

## Dosimetric comparison between VMAT and 7 fields IMRT in preoperative hypofractionated radiotherapy for rectal cancer

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**Abstract: Introduction:** The hypo-fractionated short course radiotherapy has been considered as preoperative treatment in patients with locally advanced rectal cancer (LARC). The aim of this study is to compare the dosimetric differences between volumetric modulated arc therapy (VMAT), 7 fields intensity modulated radiotherapy (IMRT), regarding the target coverage and preservation of organs at risk (OARs) in patients with locally advanced rectal cancer planned for neoadjuvant short course radiotherapy. **Methods:** Thirty LARC patients were retrospectively evaluated in this study. For each patient dual Arc VMAT and 7 fields IMRT plans were generated. In all patients, the target consisted of clinical target volume (CTV) including pelvic LNs and the whole rectum with the mesorectum. Planning target volume (PTV) was created from the CTV with a margin of 5mm in all directions. The dose prescription was 25 Gy in 5 fractions in 5 successive days. OARs were delineated: bladder, small bowel, bilateral femoral heads and pelvic bone marrow (PBM). Conformity index (CI) and homogeneity index (HI) for both plans were compared. The dose-volume histogram (DVH) of PTV and OARs for both techniques was compared. **Results:** No significant difference between RA and IMRT plans in PTV25Gy coverage. ( $p = 0.72764$ ). Both CI and HI are better with VMAT than IMRT. The maximum and minimum bladder doses are less with VMAT compared to IMRT. The mean dose to femurs, bowel and pelvic bone marrow were significantly less with VMAT. **Conclusion:** In preoperative hypofractionated radiotherapy of LARC, VMAT technique can offer better conformity and homogeneity than IMRT with better OARs preservation. Further randomized clinical trials are needed to translate this dosimetric data into significant clinical benefit.

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**Key words:** Rectal cancer, Preoperative radiotherapy, VMAT, IMRT

### 1. Introduction

Locally advanced rectal cancer (LARC) is considered a common oncological problem in most of the countries. Both local and distant spread can affect the patient survival and quality of life. The neoadjuvant concurrent chemo-radiotherapy (CCRT), followed by radical surgery by total mesorectal excision (TME) has been considered the standard approach for treatment. Many studies have shown that the neoadjuvant CCRT resulted in less local recurrence rate with less acute and chronic toxicities as compared to adjuvant CCRT. Neoadjuvant CCRT also has the advantages of increase the possibility of sphincter preservation operations [1,2].

The short course of neoadjuvant radiotherapy in rectal carcinoma was proved to be efficacious in the Scandinavian studies, which reported less local recurrences and better overall survival, compared to long course radiotherapy. It is now used as a standard protocol in many radiotherapy centers [3,4].

For many years and till now, three-dimension conformal radiotherapy (3D-CRT) has been used as

the preferred technique of radiotherapy for patients with rectal cancer in many centers; however, the resultant acute and late bowel toxicity remains a challenge as it affects the quality of life, especially with the addition of concomitant chemotherapy [5].

Many studies have found a relationship between the volume of irradiated bowel and the risk of gastrointestinal toxicity [6–9].

Many planning studies identified the dosimetric advantages of IMRT and VMAT over 3D CRT in PTV coverage and also preservation of organs at risk (OARs). Both techniques have the advantage of generating concave isodose lines around the OARs, and thus improving the therapeutic ratio, through more homogenous dose to the target volume and less dose to the surrounding risk structures [10].

The aim of this study is to identify the optimal radiotherapy technique of short course neoadjuvant radiotherapy to patients with LARC through dosimetric comparison between volumetric modulated arc therapy (VMAT), and 7-field intensity modulated

radiotherapy (7F-IMRT), regarding the target coverage and organs at risk preservation.

## 2. Patients and Methods

### Patient characteristics

Thirty patients with LARC who already received neoadjuvant chemoradiotherapy were retrospectively evaluated in the study. There were 17 males and 13 females. The median age was 58 years (range 33 - 70 years). All patients had pathologically confirmed adenocarcinoma by colonoscopic biopsy. 14 patients had stage cT2-4bN0M0 and the other 16 were staged cT3-4bN1a-1bM0 according to the AJCC/UICC TNM (2010) staging system. The median tumor length was 4.5 cm (range from 3 cm to 9 cm) and the median distance from the anal verge was 4 cm (range from 1 cm to 9 cm).

