

## Evaluation of Dose Distribution Indices by using RapidArc Technique for the Treatment of Gynecological Cancer

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### Abstract

*This study describes the distribution of radiation doses to investigate the planned target volume (PTV) of gynecological cancers using the RapidArc technique. The optimal treatment plan options are developed by involvement of different dosimetric parameters including Homogeneity index (HI), Conformity index (CI), Uniformity index (UI), Radical dose homogeneity index (rDHI) and Moderate dose homogeneity index (mDHI).*

*Thirteen patients diagnosed with gynecological cancer were treated through RapidArc on DHX Varian linear accelerator with 6MV and 15MV photon beams. This therapy was carried out with linac.*

*The calculated dosimetric parameters for planning target volume were found in the ranges; HI (1.08 to 1.20), CI (0.985 to 0.997 in RTOG), CI (1.003 to 1.005 in ICRU), UI (1.05 to 1.13), rDHI (0.57 to 0.75) and mDHI (0.88 to 0.93).*

*It has been concluded that all the calculated indices are within the range specified by radiation therapy oncology group (RTOG; 1993), International Commission on Radiation Units and Measurements (ICRU) and OLIVER; except in rare cases may be due to complex geometry, tumor volume range, and low radiation dose. This treatment can be further added to calculate other dose indices by using higher energy beams and different prescription doses for different fractions.*

**Keywords:** RapidArc, gynecological cancer, homogeneity index, conformity index, radical dose homogeneity index, moderate dose homogeneity index, uniformity index

### I. Introduction

The human female reproductive tract (FRT) is a complex system that combines various organs, including the ovaries, uterus, fallopian tubes, vulva, and vagina. Each of which has unique cellular properties and functions. This versatility in turn allows for the development of a wide range of distinctly characterized elliptical gynecological cancers. Thus, reliable model systems are needed to better understand the various processes involved in the regional pathogenesis of the reproductive tract and to improve treatment strategies (Löhmußaar, Boretto, & Clevers, 2020).

Radiation Oncology is a clinical and scientific discipline using ionizing radiations for the cancer management. Hence giving the precise dose measurement to target volume and

minimizing damage to healthy tissues (Perez & Brady, 2011). Radiation oncologists must work closely with physicians, treatment planners, and dosimetrists in radiotherapy facilities to ensure that their designs are as accurate, practical and cost-effective as possible treatment plan (Govindan, 2008). Radiation therapy (RT) plays an important role in the treatment of gynecological malignancies, especially for those patients with one or more pathological risk factors such as positive lymph nodes, precancerous infiltration, surgical margins, tumor size, deep matrix invasion or invasion Lymphatic space (Rotman et al., 2006). Gynecologic cancer is unique in its effects on reproductive system, sexuality and body image (Ayana, Negash, Yusuf, Tigeneh, & Haile, 2018).

RapidArc is advanced IMRT optimization that combines a gantry rotation with Variable Dose Rate, Variable Gantry Speed, and Dynamic MLC features. This technique provides a highly effective treatment plan optimization and delivery platform and also, delivers highly conformable dose distribution with excellent accuracy (Otto, 2008). A series of studies have shown that RapidArc has obvious benefits of dose distribution and organ protection. Increasing the therapeutic sensitivity of tumor cells may help improve local control of disease and survival (Ji et al., 2018). It delivers Monitor Units (MU) with high efficiency and both total body dose and overall treatment time reduces through it (Alexander et al., 2008).

The linear accelerator is used for the treatment of cancer patients with high accuracy and efficient results used in the radiation oncology department especially in cancer hospital. The clinical quality of linear accelerators in a flattening filter free mode (FFF) results in a much higher dose rate than in a standard flat beam mode (FB) (Treutwein, Hipp, Koelbl, & Dobler, 2017).

Dose volume histograms (DVHs) and isodose lines are used for the investigating maximum, minimum, average and mode of delivered dose parameters for each volume of interest (Kataria, Sharma, Subramani, Karrthick, & Bisht, 2012). The DVH provides all information about absorbed dose in a larger volume and summarizes the entire dose distribution for each anatomy into a single curve (Manikandan, Supe, & Katke, 2012). International Commission of Radiation Unit (ICRU) Report No. 83 provided the necessary information to standardize techniques, procedures, coordinate prescription and record. This report discussed about the use of dose volume histogram for specified absorbed dose for treatment goals and median recommendations (Grégoire & Mackie, 2011). ICRU and measurement committee report no.50 and 62 define the gross target volume (GTV), an appropriate computed tomography (CT), clinical target volume (CTV): includes GTV plus areas considered as potential microscopic diseases. Planning target volume (PTV): providing an edge around the CTV to allow internal target motion, other anatomical movements during treatment, and changes in treatment settings (Sharyan, Allehyani, & Tolba, 2015).

In recent years, a number of efforts have improved PTV processing to help consistently plan products and reduce mandatory optimum time (W. Cao, Zhuang, Chen, & Liu, 2020). By choosing the best plan from a variety of plans has always been a difficult task, depend on dose volume histogram metrics and visual inspection of isodose distributions to provide vague assessments (Cilla et al., 2020).

