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Biological evaluation of spatially fractionated radiotherapy versus three-dimension conformal radiotherapy for organs at risk in the bulky sarcoma tumors

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ABSTRACT

Spatially fractionated radiotherapy (SFRT) is one of the radiotherapy techniques utilized to treat patients with advanced bulky tumours. This study aims to estimate the difference in biological and dosimetric parameters of the SFRT technique and compare it to the three-dimension conformal radiotherapy (3D-CRT) of bulky shoulder and pelvic sarcoma tumours. 3D-CRT and SFRT were designed by the Monaco treatment planning system. Sex bulky shoulder and pelvic sarcoma cases were selected, a single fraction 15Gy were used. Dose-volume histogram of the organs at risk (OARs) was used to calculate the equivalent uniform dose (EUD) (Gy) by Matlab program. SFRT achieves more EUD (Gy) for OARs were compared to 3D-CRT. In SFRT, where organs at risk in close to the tumours and the shielding it by multi-leaf (1 cm) that leads to more effective than other techniques, and lead to a decrease of EUD(Gy) according to its definition by Niemierko. EUDs showed significant differences between the two methods for OARs in right and left lungs and heart as p-value = 0.001,0.001 and 0.03, respectively. While, others OARs, right and left femurs, bladder, rectum and bowel is non-significant different between them as p-valve > 0.05. The OARs have differed from patient to patient, that is due to differences in tumours site, shape, size, depth and how far from OARs, such as pelvic sarcoma tumours. SFRT achieves more sparing and fewer complications for OARs and provides an accurate assessment of the radiation dose that is actually received.

1. INTRODUCTION

Spatially fractionated radiotherapy (SFRT) is one of the treatment techniques applied to treat patients with advanced bulky tumors. It is employed as an effective curative and palliative hypo-fractionation technique. SFRT plan is achieved via the utilization of many small beams in the field with a high dose single fraction radiation. Specific areas of the target tissue are directly irradiated, while the surrounding areas are protected

from direct the high doses radiation [1]. Many researchers suggested that bystander response, which refers to effects seen in cells that are indirectly radiated, abscopal effect, vascular damages, and immunomodulation reactions occur by radiobiological mechanisms in SFRT. Cilla and co-workers investigated that SFRT RT challenges the three-dimension conventional radiotherapy (3D-CRT) technique by aiming to deliver a highly heterogeneous radiation dose to the tumor volume while minimizing the dose to organs that are close to the tumor [3]. Soft tissue sarcomas malignancies can appear everywhere in the body and form in supporting or connective tissue, such as muscles, nerves, tendons, blood vessels, and fatty and fibrous tissues [4].

This study aims to estimate the difference in biological and dosimetric parameters in SFRT and 3D-CRT techniques for soft tissue sarcoma shoulder and pelvic tumors cases (as scenarios) in radiotherapy plans and evaluate the differences between two methods for these parameters. This study is the first practical experiment in this subject.

2. Subjects and Methods

1. Computed Tomography (CT) Simulator: CT simulator of type (Siemens, Somatom AS, Garmany), provided with 24 multi-slices per rotation, was used to scan the cases in this study.
2. Monaco Sim Workstation: Three-dimensional RT treatment planning system (TPS) of type (Monaco, Elekta, Sweden) was used in this study.
3. Equivalent Uniform Dose (EUD) (Gy): Niemierko first defined the EUD(Gy) as the absorbed dose, that is, if given uniformly, would tend to the same cell death as the actual heterogeneous absorbed dose. EUD(Gy) can be used for both tumors and normal tissues. It can be computed directly from calculating dose points or from the corresponding dose-volume histograms (DVHs) such as:

$$EUD\ (Gy) = (\sum Vi\ Di^{a})^{1/a} \quad \ldots\ldots.1$$

where v_i is the partial volume with absorbed dose D_i.

4. Matlab Program: The MATLAB R2018a (Math Works Inc., Natick, MA, USA) software has served as an excellent tool for processing the pencil beam data sets. Matlab is a numeric computation and visualization software system [5].
Dose volume histogram (DVH) for each case in both plans exported to Matlab program to calculate EUD(Gy) for tumor and OARs.
5. Data Collection: Six cases were selected with shoulder and pelvic sarcoma bulky tumors > 6 cm, taken from TPS. They were scanned on a Siemens CT simulator, following by the export of CT images to the Monaco sim workstation, bulk mass and organs at risk, which were close to the tumor, were delineated. When the delineation is completed, the CT images are sent to the Monaco workstation to design the treatment plans of the SFRT. Each radiation field is divided into several sub-fields with an area of 1 cm2, while the distance between two sub-fields is 2 cm and 3D- conformal therapy plan for each case was performed by TPS figure 1.

