1.1 RADIATION-THERAPY OVERVIEW:

Radiation-therapy is a clinical medicine branch utilizing ionizing radiation to treat the cancer. Radiation is classified in two categories ionizing and non-ionizing radiation. Ionizing radiation is sub-divided in direct and indirect radiation which includes the different type of radiation[1] (Figure 1).

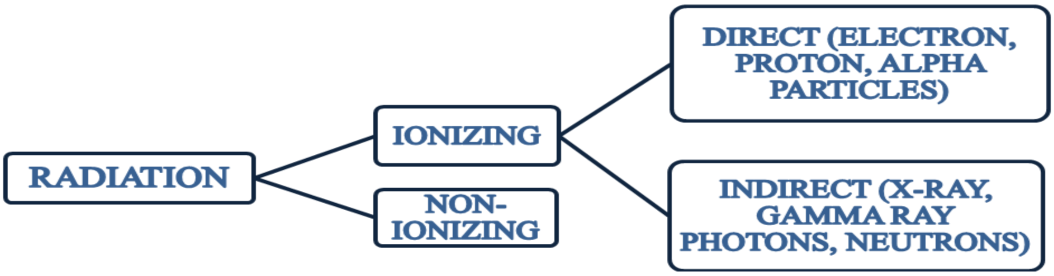

Figure 1: Showing the classification of radiation

The ionizing radiation produces high damage to the cancer cell than the surrounding healthy tissue in the cancer treatment. Radiation can be delivered to the tumor either externally and internally or combine both[1].

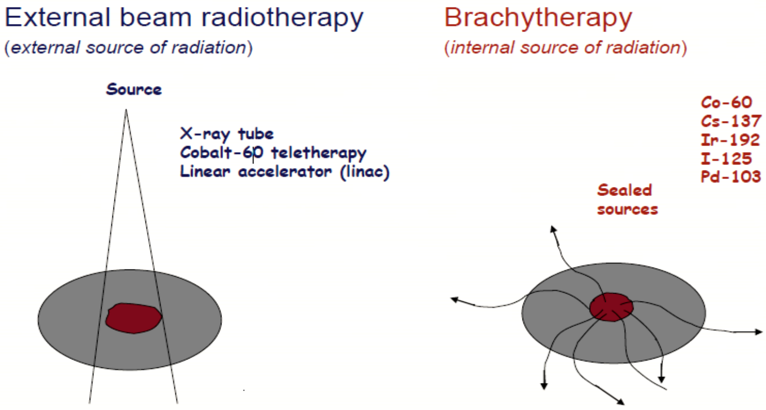

Figure 2: Showing the type of radiation therapy delivery

High energy X-rays are generated in Linear Accelerator and delivered externally to the patient in External Beam Radiotherapy (EBRT). EBRT with megavoltage photon beam is commonly used for the radiation-therapy treatment with skin sparing properties. The advantage of skin sparing effect gives freedom to treat deep seated tumor within the patient. Initially with the conventional EBRT technique large volume is treated with homogeneous dose distribution, as per the International commission of radiation units and measurement (ICRU) the acceptable dose range of the prescribed dose is 95% to 107%. In this situation Organs at risk (OARs) may received higher doses and exceeded their tolerance doses. To increase the tumor control probability and minimize the normal tissue complication probability, the normal tissue and target volume structure confirmation is needed which helps us in delivering desired dose to the tumor and minimize doses to the OARs.

After a long time, introduction of computed tomography and multileaf collimator along with Treatment planning system (TPS), field shaping is possible in the treatment planning. Three-dimensional conformal radiotherapy (3DCRT) techniques introduced where field shaping is possible. In next technique called Intensity Modulated Radiotherapy (IMRT) along with field shaping intensity modulation is possible in the TPS. In addition to the intensity modulation there is another development in which imaging system is added in the treatment unit and an image is acquired just before the delivery of the radiation beam known as Image guided radiotherapy (IGRT) technique[2]. In these techniques it is ensured that the therapeutic ratio achieved in radiation therapy treatment.

