INTRODUCTION

In recent years, there have been significant improvements in the field of radiotherapy. Advances in computer hardware and software, and medical imaging have led to the development of new technology for improving external beam treatment planning, dose delivery and verification or radiotherapy. The principle of treatment planning is based on the attempt to arrange the treatment field so as to conform the high dose region to the target. It also attempts to minimize the radiation dose to normal structures and constrain the dose to critical structures below tolerance. Poor local tumour control or increased normal tissue complications may arise from inaccurate targeting of the tumour, failure to conform the high dose distribution to the target volumes and inaccurately delivered radiation doses.

High radiation doses can cause severe health complications or death if delivered to the normal tissues, but these are critical and sometimes necessarily needed to be given to a patient for his survival. Delivery of high radiation dose to the tumour without injuring proximal normal tissues requires accuracy and precision in the delivery of radiation to the tumour. Treatment outcome can be improved by improving accuracy and precision in delivering dose to the conformed target with the help of recently developed three-dimensional imaging techniques. Confirmation of the accuracy of optimized calculations with verification evaluation techniques is vital in order to assure the quality of treatment.

There are different possible errors and uncertainties that may exist in different areas in radiotherapy treatment of a patient. These errors need to be identified, and then removed where possible. The present review discusses in detail about the possible errors and uncertainties in radiotherapy treatment planning, by underscoring the significant areas in accuracy point of view, which broadly are accuracy of immobilization, organ movement, imaging, definition of target volumes, choice of dose distribution, treatment verification, machine checks, and Dosimetry protocols, planning checks, patient documentation and treatment scheduling.

Target volume determination: Defining the target volume is one of the important steps in treatment planning. Radiation oncologists currently define Planning Target Volume (PTV) empirically. Different problems of tumour localization and geometrical reconstruction has been investigated and solved in research works done previously. For accurate dose reporting, the volume of interest description is a pre-requisite for meaningful 2-D and 3-D treatment plans.

These regions of interests, target and normal structure, delineation should follow the International Commission on Radiation Units and Measurements (ICRU) -50 and 62 Reports. Volumes of interests for target delineation started from gross tumour volume to planning target...
volume. A radiation oncologist usually determines these anatomical clinical volumes, often after other relevant specialists such as pathologists or radiologists have been consulted. These entire volumes required different dose levels around there self for the best achievement of goal of radiation therapy.7

In some cases Grass Tumour Volume (GTV) and Clinical Target Volume (CTV) are considered as same volume but in other cases these volumes usually differ by different margins as GTV plus very small cm values for regular or irregular GTV.8

To determine the target volume, any palpable masses are marked with wire and contrast medium may be placed in the bladder, rectum, vagina or esophagus.9

The most difficult and subjective step in treatment planning is to quantify margins around grass tumour volume to define clinical target volume.10 It needs a lot of practice, clinical experience and the knowledge of the patterns of tumour recurrence so that precise data be used to define the margins around GTV. Different factors like age of the patient and considerations of normal tissue tolerance, may influence the maximum volume considered to be appropriate for treatment. The concepts of defining target volumes are also based on the risk of microscopic spread of the disease.8

There is a chance of error in defining PTV by different oncologists, and sometimes even by the same oncologist on different occasions.11,12 National Cancer Institute (NCI) photon treatment group made efforts to standardize the process of defining PTV13 and international commission on radiological Units14 resulted in the definition of the PTV in relationship to the GTV and the clinical target volume (CTV).

