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Radiobiological approach for evaluating the outcome of radiotherapy treatment planning

Thesis Submitted for Ph.D. degree in (Biophysics)

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Abstract

Radiation therapy (RT) plays a critical role in the management of cancer patients. The goal of radiotherapy is to achieve tumor control without causing complications. The use of the modern linear accelerator has become a very precise tool, capable of depositing a defined dose to a specific volume of tissue. This has been made possible by rapid advances in technology, including intensity modulation and image guidance in real time. These developments have been particularly useful in allowing sparing of normal tissues lying in close proximity to tumors.

Each patient who undergoes curative radiotherapy has an individualized treatment plan. Often the ideal plan cannot be created and the chosen clinical approach represents a trade-off between ensuring that the dose to the tumor is acceptable whilst minimizing the risk of complications to normal tissue. Understanding how this dose distribution translates into a biological effect is a key in producing successful treatment plans.

Currently, the treatment planning process is defined and evaluated only in terms of physical dose and physical volume, by dose volume histogram and dose distribution homogeneity but this is not enough because there are different factors affecting the treatment outcome, these factors are;

- Number of fractions and fraction size (dose fractionation).
- Overall treatment time.
- Type of tumor (it's radiosensitivity)
- Dose and volume of healthy tissue

These factors are considered as biological parameters. Biologic indices represent an alternative method for evaluating treatment plans to take in consideration the biological parameters. Criteria for an optimal plan include both the biological and the physical aspects of radiation oncology. By definition, an optimal plan should deliver tumoricidal dose to the entire tumor and spare all the normal tissues. These goals can be set, but are not attainable in the absolute terms. To achieve quantitative biologic endpoints, models have been developed involving biologic indices such as tumor control probability (TCP) and normal tissue complication probability (NTCP).

So the aim of this work was to estimate a radiobiological method to represent the outcome of different treatment plans, in external beam radiotherapy and to apply the new method in evaluation and comparison of different treatment plans and to use the biological dose distribution to recommend an optimal fractionation schedule as well as an optimal treatment plan.

In an attempt to launch a model to evaluate treatment plans in advanced radiotherapy, we have studied some common evaluation indices. In physical evaluation, we studied dose homogeneity indices (MHI and HI), target coverage and conformity indices (PITV, TCI, CI, and CN), dose gradient (GI and GM) and an index for overall plan quality factor (QF), in addition to the total number of monitor units. In Biological evaluation we studied TCP and NTCP for tumor and critical structures, and P+ for free complication tumor control. Evaluation has been performed for twelve plans, four rapidarc plans, seven IMRT and one 3DCRT plan.

The used rapidarc plans are;

- One 300^{o} arc from 210^{o} to 150^{o} with anterior 40^{o}avoidance sector, (1FRA).
- One full rotation single arc (SA).
- Two 130^{o} lateral arcs (from 210^{o} to 340^{o} and from 20^{o} to 150^{o}) (2HA).
- Double Arcs with one full rotation (360^{o}) arc and one (260^{o}) Arc: from 230^{o} to 130^{o} (DA).

Seven IMRT plans with different number of beams have been studied. The number of beams range from 5 beams to 11 beams. The beam angles in all plans were optimized using Eclipse IMRT optimization module supplied with v13.5 of Varian Medical Systems Eclipse planning software on which all plans have been performed. In 3D conformal techniques, five fields have been used.

A conventional schedule with a daily dose of 2 Gy for a total dose of 76 Gy in 38 fractions over treatment time of 52 days has been used. The other schedule was a hypofractionated schedule with a daily dose of 3 Gy for a total dose of 69 Gy in 23 fractions in overall treatment time of 31 days. In all techniques and schedules, dose distribution was normalized and prescribed on mean dose.

We tried to convert the physical dose distribution of the twelve plans under study into a biological dose distribution by adding two tables representing the BED values of each dose level for the PTV and OARs.