Another method of radiation delivery is brachytherapy in which radiation is delivered internally with the help of a radioactive source. Brachytherapy delivers the localized dose of radiation to tumor with minimum dose to the adjacent healthy normal tissue[3]. In brachytherapy a small encapsulated radioactive source is used to irradiate the tumor volume. The advantage of brachytherapy over external beam radiotherapy is localized dose to the tumor with rapid dose fall-off in surrounding healthy tissue. Brachytherapy main applications are Surface mould, Intracavitary, Interstitial and Intraluminal. Surface mould is used to treat the skin tumor with plastic mould prepared on the skin. In the intracavitary the applicator is implanted in the body cavity close to the tumor. In the interstitial application the applicator needles or radioactive seeds are inserted to the tumor. In the Intraluminal brachytherapy, a catheter is placed in to the lumen of the body to treat the lumen having tumor in it[4].

According to “International Commission on Radiation Units and Measurements” (ICRU) report 38[5], brachytherapy defined by the dose rate range as:

1. Low Dose Rate (LDR): used 0.4 Gy/h to 2Gy/h Dose Rate

2. Medium Dose Rate (MDR): used 2Gy/h to 12Gy/h Dose Rate

3. High Dose Rate (HDR): used 12Gy/h or more dose rate[6].

The HDR brachytherapy have several advantages over the LDR brachytherapy in view of better dose optimization capability, better immobilization of applicators, outpatient treatment; use an applicator with diameter very small for patient benefit[7].

1.2. LUNG CANCER OVERVIEW:

Worldwide one of the most common cancers is Lung (2.09 million cases) and most common cause of death is by Lung cancers (1.76 million deaths). In India each year 63,000 (approximately) new lung carcinoma cases are reported[8]. The main risk factors worldwide for lung carcinoma are using Tobacco, alcohol, unhealthy diet, and physical inactivity. The cancer burden can be reduced by avoiding the risk-factors and by executing the strategies which exist for prevention. If cancer diagnosed early and treated effectively, many cancers have cure rate with high chance.

1.3. TREATMENT OF CANCER:

The treatment of cancer depends upon type of cancer and stage of the disease as each subtype needs specific treatment regimen which includes surgery, radiotherapy and chemotherapy. The main goal is to cure carcinoma and get better quality of life (QOL) of the patient which can be attained by using optimal modality of treatment as single modality or in combination[9].

Radiation Therapy is one of the principal modality used for the cancer treatment either single or in association with other available modalities of treatment. Radiation therapy is delivered by two methods, external beam radiation therapy (EBRT) and brachytherapy (BT). The EBRT is treatment of tumor from some distance and brachytherapy is precise placement of the small encapsulated radioactive source directly inside or in close proximity of the tumor. Advantage of using brachytherapy is maximum dose delivery to tumor with lesser dose to healthy tissues which is the main objective of radiation therapy[10].

1.4. TREATMENT OF LUNG CARCINOMA:

In lung cancer, radiation therapy is used in small cell carcinoma with curative intent in combination of chemotherapy. In non-small cell carcinoma of lung, surgery is the main type of treatment whereas radiation therapy is used as adjuvant or for palliation. Radiation Therapy used in lung carcinoma is mainly by EBRT however there are indication where radiation therapy is used as brachytherapy.

1.5. "AMERICAN BRACHYTHERAPY SOCIETY GUIDELINES FOR BRACHYTHERAPY":

The "American Brachytherapy Society" (ABS) issued guidelines for brachytherapy in lung carcinoma. ABS recommends that the patients with hemoptysis and post obstructive pneumonitis can be considered for palliative Endobronchial (EB) Brachytherapy[11]. The tumors involved the lumen which compresses the bronchus/ trachea and leads to cough, breath shortness with hemoptysis. EB brachytherapy generally give fast palliation of blockage than external beam radiation therapy (EBRT).

