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Influence of deleting fewer monitor units and small area segments in step and shoot IMRT in view of planning

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Abstract
The Objective of the study is to observe the nature of the Radiotherapy patient Treatment plan quality when fewer segments are deleted. Its known fact that the IMRT planning consists of numerous segments in various gantry angles. These segments are created in inverse planning module. Depending upon the seriousness of the plan, the segment number increases. In doing so the TPS system generates many smaller segments of area even 1 cm X 1 cm or 2 cm x 2 cm with smaller Monitor Units. This not only increases patient overall treatment duration but also adds wear and tear of Linear accelerator machine by multi leave in and out movement. So, this study will investigate the influences of deleting the fever MU segments in Patient planning via dose volume histogram analysis and Organs dose coverage point of view. The results and discussion are given in detail.

Keywords: Intensity modulated radiation therapy, patient specific quality assurance, gamma index, distance to agreement, linear accelerating machine, treatment planning system, planning target volume, quantitative analyses of normal tissue effects in clinics (QUANTEC)

Introduction
Cancer refers to any one of a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue.Cancer is caused by changes (mutations) to the DNA within cells. The DNA inside a cell is packaged into a large number of individual genes, each of which contains a set of instructions telling the cell what functions to perform, as well as how to grow and divide. Errors in the instructions can cause the cell to stop its normal function and may allow a cell to become cancerous. Mostly used treatment techniques for cancer are surgery, chemotherapy and radiotherapy. To increase the chance of success in treatment we make them in combine form like surgery is often followed by chemotherapy and or radiotherapy. Radiation therapy is a highly targeted treatment, aimed accurately and directly at the cancer wherever it might be in the body. This allows the cancer cells to be killed or reduced in number whilst protecting the majority of other organs and tissues in the body. Radiation therapy contributes to 40% of all cancer cures world-wide as well as relieving symptoms, such as pain, and improving the quality of life for many others.

Radiotherapy
At high doses, radiation therapy kills cancer cells or slows their growth by damaging their DNA. Cancer cells whose DNA is damaged beyond repair stop dividing or die. When the damaged cells die, they are broken down and removed by the body. Different cancers respond to radiation therapy in different ways. The response of a cancer to radiation is described by its radio sensitivity. Highly radiosensitive cancer cells are rapidly killed by modest doses of radiation. Radiation therapy uses high-energy particles or waves, such as x-rays, gamma rays, electron beams, or protons, to destroy or damage cancer cells. While chemotherapy and other treatments that are taken by mouth or injection usually expose the whole body to cancer-fighting drugs, radiation therapy is usually a local treatment. This means it's usually aimed at and affects only the part of the body needing treatment. Radiation treatments are planned so that they damage cancer cells with as little harm as possible to nearby healthy cells.

Tele therapy
Tele therapy refers to radiation therapy given by an external radiation source at a distance from the body. It is the most common type of radiotherapy used in cancer treatment and is usually given by a Cobalt unit, which delivers high energy gamma rays, or a linear accelerator, which can deliver high-energy X-rays or electrons. In the most common scheme, treatment is given daily for a period of 4-8 weeks. To deliver an even dose of radiation to the target, which may be several centimeters thick, the radiation source is placed at a distance from the patient

(usually 80-150 cm). Healthy tissue, including skin, in the path of the beam can also be irradiated. To reduce this effect, higher-energy beams are used for deeper tumors and treatment is delivered from several angles, which maximizes the dose at the intersection. External beam radiotherapy (EBRT) is the most common form of radiotherapy. The patient sits or lies on a couch and an external source of ionizing radiation is pointed at a particular part of the body. In contrast to brachytherapy (sealed source radiotherapy) and unsealed source radiotherapy, in which the radiation source is inside the body, external beam radiotherapy directs the radiation at the tumour from outside the body. Orthovoltage ("superficial") X-rays are used for treating skin cancer and superficial structures. Megavoltage X-rays are used to treat deep-seated tumours (e.g. bladder, bowel, prostate, lung, or brain), whereas megavoltage electron beams are typically used to treat superficial lesions extending to a depth of approximately 5 cm (increasing beam energy corresponds to greater penetration). X-rays and electron beams are by far the most widely used sources for external beam radiotherapy.