**Organ at risk (OARs) and normal tissue tolerance:**
Tumours arising from different regions of the body vary in pathology, size, shape etc. Added to the fact that there may be different pattern of Organs at Risk (OARs) present in close proximity, a variation of the level of treatment planning difficulties and complexity is expected. As a consequence, the degree of dose conformity to the PTV would also be affected, where certain tumours are easier to conform than the others.15

Normal tissues are also irradiated along with the tumour but there is wide variation in the intrinsic radio sensitivity of different normal tissues and susceptibility to changes in fraction size. Therefore, the site and volume of normal tissues must be defined clearly. Increased shielding of parts of normal organs is now feasible with the use of conformal blocks and multileaf collimators, with calculation of dose volume histograms for description of normal tissue doses.9 The treatment plans should be evaluated with reliable calculation systems for accurate and optimized outcome.16

Some of the organs have very small tolerance dose value for example lenses of eye are organs at risk during nasopharyngeal or brain tumour treatments as according to the American Center of Radiology, the lens of eye has just 1200 cGy tolerance dose which causes 50% injury within 5 years. In complete treatment planning, which consists of almost 32 fractions, the dose per fraction and total dose should be considered.17

**Organ movement:** Modern radiotherapy techniques intend to focus on the motion of target volumes, to guarantee the higher degree of accuracy. The treatment of lung cancer with external beam therapy presents a challenge due to the existence of breathing motion during both the simulation and treatment. The effects of normal breathing on coverage are small on the average, with a less than 4% chance of a 10% or greater decrease in Tumour Control Probability (TCP).16 However, in patients with large respiration-induced motion, the effect can be significant and efforts to identify such patients are important.

Stereotactic body frames are suggested to be used for real-time tumour-tracking, for an effective reduction in respiratory intrafractional organ motion.19

**Dose distribution and the degree of conformation:**
The geometry of the radiation fields can be defined by Three Dimensional (3-D) information in conformal radiotherapy process and then dose distribution is optimized using the Beam’s Eye View (BEV) concept. The BEV display shows the anatomy from the perspective of a viewer positioned at the beam’s source, looking at the patient along the central axis of the beam.20

Conventional dose calculation formalism, such as radiological path length and scatter integration models, is not sufficiently accurate for three dimensional conformal radiotherapy (3DCRT). The main weakness of conventional dose calculation is the inability to calculate dose accurately in regions of electronic disequilibria, such as under or near boundaries of arbitrary shaped beam defining devices.21

Sometimes dose distribution is not as it is needed, then it can be altered by using wedges so that it will compensate missing tissues as well as produce a more homogenous result.

For the treatment of deep seated tumours, skin and other superficial tissues are spared by combination of several beams. Computerized dose planning systems are used to construct an isodose distribution with beams of appropriate energy, size, weighting, gantry angle and wedge to give a homogenous result over the target volume. The combination of the beams in order to concentrate the dose at the target volume can be performed according to different methods. non-coplanar beams can be useful to spare critical organs, especially when high level of dose is required.22-24

Conformity Number (CN) has been used first to quantify the degree of conformity in radiotherapy of prostate
and then concept of Conformity Index (CI) was introduced in different documents. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) provide a 3-D model of the patient’s anatomy and tumour, which allows radiation oncologists to more accurately prescribe irradiation to the tumour while sparing neighboring critical normal organs.

**Dose calculation systems:** Diverse calculation algorithms are integrated in commercial treatment planning systems, to calculate the dose distribution in target volumes and organs at risk. Each target volume along with its surrounding healthy tissues requires specific dose distribution so that the beam capable of providing that certain distribution and having a behaviour to traverse desired dose delivery should always be selected for radiotherapy.

The reliability evaluation of calculation systems is vital otherwise they may mislead to an inappropriate set of planning parameters. In a comparison made between pencil beam and collapsed cone calculation system, it was found that both do not differ significantly in central axis fields as well as large field sizes, however, in the case of off-axis fields and small fields, there is notable variation. Figure 1 demonstrates this deviation of the collapsed cone calculation system.

**Beam shape:** Appropriate beam shaping can be made possible with the help of low-melting point alloy blocks and multileaf collimators. Conformal radiotherapy refers to a method of treatment delivery that incorporates rigid immobilization and 3-dimensional computer planning and treatment systems to produce a high dose area of radiation that conforms to the shape of the target. Enhanced conformation allows for greater dosage of radiation to reach the target volume while delivering less radiation to surrounding normal tissues. Conformal therapy uses a number of different techniques to shape the beam and miss normal tissues. The simplest technique is called multi field, static coplanar irradiation. That is, the multiple converging beams of radiation lie in a single plane.