### CT simulation

Each patient was simulated in head first supine position. Computed tomographic images with a thickness of 3 mm were taken from upper abdomen to 5 cm below the ischial tuberosities with immobilization by a custom vacuum immobilization device. I.V contrast was given. CT images were imported to the treatment planning system (TPS) and fusion with PET/CT or MRI was done whenever possible.

### Delineation of target volume and OAR

Delineation of the gross target volume (GTV) was done based on the data obtained from the diagnostic CT and MRI. CTV included the whole rectum and lymph nodes at risk including internal iliac, obturator, and presacral lymph nodes. It also included the sacral foramina, coccyx and at least 1 cm of the posterior bladder at middle and lower pelvic regions. In male patients, the posterior prostate and seminal vesicles were included, and in female patients, the posterior of vaginal wall and cervix were added to CTV. The cranial border for CTV was at the aorta bifurcation and its caudal border was at the anal verge covering the recto-sigmoid junction. PTV was created by adding 5 mm around CTV. The following organs at risk (OAR) were delineated: the small bowel, the bladder, and the femoral heads, and the pelvic bone marrow. The small bowel was delineated 2 cm above the PTV.

### Treatment planning

For each patient dual Arc VMAT and 7 fields IMRT plans were generated and optimized with similar planning objectives to each patient. For all patients, the prescription was 25 Gy in 5 fractions in 5 successive days. The treatment plan was analyzed in terms of their dose-volume histograms, target volume covered by 95% of the prescription dose (V95%), and maximum and mean structure doses (Dmax and Dmean). Calculation of all plans was done by 10 MV photon using AAA.

Planning objectives for OARs were defined as follows. Small bowel: 5% of the volume (D5) should be  $\leq 50$  Gy, max dose (Dmax)  $\leq 55$  Gy. Bladder dose: D5  $\leq 50$  Gy, Dmax  $\leq 55$  Gy. Femoral heads: D5  $\leq 45$  Gy. The pelvic bone marrow dose was analyzed with different dose volume objectives since there is no exact dose volume objective of sparing level has been recommended.

### Plan evaluation and comparison

All plans were evaluated based on dose-volume histogram (DVH) scoring values of PTV and OARs. PTV is evaluated using the conformity index (CI), homogeneity index (HI), and dose gradient index of the dose distribution.

For OARs, Small bowel was evaluated by the mean dose. The bladder avoidance was evaluated using maximum dose. For assessment of the femoral heads and PBM the mean doses for both VMAT and IMRT plans were calculated and compared.

### Statistical analysis

If p-value is  $< 0.05$ , it was considered statistically significant. The statistical values were calculated using SPSS (version 16.0.0, SPSS, Chicago, USA).

## 3. Results

### PTV 25 Gy coverage:

The 95% coverage of VMAT PTV 25 Gy plan showed mean dose of 24.64 Gy (SD  $\pm 0.52$ ), median dose of 24.45 Gy, minimum dose recorded 24.28 Gy (97.12%) and maximum dose recorded 25.6 Gy (102.4%). Meanwhile 95% of IMRT 25 Gy plans showed mean dose of 24.23 Gy (SD  $\pm 0.43$ ), median dose of 24.31 Gy, minimum value recorded 23.83 (95.32%) and maximum value recorded 26.1 Gy (104.4%). There is no significant difference between VMAT and IMRT plans in PTV 25 coverage. (p = 0.72764). (Figure.1)

### Conformity Index (CI):

Conformity index of IMRT plans showed mean value of 0.89 (SD  $\pm 0.056$ ) median value 0.82, minimum value 0.78 and maximum value 0.93 mean while conformity index of VMAT plans showed mean value of 0.97 (SD  $\pm 0.036$ ), median value of 0.95, minimum value of 0.93 and maximum value of 0.98 results. (p = 2.29369E-21). There is significant difference in favor of VMAT technique.

### Homogeneity index (HI):

Homogeneity index of IMRT plans showed mean value of 0.19 (SD  $\pm 0.023$ ) median value 0.1, minimum value 0.07 and maximum value 0.20 mean while Homogeneity index of VMAT plans showing mean value of 0.132 (SD  $\pm 0.13$ ), median value of 0.13, minimum value of 0.10 and maximum value of 0.16. Also there is significant difference in favor of VMAT.