Linear accelerator (LINAC)

The linear accelerator (linac) is a device that uses high-frequency electromagnetic waves to accelerate charged particles such as electrons to high energies through a linear tube. The high-energy electron beam itself can be used for treating superficial tumors, or it can be made to strike a target to produce x-rays for treating deep-seated tumors. There are several types of linear accelerator designs, but the ones used in radiation therapy accelerate electrons either by traveling or stationary electromagnetic waves of frequency in the microwave region (~3,000 megacycles/s).Medical linear accelerator accelerate electrons using a tuned-cavity waveguide, in which the RF power creates a standing wave. Some linacs have short, vertically mounted waveguides, while higher energy machines tend to have a horizontal, longer waveguide and a bending magnet to turn the beam vertically towards the patient. Medical linacs use monoenergetic electron beams between 4 and 25 MeV, giving an X-ray output with a spectrum of energies up to and including the electron energy when the electrons are directed at a high-density (such as tungsten) target. The electrons or X-rays can be used to treat both benign and malignant disease. The LINAC produces a reliable, flexible and accurate radiation beam. The versatility of LINAC is a potential advantage over cobalt therapy as a treatment tool. In addition, the device can simply be powered off when not in use; there is no source requiring heavy shielding – although the treatment room itself requires considerable shielding of the walls, doors, ceiling etc. to prevent escape of scattered radiation. The accelerator structure (or accelerator waveguide) consists of a copper tube with its interior divided by copper disks or diaphragms of varying aperture and spacing. This section is evacuated to a high vacuum. As the electrons are injected into the accelerator structure with an initial energy of about 50 keV, the electrons interact with the electromagnetic field of the microwaves. The electrons gain energy from the sinusoidal electric field by an acceleration process analogous to that of a surf rider. As the high-energy electrons emerge from the exit window of the accelerator structure, they are in the form of a pencil beam of about 3 mm in diameter. In the low energy linacs (up to 6 MV) with relatively short accelerator tube, the electrons are allowed to proceed straight on and strike a target for x-ray production. In the higher-energy linacs, however, the accelerator structure is too long and, therefore, is placed horizontally or at an angle with respect to the horizontal. The electrons are then bent through a suitable angle (usually about 90 or 270 degrees) between the accelerator structure and the target. The precision bending of the electron beam is accomplished by the beam transport system consisting of bending magnets, focusing coils and other components.

IMRT (Intensity Modulated Radiotherapy)

Intensity-modulated radiation therapy (IMRT) is an advanced mode of high-precision radiotherapy that uses computer-controlled linear accelerators to deliver precise radiation doses to a malignant tumor or specific areas within the tumor. IMRT allows for the radiation dose to conform more precisely to the three-dimensional (3-D) shape of the tumor by modulating—or controlling—the intensity of the radiation beam in multiple small volumes. IMRT also allows higher radiation doses to be focused on the tumor while minimizing the dose to surrounding normal critical structures. Treatment is carefully planned by using 3-D computed tomography (CT) or magnetic resonance (MRI) images of the patient in conjunction with computerized dose calculations to determine the dose intensity pattern that will best conform to the tumor shape.

Typically, combinations of multiple intensity-modulated fields coming from different beam directions produce a customized radiation dose that maximizes tumor dose while also minimizing the dose to adjacent normal tissues. Because the ratio of normal tissue dose to tumor dose is reduced to a minimum with the IMRT approach, higher and more effective radiation doses can safely be delivered to tumors with fewer side effects compared with conventional radiotherapy techniques. IMRT also has the potential to reduce treatment toxicity, even when doses are not increased. Due to its complexity, IMRT does require slightly longer daily treatment times and additional planning and safety checks before the patient can start the treatment when compared with conventional radiotherapy.