In conformal radiotherapy treatment planning, it is aimed to enhance Tumour Control Probability (TCP) by improving the spatial distribution of relative dose. Reducing normal tissue irradiation should be at minimum level and consequently increasing the prescribed dose should be preferred until normal tissue tolerance is reached.

Actually, the determination of the Tumour Control Probability (TCP) and of Normal Tissue Complication Probability (NTCP) permits to summarize with a few significant figures the potential outcome of a complex 3-D dose distribution.

The shape of the dose distribution and the value of isodose can be affected by the attenuation of X-ray beam by relative changes in tissue densities. So, inhomogeneity corrections are introduced. A pixel by pixel correction can be made to take account of all tissue densities within the body contour by conversion of CT numbers into relative electron densities.

Dimensions of treatment field are defined from external or radiological anatomical landmarks, assuming implicitly that the PTV receives adequate coverage. Simulator films and Beam Eye View (BEV) approach are used to shape the field. BEV approach which is considered superior in order to design better edges of the fields. It requires that PTV is previously acquired and reconstructed by the computer.

**Imaging:** After completion and approving the treatment plan, the CT image set is used to obtain Digitally Reconstructed Radiographs (DRRs) that are computer generated projection images produced by mathematically passing divergent rays through a CT data set and acquiring X-ray attenuation information along the rays during 3-D conformal radiotherapy treatment planning. They are essential for implementing 3-D CRT. The DRR serve as a reference image for transferring the 3-D treatment plan to the clinical setting. Its role is similar to that of a simulation film.

It should be recognized that the planning procedures is based on ‘snap-shot’ image data and there can be a significant delay between the CT session and when the images were acquired and the start of the actual treatment. Consistency between the planning set-up and the treatment set-up on a daily basis is facilitated by use of immobilization and verification devices. Verification can include comparison of portal image data with the planning or simulation images. The best possible imaging for site of interest should be used, as it has been reported that MR images can reduce the spatial uncertainty for prostate treatments. Ultrasound imaging can also be used for effective use to localize the prostate motion.
Documented and transfer of patient data: All the treatment parameters of a patient like number of fields, machine settings, monitor units and other details are stored first and then transferred to the treatment machine. This is done at the time of treatment. This all should be performed carefully and any update in detail of the patient's stored parameters should be transferred too, to the machine. Medical physicists are responsible to create treatment plans and to send it to machine via network. Modern machines have the option that technologists cannot change any parameter without the permission of medical physicists.

Machine checks: It has been shown that 3DCRT plans are more sensitive to deliver errors and, therefore, it becomes more important to verify that 3DCRT treatments are delivered correctly. Record and Verify (R and V) system can be used to check that machine parameters have been entered correctly. Machine parameters that can be verified by R and V system are gantry and collimator angles, field size, beam energy and type, monitor units and accessories such as blocks and wedges. Correct patient position should be checked by port films or electronic portal images. This position record should be compared with DRRs.

Patient positioning and immobilization: The issue of patient positioning was discussed in documents and all available data support the use of an immobilization device in order to achieve stable and reproducible patient positioning during treatment planning and delivery. The clinical aspects of treatment simulation rely on the positioning and immobilization of the patient as well as on the data acquisition and beam geometry determination.

It is important that the patient be treated in one position only, as changes may result in alterations in internal and external anatomy and risk of over or under dosage. Taking a decision on patient position and ensuring that this position is reproducible throughout the whole procedure is the first job to do in patient data acquisition. Specific immobilization systems are to be used for a conformal treatment. In brain treatment and possibly other localizations, stereotactic frames allow to reach a better accuracy.

The position of the patient, all positioning aids and anatomical measurements should be documented accurately in writing with a diagram and Polaroid photograph to ensure reproducibility through all stages of the planning process and subsequent treatment.

Localization of the target volume within the patient in relation to external reference points should be done under exactly the same conditions as subsequent treatments.