### Bladder comparison between IMRT and VMAT

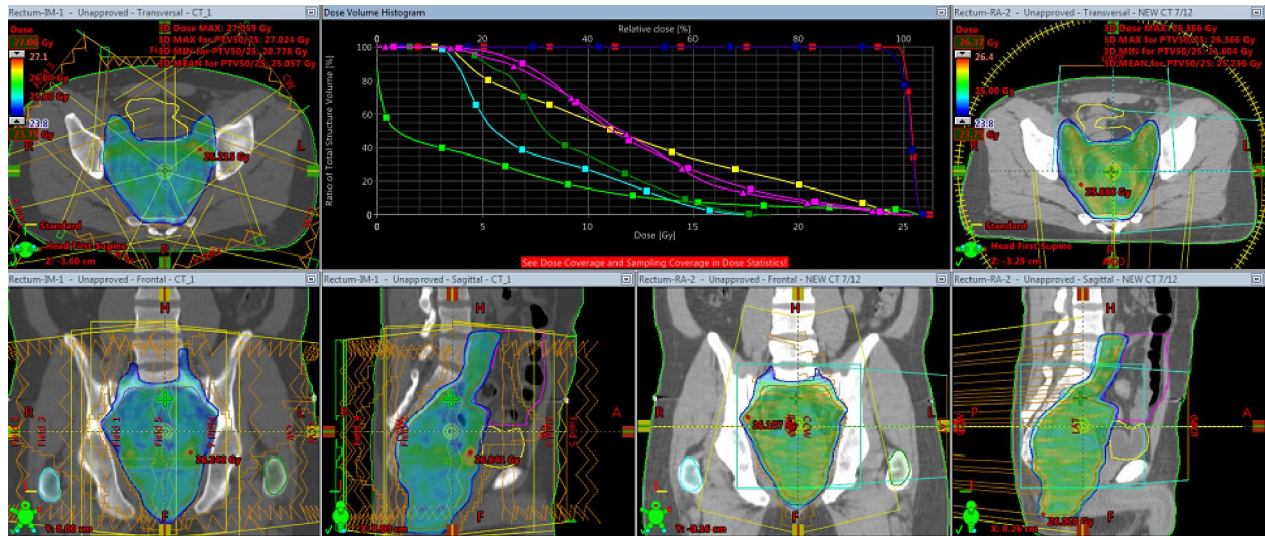


Figure 1: The different views for comparison between IMRT and VMAT plans for target volume coverage