The ABS recommends that EB brachytherapy is performed via trans-nasal technique with the help of flexible fiber optic bronchoscope under conscious sedation administered by well-trained person. A guide wire is used to visualize the catheter under fluoroscopy because through bronchoscope endobronchial lesion is visualized but not by fluoroscopy. Markings on catheter define its location relative to the tumor and helps in treatment planning. The catheter insertion is completed with the help of bronchoscope. The ABS suggests that 7.5Gy/ fraction per week for 3 weeks, 10Gy/

fraction per week for two weeks or 6Gy/fraction per week for four weeks when HDR brachytherapy is used for palliation.

The dose prescription point in endobronchial HDR brachytherapy can be selected by two ways, one is at 1.0cm from the catheter center and other one is at various distances around the catheter center which depends upon the trachea or bronchial diameter at that level. To treat the tumor adequately a margin of 1cm to 2cm is recommended at each end of the catheter.

1.6. BRACHYTHERAPY DOSIMETRY:

The optimized dose distribution is completed in the dedicated HDR Brachytherapy treatment planning system (TPS). Accurate with reliable quantification of brachytherapy dose distributions is of vital importance in clinical treatment planning. The distribution of dose around the radioactive source used in brachytherapy is classified by energy spectrum with sharp dose gradients varying rapidly about the source by means of depth in water.

1.7. DOSIMETERS FOR DOSE DISTRIBUTION MEASUREMENT:

The doses around brachytherapy sources can be determined by experimental and Monte Carlo methods. Accurately placement of the detector is important for radiation dose measurement and measured signal is proportional to the relative/ absolute dose in the absence of detector in the medium. The detectors are used in this application include small TLDs dosimeters, Gafchromic film, ionization chamber. As far as the suitability of dosimeter is concerned, TLD has already been established as a detector offering best compromise between small size, sensitivity, flat energy response and ease of accurate positioning. The “American Association of Physicists in Medicine” (AAPM) recommends that the LiF based TLD to be used for dose verification measurements for brachytherapy applications[12]. However, the method based on TLD is cumbersome and related with volume averaging, positioning errors and self-attenuation factors. The ionization chamber is capable of real time dosimetry does not fulfill the requirement of resolution because of finite physical dimension of the detector. In addition, ionization chamber positioning corresponding to HDR brachytherapy Ir-192 source is labor intensive and time consuming.

1.8. FILM AS DOSIMETER IN BRACHYTHERAPY DOSIMETRY:

In recent times radiochromic film such as Gafchromic EBT series films are in use for experimental dosimetry in brachytherapy[13-15]. EBT films provide nonlinear dose response. Gafchromic EBT3 film is the most recent version of EBT series films. EBT3 film exhibits high resolution which makes it appropriate for measuring rapidly falling doses around brachytherapy sources. The film is nearly tissue equivalent and possesses low energy dependency within the range of calibration. In addition, dosimetry with Gafchromic film is a user friendly and cost-effective method which is convenient to be used even in a busy clinical set-up.

1.9. BRACHYTHERAPY TREATMENT PLANNING SYSTEM (TPS):

An important part of brachytherapy TPS is the calculation of absorbed dose along with distribution in a patient body. In an attempt to minimize the large variation of dosimetric information determined by various investigators, the AAPM Task Group 43 (TG 43/TG43U1) has recommended formalism for determining the distribution of dose rate in water medium about a single sealed source used in brachytherapy[16]. The algorithm of dose calculation in the most brachytherapy TPS) is based on this formalism which assumes a homogeneous water equivalent medium around the source[17, 18]. This difference between the planned and the actual condition include the effects of patient heterogeneities, applicators attenuation and the altered scatter conditions etc. Inaccurate treatment causes late complications and significantly reduces quality of life. Thus, it is important to quantify the difference among TPS calculated and actual dose delivered[19].

1.10 IMAGING AND TREATMENT PLANNING:

It is evident that treatment outcome entirely depends on the accuracy with which tumor has been delineated, precision of treatment planning using radiation dosimetry. The advance modality for imaging such as multi-slice C.T. scanner, functional-MRI and P.E.T.-C.T. provided newer approach in delineating target volume and OARs for accurate dose delivery[20]. In actual patient different types of tissues are present in between the source and point of interest. The inhomogeneities present around the source affects distribution of dose is investigated by researchers.