The dose distribution and DVH's of the twelve plans for 18 patients of cancer prostate have been calculated and analyzed and they were not sufficient to rank the different plans. The analysis of

Dose statistical quantities of PTV showed a homogeneous dose distribution in all plans. The same result was obtained by calculating Seven different forms of HI. Target coverage indices and conformity indices pointed out that all plans are well covered with conformed dose. Gradient indices were almost equal in all plans. So we found that all those physical indices are not enough in comparison of different treatment plans. Therefore, we added all the physical evaluation indices in a single factor. This factor is the quality factor QF. The difference in plan quantitative quality was very clear and statistically significant between different plans. The higher values of QF were obtained in the four rapidarc plans.

Dose delivered to OARs were estimated and compared for different plans. Both rapidarc and IMRT have lower doses to bladder, rectum and heads of femur in comparison with 3DCRT. rapidarc plan with avoidance sectors (2HA) is demonstrated to deliver the lowest doses to all OAR's.

In biological evaluation we pointed that, all plans have almost similar TCP values. On the other hand, there is significantly difference in the NTCP values and accordingly in P^+ values. The lowest value of P^+ was obtained in the rapidarc teqnique with avoidance sectors.

Both rapidarc and IMRT have lower doses to bladder, rectum and heads of femur in comparison with 3DCRT. The reason of that finding is the usage of inverse planning of both IMRT and rapidarc. In IMRT technique we pointed out that the directions of the beams is more critical in OARs dosimetry than the number of beams. IMRT plans with beams facing any OAR produce a higher dose to that organ regardless the number of beams. In rapidarc plans the reason of

The low dose to OARs is the using of avoidance sectors in front of the OARs.

In applying avoidance sectors in rapidarc treatment planning, it is very important to notice that the starting and ending angels of the treating arcs will affect the dose to OARs.

In order to evaluate treatment plans created in different fractionation schemes BED distribution has been calculated. The BED values of the PTV were higher in conventional dose fractionation schedule than that in hypofractionation. In the same time the BED values of OARs were lower in conventional dose fractionation schedule than that in hypofractionation because of its low α/β value (3 Gy).This method of presenting the planning outcome allowed us to judge both of the physical treatment planning quality and the effectiveness of the fractionation schedule.

According to the results obtained in this study we concluded that BED distribution is essential in physical and biological evaluation of treatment planning and dose fractionation.

Contents

Chapter 3

Materials and Methods

List of Abbreviations

Abbreviation	Meaning
BED	Biological Effective Dose
2D	Two dimension
3D	Three dimention
2-DRT	Two-Dimensional Radiation Therapy
3DCRT	Three Dimensional Conformal Radiation Therapy
cGy	centi-Gray, the unit of absorbed dose
CI	Conformity Index
CN	Conformity Number
CT	Computed Tomography
CTV	Clinical Target Volume
CRT	Conformal Radiation Therapy
CRE model	Current Radiobiological model
D	Dose
DA	Double Arc
DICOM	Digital Imaging and Communication in Medicine
d_{max}	Depth of maximum dose
D_{max}	Maximum dose
D_{ref}	The total dose normalized to a reference fraction
d_{ref}	The reference dose per fraction used
DMLC	Dynamic Multi-Leaf Collimator
DMPO	Direct Machine Parameter Optimization
DRR	Digitally Reconstructed Radiography
DV	Dose volume
DVH	Dose Volume Histogram
EBRT	External Beam Radiation Therapy

EQD	Equivalent conventional Dose
EPID	Electronic Portal Imaging Device
EUD	Equivalent Uniform Dose
gEUD	Generalized Equivalent uniform dose
ERP	External Reference Point
fMRI	Functional Magnetic Resonance Imaging
GTV	Gross Target Volume
GI	Gradient Index
GM	Gradient Measure
Gy	Gray
HT	Helical Tomotherapy
HI	Homogeneity Index
ICRU	International Committee of Radiation Unit
IGRT	Image Guided Radiation Therapy
IM	Internal Margin
IMAT	Intensity-Modulated Arc Therapy
IMRT	Intensity Modulated radiation therapy
ITV	Internal Target Volume
IRP	Internal Reference Point
IRV	Irradiated Volume
LET	Linear Energy Transfer
Linac.	Linear Accelerator
LQ	Linear Quadratic
MeV	Million electron Volt
MLCs	Multi-Leaf Collimators
MUs	Monitor Units
NTCP	Normal Tissue Complication Probability