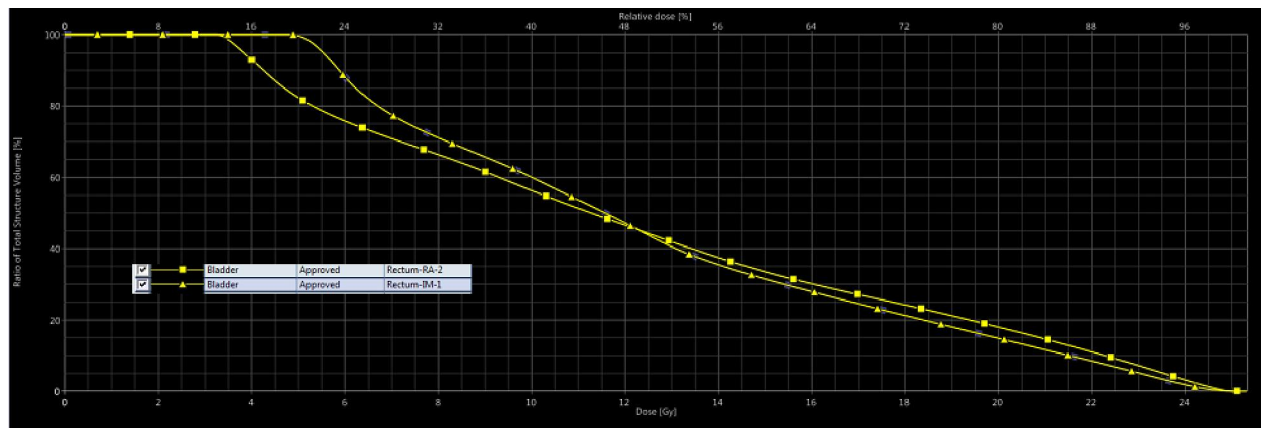


Figure 2: Bladder dose comparison for both plans

The maximum dose of the urinary bladder in IMRT plans showed mean value of 21.26 Gy (SD  $\pm 0.669$ ), median value of 18.15Gy, minimum value of 15.43Gy and maximum value of 16.90Gy, meanwhile the urinary bladder maximum dose in VMAT plans showing mean value of 16.80Gy (SD  $\pm 2.915$ ), median value of 15.45Gy, minimum value of 14.14Gy and maximum value of 18.91 Gy, comparing this data together, There is significant difference in favor of VMAT technique. (Figure.2).

#### Both Femoral heads

Right femur head and neck mean dose in IMRT plans showed mean value of 12.93 Gy (SD  $\pm 3.71$ ), median value of 12.16Gy, minimum value of 12.54 Gy and maximum value of 12.34 Gy, meanwhile mean dose VMAT plans showing mean value of 11.95 Gy (SD  $\pm 3.42$ ), median value of 10.81Gy, minimum value of 4.80Gy and maximum value of 16.39Gy. There is significant difference in favor of VMAT technique. Left femur head and neck mean dose in IMRT plans showed mean value of 12.32 Gy (SD  $\pm 4.86$ ), median

value of 10.63Gy, minimum value of 15.39 Gy and maximum value of 16.34 Gy, meanwhile mean dose VMAT plans showing mean value of 11.95 Gy (SD  $\pm 3.27$ ), median value of 11.81Gy, minimum value of 5.79Gy and maximum value of 16.81, The significant difference was in favor of VMAT technique. (Figure.3)

#### Bone marrow mean dose:

Bone marrow mean dose in IMRT plans showed mean value of 15.88Gy (SD  $\pm 2.75$ ), median value of 15.30Gy, minimum value of 14.3Gy and maximum value of 16.34 Gy, meanwhile mean dose VMAT plans showed mean value of 13.08 Gy (SD  $\pm 2.731$ ), median value of 12.45Gy, minimum value of 10.89Gy and maximum value of 14.691Gy, There is significant difference in favor of VMAT technique. (p = 1.08849E-8). (Figure.4)

#### Bowel volume 195cc dose:

Bowel mean dose in IMRT plans showed mean value of 12.49Gy (SD  $\pm 5.33$ ), median value of 12.92Gy minimum value of 3.20Gy and maximum

value of 20.74 GY, meanwhile bowel mean dose in VMAT plans showing mean value of 11.78Gy (SD±4.20), median value of 11.085Gy, minimum value of 4.70GYand maximum value of 14.57GY,

comparing these data together showing significant difference in favor of VMAT technique. (p = 0.00464). **(Figure.5).**