In the traditional external beam photon radiation therapy, most treatments are delivered with radiation beams that are of uniform intensity across the field (within the flatness specification limits). Occasionally, wedges or compensators are used to modify the intensity profile to offset contour irregularities and/or produce more uniform composite dose distributions. This process of changing beam intensity profiles to meet the goals of a composite plan is called intensity modulation. Thus, the compensators and wedges may be called intensity modulators, albeit much simpler than the modern computer-controlled intensity modulation systems such as

dynamic multileaf collimators. The clinical implementation of IMRT requires at least two systems: (a) a treatment-planning computer system that can calculate nonuniform fluence maps for multiple beams directed from different directions to maximize dose to the target volume while minimizing dose to the critical normal structures, and (b) a system of delivering the nonuniform fluences as planned. Each of these systems must be appropriately tested and commissioned before actual clinical use.

Treatment planning system used in IMRT planning

Radiation treatment planning represents a major part of the overall treatment process. Treatment planning consists of many steps including patient diagnostic, tumor staging, image acquisition for treatment planning, the localization of tumor and healthy tissue volumes, optimal beam placement, and treatment simulation and optimization. Computerized Treatment Planning Systems (TPS) are used in external beam radiation therapy to generate beam shapes and dose distributions with the intent to maximize tumor control and minimize normal tissue complications. Treatment planning prior to the 1970s was generally carried out through the manual manipulation of standard isodose charts onto patient body contours that were generated by direct tracing or lead-wire representation and relied heavily on the judicious choice of beam weight and wedging by an experienced dosimetrist. Simultaneous development of computerized tomography, along with the advent of readily accessible computing power from the 1970s on, lead to the development of CT-based computerized treatment planning, providing the ability to view dose distributions directly superimposed upon patient's axial anatomy. Advanced TPS are now able to represent patient anatomy, tumor targets and even dose distributions as three-dimensional models.

Successive improvements in treatment planning hard-ware and software have been most notable in the graphics, calculation and optimization aspects of current systems. Systems encompassing the "virtual patient" are able to display: Beams-Eye Views (BEV) of patient's anatomy. Computerized treatment planning is a rapidly evolving modality, relying heavily on both hardware and software. As such it is necessary for related professionals to develop a workable Quality Assurance (QA) program that reflects the use of the TP system in the clinic, and is sufficiently broad in scope to ensure proper treatment delivery. In the 1970s and 1980s treatment planning computers became readily available to individual radiation therapy centers. As computer hardware technology evolved and became more compact so did Treatment Planning Systems (TPS). Principal hardware components are described in the following slides.

Inverse Treatment Planning system

Recent advances in computer technology have led to evaluation of designing inverse treatment planning system. The principle of inverse treatment planning system is the specification of doses to target and critical structures. The treatment planning system will perform a systematic search for a plan that satisfy the dose constraints to the target volume and critical structures. Because of the physics of radiation, satisfying all the dose constraints simultaneously may not be possible. As such, acceptance of higher doses to certain structures is unavoidable. Since a computer does the search for an optimal plan, a computerized method of evaluation or objective function is needed. The object function is an expression that adds relative weights to each constraint such that the overall value expresses the goodness of the plan.

A minimum or maximum value would indicate an optimal plan or a plan that nearly satisfy the dose constraints. In principle, an inverse treatment planning system would need CT data of patients, definition of target and critical structures and relative weight assigned to the dose constraints. The computer would then create a dose distribution using various beam size and direction. After creating the dose distribution, the value of the objective function is computed. An iterative method is initiated by designing another dose distribution using other field arrangements. These dose distributions are compared until find a plan that yielded a minimum objective function value. Since inverse treatment planning system is based on satisfying dose constraints, the ability to deliver a beam with varying radiation intensity is not possible using traditional linear accelerator technology. Radiation therapy involving the use of varying intensity beam is called intensity modulated radiation therapy (IMRT). A method of producing varying intensity within a beam is the use of a series of uniform beam segments.

Materials and Methods.