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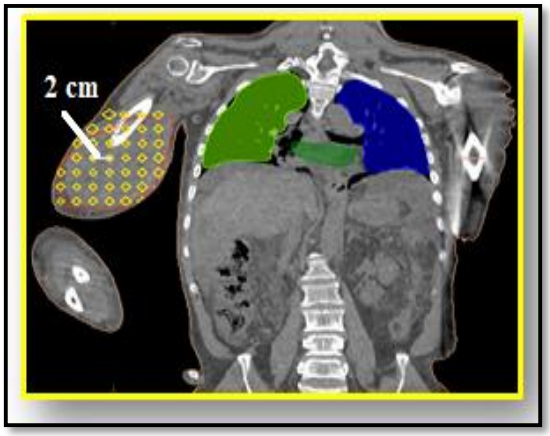

Figure 1: Screenshots for SFRT plan design by MLCs show the distance between two open and close sub volumes.

3. Results

3.1 Spatially fractionated radiotherapy plan design

Figure 2 and figure 3 displayed sarcoma tumor cases with two different treatment regimens, SFRT, and 3D-CRT radiotherapy, showing the change in the shape of the shield modified by MLCs to protect the lung which is OARs and is very sensitive to radiation. The SFRT plan, in this case, shows a perfect shielding of the lung from radiation.

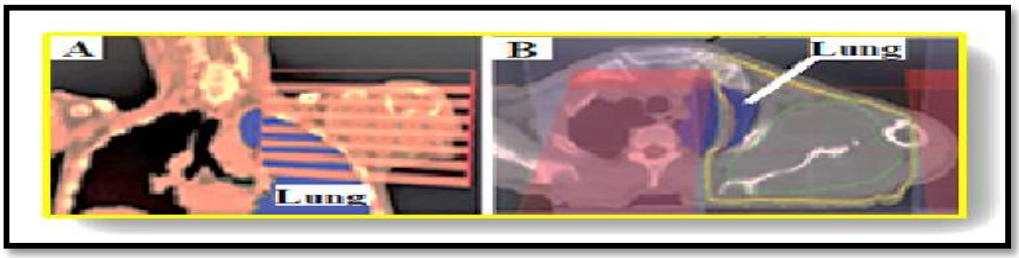

Figure 2: An axial view of sarcoma tumor, lung shielding with SFRT plan (A) and 3D-CRT plan (B).

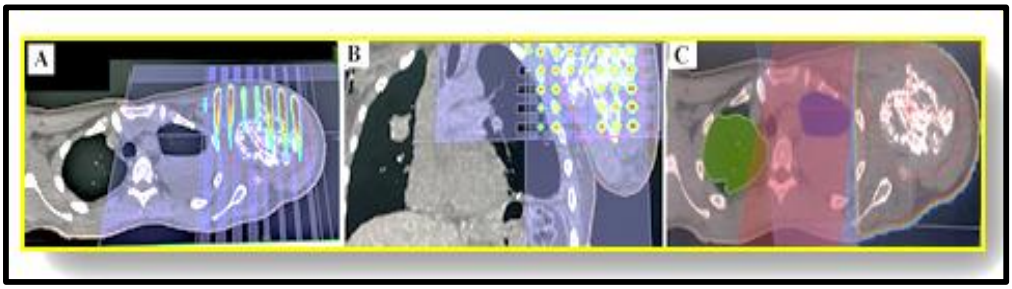

Figure 3: An axial view of sarcoma tumor, the isodose distribution of SFRT plan with MLCs (A), lung shielding with SFRT plan (B), and 3D-CRT plan (C).

For bulky pelvic sarcoma tumors in this study as in figure 4. Two plans for each case were designed, as SFRT and 3D-CRT radiotherapy. To highlight the difference in the protective shields of OARs by MLCs.