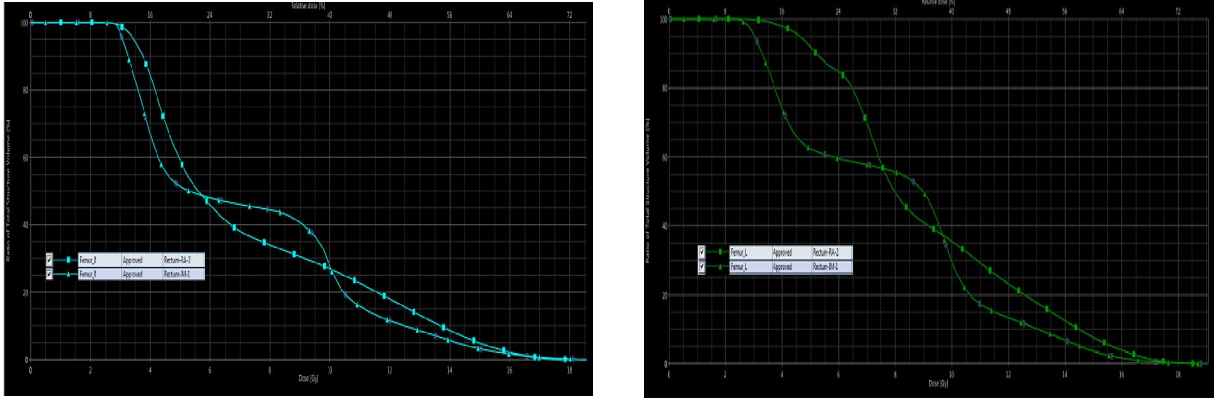


Figure.3: Both femoral Heads mean dose for both plans

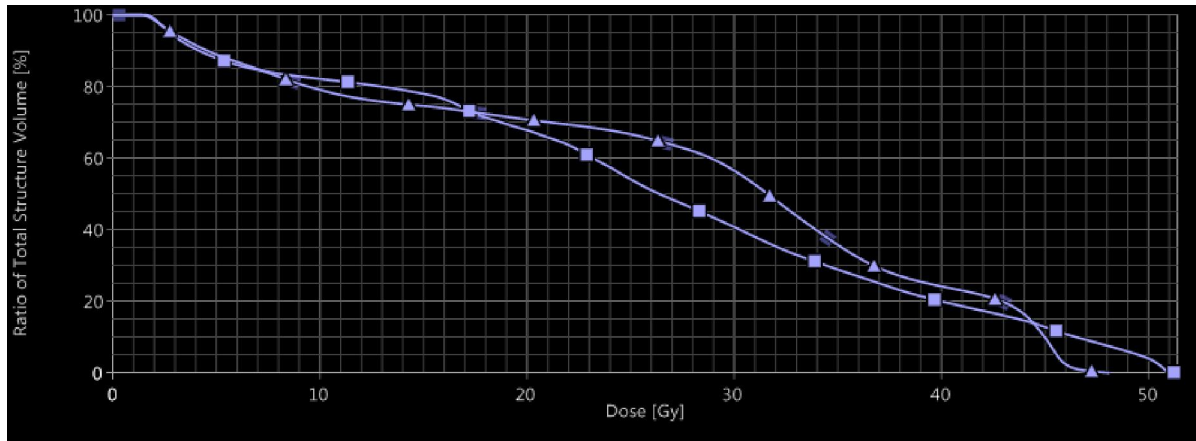


Figure.4: Bone marrow dose for both plans

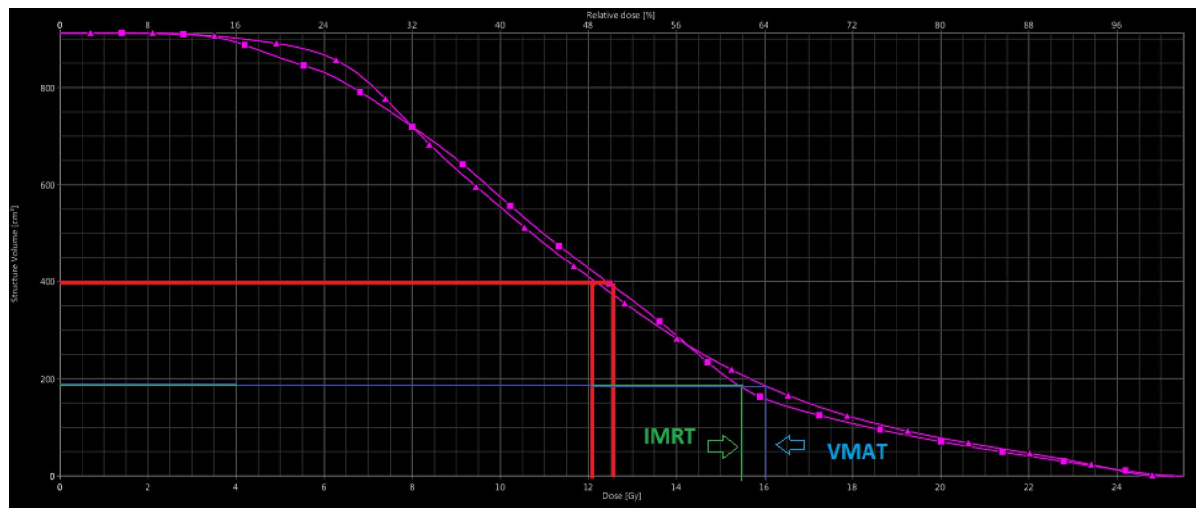


Figure.5.: The comparison between volume of 195cc of bowel in IMRT and VMAT plan



#### 4. Discussion

Radiotherapy is necessary to control the rectal cancer locally in the pelvis. Combination of radiotherapy and surgery reduced the local relapse rate from 46% to 37% in comparison to surgery alone [11-13]. However, the radiotherapy related toxicity is a major concern especially with the addition of chemotherapy [14]. Advanced radiotherapy techniques can reduce the irradiation of OAR [15].