IMRT treatment plan were generated on CT with beams, 6MV fields on the Elekta Xio treatment planning system. Here we consider different number of beams for different treatments sites like brain, head and neck, pelvic cases. The IMRT plan were optimized using inverse planning algorithm. Consider the dose received to PTV is of two kinds 107% and 95% of prescribed dose. Mainly we considered 5 Head and Neck patients Plans, because there may be two or three PTVs may be involved very frequently. So, in these cases we can come across very fever segments of less area not more than 3 x 3 Sq.Cm. Also, we notice that this less area segments has fewer MU's in range from 2 to 8, which two factors considered for our study. For each patient plans, the plan acceptance criteria were 95% of PTV should receive at least 95% of prescribed dose and 1% of PTV should not exceed 107% of prescribed dose. Dose for the organs at risk were respected as per the QUANTEC guidelines. These plans after being accepted by oncologist for patient treatment. Again, the plans were reanalyzed with same criteria by deleting the segments with above said factors like less area segment and fewer MUS. We notice that there is not much significant or no change in DVH of PTV coverage point of view. Similarly in OARs. This accepted plan which are to be treated for patients are then done with patient specific QA procedure.

Patient selection and dose constraints for study

9 patients are taken for the study in which 3 were brain cases, 3 head & neck cases and 3 pelvic cases.

- 3 patients are selected for brain cases with planned fields of 9 beams:
- Patient A, Prescribed dose – 60Gy
- Patient B, Prescribed dose – 60Gy
- Patient C, Prescribed dose – 60Gy

Dose constraints: 95% of PTV should get 95% of prescribed dose for PTV -60

- Eyes (right & left)- maximum dose less than 5000cGy
- Optic nerves(right & left)-maximum dose less than 5400cGy
- Eye lens(right & left)- maximum dose less than 2500cGy
- Brainstem(right & left)- maximum dose less than 5400cGy
- Chiasma(right & left)- maximum dose less than 540cGy

- 3 patients are selected for head & neck cases with planned fields of 9 beams:
- Patient A, Prescribed dose – 70Gy, 63GY,56Gy
- Patient B, Prescribed dose – 70Gy, 63GY
- Patient C, Prescribed dose – 70Gy, 56Gy

Dose constraints: 95% of PTV should get 95% of prescribed dose for both PTVs

- Spine-maximum dose less than 4700Gy.
- Brainstem- maximum dose less than 5400Gy.
- Parotid -50% volume maximum dose less than 3000Gy.
- Mandible- maximum dose less than 7000Gy.

- 3 patients are selected for pelvis cases with planned fields of 9 beams:
- Patient A, Prescribed dose – 55.8Gy,50Gy
- Patient B, Prescribed dose – 70Gy,
- Patient C, Prescribed dose – 50Gy

Dose constraints: 95% of PTV should get 95% of prescribed dose for both PTVs.

- Rectum-50% volume should get less than 50Gy
- Bladder-50% volume should get less than 65Gy
- Femoral head-40% volume should get less than 40Gy
- Bowel-200cc volume should get less than 45Gy

Data Colletion Method

Dose distribution in the form of isodose curves or surfaces is useful because it shows not only regions of uniform dose, high dose, low dose but also their anatomic location and extent. The dose volume histogram is created by initially dividing the dose distribution into three-dimensional grid. The size of the grid or volume element called voxel is assumed to be sufficiently small such that the dose within the voxel is constant. The volume elements are regrouped according as a function of dose to form the dose volume histogram. The variation of volume as a function of dose is called differential dose volume histogram. If the volume is integrated below a certain dose, the dose volume histogram is called cumulative dose volume histogram. Dose volume histogram provides a means of condensing a large amount of dose data into a manageable size. It is a tool to rapidly determine the presence of cold and hot spots in the dose distribution. The dose-volume histogram can also be used to compare different treatment plans. Dose variations within the treatment volume can be compared from plan-to-plan using dose volume histograms. Similarly, the doses received by normal structures can be evaluated and presented in a statistical form. Since dose volume histogram discarded spatial information, it should not be used alone for assessment, instead it can be used to highlight

In modern radiation therapy, 3D dose distributions are typically created in a computerized treatment planning system (TPS) based on a 3D reconstruction of a CT scan. The "volume" referred to in DVH analysis is a target of radiation treatment, a healthy organ nearby a target, or an arbitrary structure. DVHs can be visualized in either of two ways: differential DVHs or cumulative DVHs.