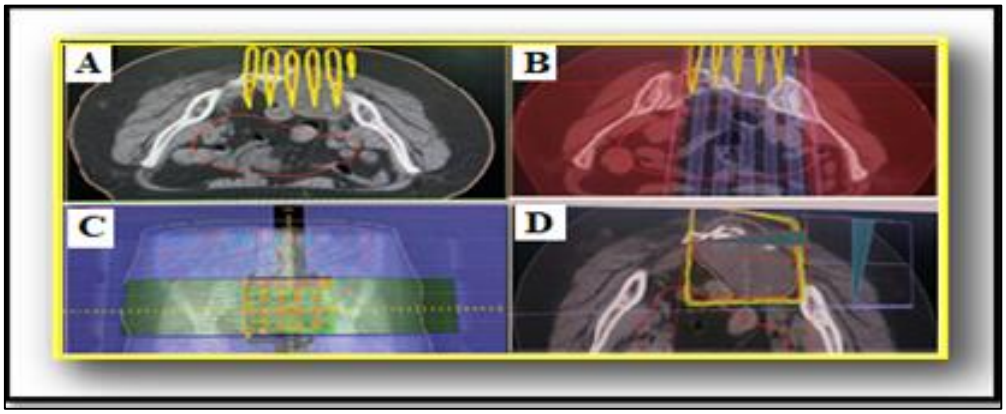

Figure 4: An axial view of pelvic sarcoma tumor with SFRT plan (A) a coronal view with MLCs for SFRT plan (B, C), and a coronal view of 3D-CRT plan (D).

In summary, the figures in this section indicate that SFRT therapy is can be used for different bulky tumors treatment and preformed more protection for OARs when comparison with 3D-CRT plans. Emphasized that SFRT manner of RT has been highly renewed. Two years ago, the Radiology workshop with three working groups (clinical, biological, and physics) was co-conducted by the National Cancer Institute and the Radiation Society to give strong testimony to the therapy and potential clinical application [6].

The patrons of SFRT design in this work are directly in agreement with prior reports of when summarizing the clinical application studies of SFRT radiotherapy from 1990 to 2019 [7].

3.2 Biological model equivalent uniform dose evaluation of SFRT versus 3D-CRT by Matlab program for organs at risk in bulky shoulder sarcoma tumors

Our results in this section shed a new light on a biological model EUD (Gy) for SFRT and compared with 3D-CRT plans in vivo cases of the bulky tumors of patients, and used as scenario plans. EUD (Gy) is ideally adapted to obtain the biological effect of heterogeneous irradiation in a volume of interest such as tumors and normal tissues. This work is to large extent in agreement with suggestion and when investigated the difference between megavoltage therapy plans generated by MLCs and cerrobend collimators. However, it was estimated that an optimal therapy plan that can provide the best tumor control with the least amount of toxicity should come from and radiobiology studies [8], [9]. Developed their studies using biological methods to investigate the dosimetric characteristics of collimators for different sizes and patterns. As well as (EUD) for treating tumors of different sizes and depths. A single fraction was used beneficially for sparing interspersed normal cells when melanomas were treated to a dosage of 15 Gy or higher [10].

Comparison of mean EUD(Gy) for OARs of bulky shoulder sarcoma tumors with 3D-CRT and SFRT plans showed that the decrease in the mean EUD(Gy) for OARs in SFRT plan more than 3D-CRT as shown in figure 5. The mechanical of SFRT plan by MLCs leads to increase the dose-volume effect, which is the tolerance doses for biological tissues increased when beam size of radiation decreased. Furthermore, SFRT treatment causes normal cells' superior healing ability over malignant cells. The non-irradiated cells can function as regrowth centers for normal tissues, heal damaged areas, and reduce complications [11]. These our finding are agreeing with when, shown that SFRT therapy for bulky cancer, generated by MLCs and TPS with a single-dose 20 (Gy) showed consistent dosimetric quality results and a great advantage in accommodation targets and maximally sparing normal structures, also spare more than nine times more radiosensitive normal cells comparing with the open-field radiation boost at the same cancer cell killing [12].

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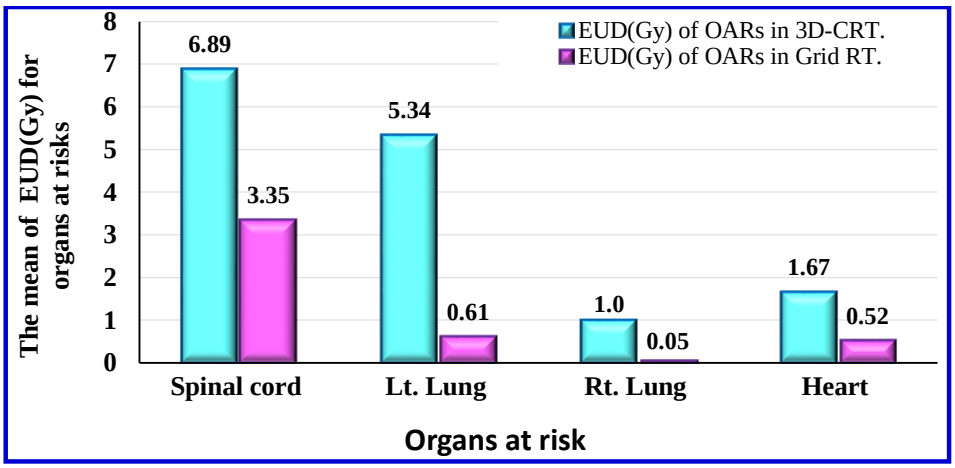

Figure 5: Comparison between the mean of EUD (Gy) for OARs in the sarcoma tumors with 3D- CRT and SFRT plans calculated by Matlab program.