The brachytherapy treatment planning system adopted the three-dimensional computed tomography (3D CT) of the patient for treatment planning which gives the more realistic outcomes of the dosimetry on anatomy of the patient[21].

In the literature there are few studies available where the dosimetry was performed either by measurement or with the Monte Carlo methods to estimate heterogeneity medium/ applicator effect on the measured dose from TPS calculated dose. The TPS calculated dose and measured dose at desired location has discrepancy which should be accurately assessed to evaluate the clinical-outcome to dosimetric-parameters. In Bronchial lesion Brachytherapy, there are some tissues of different densities and which can affect brachytherapy source dose distribution[22]. The treatment planning system available commercially does not include the heterogeneity corrections for different types of tissues present around the source in brachytherapy dosimetry[23-26].

There is very less data available on the dosimetry of carcinoma lung brachytherapy. Primary objective of the research work is to perform a dosimetric analysis in carcinoma lung for palliative treatment and verify the doses to OARs in TPS planned and actually delivered doses in a phantom designed for site specific with the help of Gaf-chromic film dosimeters. This study is helpful in accurate treatment delivery and improvement in the quality of life of the patient.

Endobronchial brachytherapy (EBBT) treatment planning is carried out on the carcinoma lung patient's CT scan. A Lumencare Intraluminal catheter insertion into the bronchus tumor lesion is done by the expert physician where radiation is to be given. A remote afterloading brachytherapy machine (microselectron HDR V3; Nucletron Make) is used to irradiate the tumor by Ir-192 source[27]. When the radiation treatment planning is made in TPS, reference isodose of prescribed dose is covering target volume and dose to OAR's nearby target volume is evaluated before the final plan approval[28]. The advantage of brachytherapy source characteristics of rapid dose falls up with distance which gives maximum tumor dose with minimal doses to nearby OARs. An EBBT treatment in carcinoma lung is given in three sessions with one week time period gap in between the sessions.

The treatment procedure time in brachytherapy can be made shorten for the standard doses and lengths with start the treatment with no delay. It is feasibly to reduce the treatment planning time if one catheter with lesser curvature is used in the treatment area and implementing pre calculated standard plans of treatment for 3-10cm tumor length and 5-10Gy dose prescription at 1cm from center of the source with same dwell-time[26, 29].

1.11 TISSUE INHOMOGENEITIES:

An area of concern belongs to the effect of backscatter on the dose delivered to the wall of the lumen. The air present in the lumen posed affects on the dose distribution about the source, thereby affecting treatment accuracy. Generally, treatment planning and dose distribution within the body are performed by a commercially available treatment planning system (TPS), which uses axial CT images to construct a three-dimensional image of the target volume and organs at risk based on the user defined shape and location of these structures. The TPS calculates the doses delivered to any point about the source by assuming an infinitely large, homogeneous, water equivalent medium surrounding the source. This means the dose calculation algorithm of the TPS does not account for the effect of heterogeneities present in the patient treatment. This implies a mismatch between the planned and real doses delivered to the tumor and organs at risk.

In addition of a dosimetric method used, the dose distribution in the anatomy of interest may depend on composition of its organs at the time of treatment. The tissue inhomogeneities around the source and target volume may perturb the doses to nearby OARs doses, due to the organ's closeness to source in brachytherapy treatment, a requirement exists to experimentally ensure the effect of tissue inhomogeneities on different points located nearby the source for OARs. A number of experiments and Monte Carlo (MC) studies have been reported in literature demonstrating the effect of inhomogeneity in brachytherapy treatments[13].

The secondary objective (1) of the research work is to perform the "volumetric and dosimetric evaluation in endobronchial brachytherapy to assess the affect of tumor site, either left lung or right lung, and tumor location in the bronchus on doses to OARs and effect of tumor volume on the doses to OARs during the EBBT treatment sessions".

The secondary objective (2) of the research work is "to analyze the variation in the target volume after the three endobronchial brachytherapy treatment sessions to the patients of carcinoma lung".