A DVH is created by first determining the size of the dose bins of the histogram. Bins can be of arbitrary size, e.g. 0–1 Gy, 1.001–2.000 Gy, 2.001–3.000 Gy, etc. In a differential DVH, bar or column height indicates the volume of structure receiving a dose given by the bin. Bin doses are along the horizontal axis, and structure volumes (either percent or absolute volumes) are on the vertical. The differential DVH takes the appearance of a typical histogram. It reads like the volume of the organ that receives the dose of the correspondent dose - bin. It is built by the sum of the number of voxels characterized by a specified range of dosage for the organ considered. It is helpful in providing information about changes in dose within the structure considered and to easily visualize minimum and maximum dose. The cumulative DVH is plotted with bin doses along the horizontal axis, as well. However, the column height of the first bin (0–1 Gy, e.g.) represents the volume of structure receiving greater than or equal to that dose. The column height of the second bin (1.001–2.000 Gy, e.g.)

represents the volume of structure receiving greater than or equal to that dose, etc. With very fine (small) bin sizes, the cumulative DVH takes on the appearance of a smooth line graph. The lines always slope and start from top-left to bottom-right. For a structure receiving a very homogenous dose (100% of the volume receiving exactly 10 Gy, for example) the cumulative DVH will appear as a horizontal line at the top of the graph, at 100% volume as plotted vertically, with a vertical drop at 10 Gy on the horizontal axis.

Results

Below Table 1, Table 2 and Table 3 shows the respective patient site and the dose its achieved when deleting the fever segment in associated plans.

Table 1: Site: Brain

Patient A						
			Complete Plan		**Fewer Segment Deleted plan**	
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV	95%	107%	5870	*	5800	*
Eyes [RT]	Max. dose 5000cGy		3525		3488	
Eyes [LT]	Max. dose 5000cGy		2540		2470	
Optic nerves [RT]	Max. dose 5400cGy		4875		4813	
Optic nerves [LT]	Max. dose 5400cGy		2450		2360	
Eye lens [RT]	Max. dose 2500cGy		1925		1901	
Eye lens [LT]	Max. dose 2500cGy		2100		2077	
Brain stem	Max. dose 5400cGy		4650		4633	
Chiasma	Max. dose 5400cGy		4570		4531	
Patient B						
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV	95%	107%	5921	*	5901	*
Eyes [RT]	Max. dose 5000cGy		2976		2926	
Eyes [LT]	Max. dose 5000cGy		3860		3830	
Optic nerves [RT]	Max. dose 5400cGy		650		622	
Optic nerves [LT]	Max. dose 5400cGy		675		657	
Eye lens [RT]	Max. dose 2500cGy		761		761	
Eye lens [LT]	Max. dose 2500cGy		1052		1042	
Brain stem	Max. dose 5400cGy		1121		1111	
Chiasma	Max. dose 5400cGy		1136		1101	
Patient C						
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV	95%	107%	5888	*	5868	*
Eyes [RT]	Max. dose 5000cGy		754		733	
Eyes [LT]	Max. dose 5000cGy		809		801	
Optic nerves [RT]	Max. dose 5400cGy		757		748	
Optic nerves [LT]	Max. dose 5400cGy		1393		1379	
Eye lens [RT]	Max. dose 2500cGy		611		602	
Eye lens [LT]	Max. dose 2500cGy		574		554	
Brin stem	Max. dose 5400cGy		3933		3913	
Chiasma	Max. dose 5400cGy		1505		1491	

'*' = volume does not receive any dose at 107%.