3.3 Equivalent uniform dose evaluation of SFRT versus 3D-CRT by Matlab Program of organs for risk in bulky pelvic sarcoma tumors

Results of the calculating EUD(Gy) by Matlab program for OARs of bulky pelvic sarcoma tumors in the SFRT and compared with the 3D-CRT techniques show in figure 6.

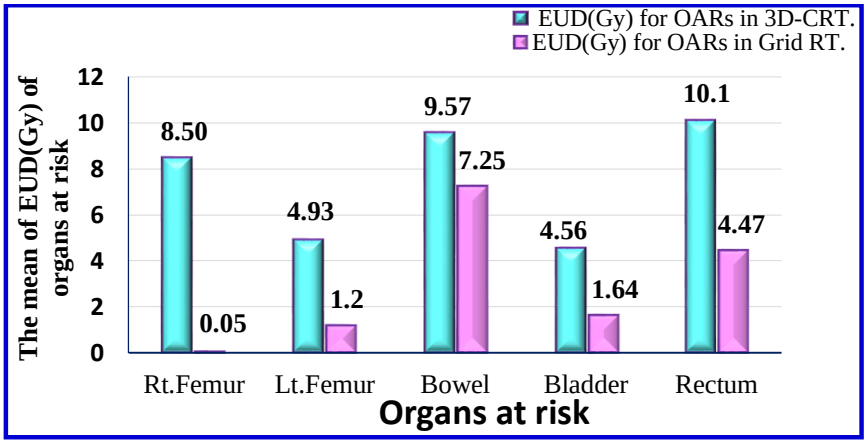

Figure 6: Comparison between the mean of EUD(Gy) for OARs of bulky pelvic sarcoma tumors in SFRT and 3D-CRT by Matlab program.

Described a simple clinical useful 3D-conformal MLCs-based on the SFRT-therapy technique that resulted in enhanced target coverage for the deep-seated bulky tumors with reduced skin toxicity and other internal critical structures and a higher significance to repair normal tissues [13]. This is to large extent in agreement with our findings.

3.4 Statistically analysis aata of EUD(Gy) in 3D-CRT and SFRT

Table 1 shows the different bulky tumors, which are comparing the EUD by Matlab program mean ± stander division (SD) for each OAR of the two plans, SFRT and 3D-CRT. Statistical analysis was performed using Microsoft Excel 2016, data analysis program. Two- sided paired student's t-test was used to analysis parameters and consider p-value ≤ 0.01,0.001, and 0.05 is significant difference between two methods and non -significant when p value > 0.01, 0.001 and 0.05.

This table shows a significant relationship between SFRT and 3D-CRT plans in right and left lungs and heart

as p value (0.001, 0.001 and 0.03), respectively. While left femur, rectum and bladder as OARs in this study showed non-significant difference between 3D-CRT and SFRT plans as p-value (0.008, 0.0009 and 0.25), respectively. In fact, those organs are far away from tumors. In addition, the right femur and bowel were one case. Mentioned as SFRT provides another technique for a high dose while sparing skin and soft tissues between beamless. This is to large extent in agreement with our findings [14].

Table 1: Comparison (Mean ± SD) of EUD (Gy) calculated by Matlab program for OARs between 3D-CRT and SFRT plans for different bulky tumors.

Organs at risk	Mean ± SD of the EUD (Gy) of OARs		P-Value
	3D-CRT	SFRT	
	Mean± SD	Mean± SD	
Right Lung	1 ± 0.18	0.05 ± 0.369	0.001
Left Lung	5.34 ± 5.44	0.61 ± 1.12	0.001
Heart	1.67 ± 1.2	0.526 ± 0.509	0.03
Rectum	10.1 ± 5.2	4.47 ± 2.85	0.009
Left Femur	4.93 ± 2.92	1.2 ± 1	0.08
Right Femur	8.501	0.052	_
Bowel	9.574	7.25	_
Bladder	4.56 ± 6.17	1.64 ± 1.87	0.25

4. Conclusion

1. EUD is an essential criterion for evaluating SFRT therapy plans. In hypo-fractionated SFRT treatment regimens, a fraction dosage of at least 15 Gy with a single fraction should be employed.
2. Although the mean dosage ranges of OARs may differ from patient to patient, that is due to differences in tumour location, shape, size, depth and how far from OARs.
3. The MLCs-based SFRT plans described in this study have the potential to lower doses to OARs, while also providing an accurate assessment of how much radiation is actually delivered.

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