If treatment will use a beam coming posteriorly through the couch, a 'tennis-racket' insert or other window in the couch may be considered to avoid attenuation of the beam. This can lead to inaccuracy of patient positioning, and a rigid carbon-fiber insert may be used instead. If any immobilization system has been used for patient data acquisition, it must also be used for treatment verification and execution. The Figure 2 shows reinforced thermoplastic masks which add an unparalleled horizontal stability with an increased fixation force.

The protected rim around the mask and over the chin and shoulders results in great control over the actual position of the patient positioning and patients head.

Effect of the setup errors in radiotherapy treatment:

Although there are a number of studies which attempted to assess the magnitude of setup errors, analysis of their dosimetric effects is quite sparse. In an analysis of setup errors in 3-D conformal plans, it could be found more sensitive to setup errors than traditional plans. To measure setup errors, two double exposure portal films, approximately 90° apart, should be taken before each fraction of the patient. Five to seven landmarks should be identified on each film, and the rotation and translation of the patient should be calculated using a least squares algorithm. For each fraction, three dimensional dose distributions should be calculated for each fraction using the measured position of radiation isocenter relative to the patient.

One striking feature is that the nominal plan is an overly optimistic estimate of the intended treatment. As indicated by the range of daily Dose Volume Histograms (DVH) and the mean DVH, almost all daily treatments indicate less of the target at each dose level than the planned treatment. This result appears to be a consequence of the fact that almost any setup error leads to a decrease in dose to the target since the dose distribution in this case surrounds it conformally. In contrast, if the patient were treated with a traditional parallel opposed plan the range of daily dose distributions would be closer to the nominal or intended plan. Similar results and conclusions follow when DVHs for normal organs are analyzed. 
Incorporation of uncertainties in treatment plan: While online imaging in combination with protocols to correct setup errors may reduce their magnitude, it is evident that the residual systematic and random errors will still remain. Moreover, organ motion will affect the accuracy of dose delivery and these motions may be difficult or impossible to control. One approach, and the standard one, is to understand the errors inherent in a treatment site and then to apply margins around the CTV, which will account for these treatment uncertainties. Another approach is to directly include the uncertainties in the dose calculation algorithm. Conformal treatment aims to conform high dose volume, usually the prescribed dose volume; tightly to the planning target volume and spare the organs at risk in close proximity. Recent studies reported that 3DCRT, Stereotactic Radiotherapy (SRT) and Intensity Modulated Radiation Therapy (IMRT) have the potential for tumour dose escalation, better tumour control, as well as have the ability to compensate the systematic uncertainties by including multi-leaf collimator margins for better clinical outcomes.

CONCLUSION

There have been great improvements in radiotherapy techniques. Significant changes in the outcome of the radiation therapy treatment have been noted in recent years. A lot of work has been done by the physicists and oncologists to improve accuracy in the entire process of radiotherapy treatment. Improved dose calculation methods are available and their use is necessary to remove dose uncertainty as a factor in determining outcome. However, improved accuracy is usually accompanied by a reduction in the speed of calculation. It is important that the speed of calculation is fast enough for the interactive development of treatment plans. The objective is to determine what approximation can be made to enable the accurate calculation of dose, in a reasonable time and affordable system. It is necessary for different techniques, to perform a systematic analysis of the set-up uncertainties and to translate them into 3-D margins to be applied around the CTV. Uncertainties are expected in different steps of the treatment planning, which should be statistically taken into account in the planning process, resulting in an optimized dose distribution or in some biologically relevant figures. Accurate determination of irradiation dose and volume to be treated is very important; otherwise inaccuracy in these can cause severe complications. This depends on the anatomic location, histological type, tumour stage, potential lymph node involvement, other tumour characteristics and normal structures present in the area to be irradiated. In an accurate delineation of target volume, BEV approach is considered superior than the simulator approach. The professionals involved in radiotherapy need to be aware of developments in related fields. It is important that key members of all the disciplines within radiotherapy be aware of developments in different concerned areas.

REFERENCES