Table 2: Site: Head and Neck

Patient A						
			Complete Plan		**Fewer Segment Deleted plan**	
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV 1	95%	107%	6655	*	6618	*
PTV 2	95%		5570		5554	
PTV 3	95%		5274		5257	
Spine	Max. dose 4700cGy		4618		4601	
Brain stem	Max. dose 5400cGy		4680		4666	
Parotid [RT]	50%		1940		1913	
Patient B						
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV 1	95%	107%	6645	*	6637	*

PTV 2	95%		6292		6267	
Spine	Max. dose 4700cGy		4684		4662	
Brain stem	Max. dose 5400cGy		4876		4852	
Parotid [LT]	50%		2066		2051	
Patient C						
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV 1	95%	107%	6311	*	6300	*
Spine	Max. dose 4700cGy		4343		4319	
Mandible	Max. dose 7000cGy		5111		5100	
Parotid [LT]	50%		1791		1771	

'*' = volume does not receive any dose at 107%

Parotid - consider any one side of parotid [i.e. left or right] as per the patient orientation.

Table 3: Site: Pelvis

Patient A						
			Complete Plan		**Fewer Segment Deleted plan**	
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV 1	95%	107%	5399	*	5387	*
PTV 2	95%		4876		4863	
Rectum	50%		4060		4041	
Bladder	50%		4135		4121	
Femoral head [RT]	40%		2102		2088	
Femoral head [LT]	40%		2257		2241	
Bowel	200cc		2545		2533	
Patient B						
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV 1	95%	107%	6780	*	6760	*
Rectum	50%		5800		5788	
Bladder	50%		5228		5217	
Femoral head [RT]	40%		2800		2791	
Femoral head [Lt]	40%		2944		2927	
Bowel	200cc		4405		4399	
Patient C						
Organs	Volume [%]		Dose [cGy]		Dose [cGy]	
PTV 1	95%	107%	4860	*	4850	*
Rectum	50%		3640		3627	
Bladder	50%		3920		3908	
Femoral head [RT]	40%		2627		2616	
Femoral head [LT]	40%		2540		2523	
Bowel	200cc		3687		3661	

'*'= volume does not receive any prescribed dose at 107%

Discussion

Intensity Modulated Radiotherapy technique in cancer treatment has become most sophisticated and matured way of giving treatment to patients. It has grown to the extent that it became minimum requirement to set up a Radiotherapy Department. As advancement of technique like VMAT, IGRT, SRS and SRT increases, precision and accuracy also increases. However, the technique or modality increases, Step and Shoot IMRT remains baseline for a department. Step and Shoot IMRT is considerably practiced in across all depts. So, in Step and shoot IMRT treatment, to decrease overall patient treatment time and to reduces Linear accelerators down time due to non-working of multi leave assembly motors, this study was carried out. This study enables us to delete fewer MUs and small area segments. The different beams considered for each cases of brain, head & neck and pelvis cases showed the accuracy level of dose deposition on tumor as well as body. From DVH analysis and then by tables we could find out that by deleting the fewer segments plan quality is reduced but not to greater extend of neglecting the plan for the reason it has not met the primary goal of radiotherapy. So ultimately deleting the segment will lead to lesser treatment time as well as lesser work load on machine performance.

References

1. The International Commission on Radiation Units and Measurements Report No. 83, Bethesda, MD, USA, 2010.
2. Computerized medical systems (Cms) Xio version 4.71, Elekta instruments AB Stockholm. Stockholm.
3. Knoos T *et al*. Comparison of dose calculation algorithm for treatment planning in external photon beam therapy for clinical situations. Phy. Med. Biol, 2006.

4. International Commission on Radiation Units and Measurements Report 50, “Prescribing, Recording, and Reporting photon beam therapy”. Andre Allisy, chairman, Bethesda, MD: ICRU, 1993.
5. Brahme A. “Optimization of radiation therapy and the development of multi leaf collimation”, Int J Radiat Oncol Biol Phys,1993:25(2):373-375.
6. Sohn JW, Dempsey JF, Suh TS, Low DA. “Analysis of various beamlet sizes for IMRT with 6MV photons”. Med.phys,2003:30:2432-2439.
7. Chen Y, Michalski D, Houser C, Galvin JM. A deterministic iterative least- squares algorithm for beam weight optimization in conformal radiotherapy. Phys. Med. Biol,2002:47:1647-1658.