The expanding use of neoadjuvant short course radiotherapy to LA rectal cancer highlights the need for choosing the best technique of radiotherapy, that can lower the dose to OAR to reduce the late effects of radiotherapy especially with the use of such high dose per fraction in the short course.

VMAT and IMRT were confirmed to have dosimetric advantages over 3D conformal technique in neoadjuvant radiotherapy of rectal carcinoma. In many studies evaluating pelvic malignancies, VMAT had better OAR protection than IMRT, with the advantages of less monitor units, less treatment time and higher dose rate [16,17]. This was comparable with our results which confirmed better PTV coverage using VMAT technique in comparison to IMRT. This was evidenced by better CI and HI.

The major concern during preoperative radiotherapy of rectal cancer is to avoid radiation enteritis [18]. The volume of irradiated small intestine was found to have a significant correlation with the incidence of diarrhea in patients with locally advanced rectal cancer in the neoadjuvant setting [19].

Another study in anal canal cancer patients treated with chemoradiation showed significant dosimetric difference between VMAT and VMAT in small intestine sparing in favor of VMAT which reduced significantly V35 - V45 of small bowel [20]. This data is compatible with our results which showed less bowel mean dose in VMAT plans (11.78Gy), than bowel mean dose in IMRT plans (12.49Gy) with significant p value  $p = 0.005$ ). However another study evaluating patients with locally advanced rectal cancer treated with neoadjuvant radiotherapy with simultaneous integrated boost, showed that there is no significant difference between VMAT and 7 fields IMRT in reduction of the irradiated small bowel volume [21].

The irradiated bladder volume may not have a significant clinical benefit due to relatively high tolerance of the bladder and relatively lower dose given in the rectal cancer in comparison to escalated doses as given in prostate cancer. Our study showed a difference between VMAT and IMRT in bladder preservation in favor of VMAT. VMAT had less maximum dose to the urinary bladder with a mean value of 16.80Gy (SD  $\pm 2.915$ ), in comparison to

IMRT plans showing mean value of 21.26 Gy (SD  $\pm 0.6$ ). Our data is compatible with another study done by Wolff HA et al, which compared between VMAT and IMRT in patients with locally advanced rectal cancer, and revealed that bladder volume V40 is significantly less in VMAT than IMRT plans [9]. A different result was published by Myerson et al, who did not find a significant difference in bladder volume, V15, V30, V40, V50, V55, and Dmax of the bladder between VMAT and IMRT in treatment of anorectal cancer [22].

Reduction of the dose to the head and neck of femur may reduce the risk of avascular necrosis. In our analysis, the mean dose to the proximal femur was significantly less in VMAT (11.95Gy, SD  $\pm 3.27$  than IMRT (12.32Gy, SD  $\pm 4.86$ ). A similar published study found that Dmax and V30 of the bilateral proximal femurs and the V40 of the right proximal femur were significantly reduced by VMAT in comparison to IMRT. ( $P < 0.01$ ) [10].

Many studies revealed a correlation between the hematological toxicity and the BM dosimetric parameters in anal cancer patients [23].

Our data showed that bone marrow mean dose in IMRT plans had mean value of 15.88Gy (SD  $\pm 2.75$ ), which is significantly higher than mean dose of VMAT plans 13.08 Gy (SD  $\pm 2.731$ ). Similar results was reported in a another study, in which VMAT had better PBM preservation than IMRT in patients with cervical cancer receiving pelvic LNs irradiation and the bone marrow mean and D40% dose with VMAT and IMRT were 30.128 $\pm$ 1.94, 34.399 $\pm$ 2.09; 32.216 $\pm$ 2.72 and 37.397 $\pm$ 2.87 respectively [24].

#### Conclusion

In preoperative short course radiotherapy for locally advanced rectal cancer, VMAT has dosimetric advantage than IMRT in PTV coverage and OAR sparing, with less treatment time and MU. However further clinical trials with long term follow up are needed to translate this dosimetric advantage into clinical benefit.

This study was done in the Department of Radiation Oncology, Dar Al Fouad Hospital, Egypt.

Conflict of interest notification: No authors have any conflicts of interest.

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