therapy (i.e., neutron/proton) and 25 received photon therapy. There was a significant

advantage in local control for patients in the neutron group over the MBT and the proton group. The recurrence rate was lower in the neutron group over the other two groups. It was concluded that neutron therapy could be recomended in patients with bad prognosis with gross residual disease, unresectable tumors, or inoperable tumors.[29]

Cohen studied the assessment of dose relationships for neutron beam therapy (NBT) and x-ray radiotherapy (XRT) in treatment of epidermoid head and neck tumors. About 116 patients were included in the study stage T3 or T4 epidermoid tumors of the head and neck with or without cervical node involvement who chose neutron beam therapy(NBT) for personal and logistic reasons or received x-ray radiotherapy (XRT) as controls in a randomized trial during approximately the same time period. Minimum follow up of two years was done- NBT and XRT led to similar local tumor control (43% and 44%) but NBT led to considerably more frequent severe complications (19% versus 5% for XRT; P value not reported). The dose effect analysis showed that median dose needed for tumor control was 26 Gy for NBT and 74 Gy for XRT; be substantial deterrents.

The treatment of cancers as a form of radiotherapy is totally dependent upon type of Linear Energy Transfer. DNA damage is one of the major effects in cases of low linear energy transfer, whereas in cases of linear energy transfer, it acts by cutting the DNA strands. Conventional radiotherapy is also effective against various types of carcinomas but neutron beam therapy is an important part of radiation therapy as a high Linear Energy Transfer (LET) radiation. Neutron beam therapy has some selective advantages. Treatment done with low LET radiation such as electrons, photons and protons, the chances of damaged cancer cells to get repair by itself and continue to grow are more than that of neutron therapy. In cases of neutron therapy the required radiation dose is also very low as compared to low LET to kill the same number of malignant cells. Clinical data indicate that neutron beam therapy is selective and unique type of radiation modality as it requires less number of sessions approximately 12 treatment sessions(three times a week for four weeks).

the median dose resulting in significant radiation injury was 31 Gy for NBT and 90 Gy for XRT; and the therapeutic ratio, defined as the ratio of the median dose for normal tissue injury to the median dose for tumor control, was 1.2 for both NBT and XRT. The study was limited by small sample size, lack of randomization and blinding, poor description of treatment groups, and failure to describe the relative distribution of demographic and disease characteristics between treatment groups. Cohen concluded that NBT offers no therapeutic advantage over XRT and is associated with greater toxicity at doses required for tumor control, when used for treating T3 or T4 epidermoid tumors of the head and neck with or without cervical node involvement.[30]

DISCUSSION

Various lines of treatment are available for treating malignancies and amongst all surgery is the most common and oldest treatment. However, surgery is not always effective or possible, and sometimes the risks involved and the potential side effects can

where low LET treatment contains 30-40 sessions (five times a week for six weeks).[31]

A Coordinated Research Program (CRP) was organized by International Atomic Energy Agency in 1987 on nuclear data on neutron therapy. A Coordinated Research Program (CRP) between 1987 and 1993 and a report was prepared that include an evaluation of all clinical reports conducted with neutron beam therapy. Good summary of clinical trials was provided by CRP, because funding for clinical trials terminated in the mid-nineties and the handful of studies conducted after 1995 obtained results that were consistent with the earlier findings. The CRP concluded that there are tumours where fast neutrons are superior to photons:

Paranasal sinuses - adenocarcinoma, mucoepidermoid, squamous, adenoid cystic.

Soft tissue sarcoma, osteosarcoma, and chondrosarcoma.

Head and Neck - locally extended, metastatic tumour.

Melanomas-inoperable/recurrent

Locally advanced prostate.

- Salivary glands - locally extended, well differentiated

The CRP also listed the tumours for which more clinical studies are needed:

- Esophagus
- Inoperable Pancreatic
- Bladder
- Locally advanced uterine cervix
- Neutron boost for brain tumors
- Recurrent or inoperable rectal

Most significantly they concluded that: "The proportion of patients suitable for neutrons ranges from 10- 20%, but this is probably a lower limit with high energy modern cyclotrons neutron therapy will be useful for a larger proportion of patients." In fact, most of the neutron patients today are being treated with a high-energy proton linac.[11]

Clinical studies and researches have showed that neutron beam therapy is a novel treatment option for treating radio resistant tumors such as salivary gland tumors, sarcomas, melanomas and locally advanced prostate tumors. Lack of neutron beam facility centres has limited the scientific studies and comparison of outcomes due to variation in the delivery of treatment with NBT. The safety and efficacy of the use of NBT for the treatment of other forms of cancer has not been proven.

CONCLUSION

The advantage of radiation effect of neutron beam is its higher Relative Biological Effectiveness (RBE) than conventional X or gamma ray because the neutron beam is densely ionizing radiation which is presented by high Linear Energy Transfer (LET). This physical and radiobiological characteristic does more effective role in killing of cells in the state of biologically radio resistant to the conventional radiation. Neutron beams are used for some cancers of the head, neck, and prostate and for certain inoperable tumors. The way each type of radiation behaves is important in planning radiation treatments. The treatment of malignancies can be improved by development of treatment technique of fast neutron beam.

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