The main function of conformity index (CI) is to measure how well the prescribed dose is compatible with the TV, and the main function of HI is to assess the uniformity of the dose distribution within the target. On the other hand, the main function of gradient index (GI) is to evaluate the steepness of external dose attenuation target (T. Cao, Dai, Ding, Li, & Quan, 2019).

## 2. Materials and Methods

Thirteen patients suffering from gynecological cancer were brought for the treatment. VMAT/Rapidarc technique was used to treat these patients using a 6 MV and 15 MV photon beam of the DHX linear accelerator Clinac DHX (Varian Medical Systems Inc., Palo Alto, CA) placed at SKMCH (Shaukat Khanum Memorial Cancer Hospital and Research Center). In this treatment method, we used 5040cGy total dose in 28 fractions to the PTV. In this method, treatment is delivered by using arc rotation of linear gantry.

In order to accelerate charged particles such as electrons to high energy through a linear tube, a device called a linear accelerator using high-frequency electromagnetic waves is used. The linear accelerator used for treatment planning is Trilogy with the Millennium Multi-Leaf Collimator by Varian Medical Systems. It can provide both electrons and photons beam. In this study, only photon beams were used in all cases with energies of 6 MV, 15 MV, and 18 MV (Allehyani, Sharyan, Tolba, & Hassan, 2017; Khan & Gibbons, 2014).

The treatment plan was generated using eclipse treatment planning software and each patient's computed tomography data set. Eclipse treatment planning system is the complete solution of the treatment plan for a vast variety of disease that allows the quick processing with accuracy. Advanced eclipse treatment planning strategies enable patients to provide better care and services.

To analyze our plan, we calculated the homogeneity index, conformity index by ICRU and RTOG, uniformity index, radical dose homogeneity index and moderate dose homogeneity index for the PTV by perceiving the dose volume histogram DVH of the patients (Oliver, Chen, Wong, Van Dyk, & Perera, 2007). The following formula is used to calculate the dose index for PTV described above.

$$\text{homogeneity index} = \frac{D(\text{max})}{P.D}$$

Where PD is the prescription dose

In RTOG

$$\text{conformity index} = \frac{V_{95}}{T.V}$$

In ICRU

$$\text{conformity index} = \frac{T.V}{V_{95}}$$

$V_{95}$  is the reference isodose volume in 95% and T.V is the target volume (Feuvret, L., Noël, G., Mazon, J. J., & Bey, P. (2006), Surber, G., Hamm, K., & Kleinert, G. (2004).

$$\text{uniformity index} = \frac{D_5}{D_{95}}$$

$D_5$  is the minimum dose to 5% of the target volume indicating the “maximum dose” and  $D_{95}$  is the minimum dose to the 95% of the target volume, indicating the “minimum dose” (Prabhakar, R. (2010).

$$\text{Radical DHI} = \frac{D_{\text{min}}}{D_{\text{max}}}$$

Where  $D_{\text{min}}$  is the “minimum dose” value and  $D_{\text{max}}$  is the “maximum dose” value (Yoon et al., 2007).

$$\text{moderate DHI} = \frac{D_{95}}{D_5}$$

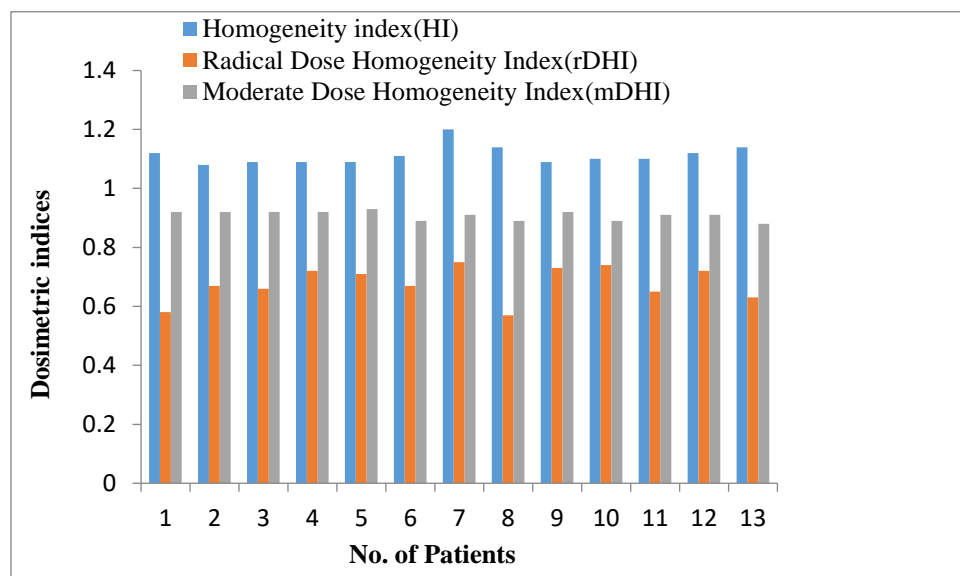
$D_5$ , is the the minimum dose to 5% of the target volume indicating the “maximum dose” and  $D_{95}$  is the minimum dose to the 95% of the target volume, indicating the “minimum dose” (Kataria et al., 2012).

RapidArc plans generated with 6 and 15 MV photon beams for the prescribed dose of 5040cGy in 28 fractions to the PTV.RapidArc showed the improvement in organ at risk and in healthy tissue sparing.

### 3. Results and Discussion

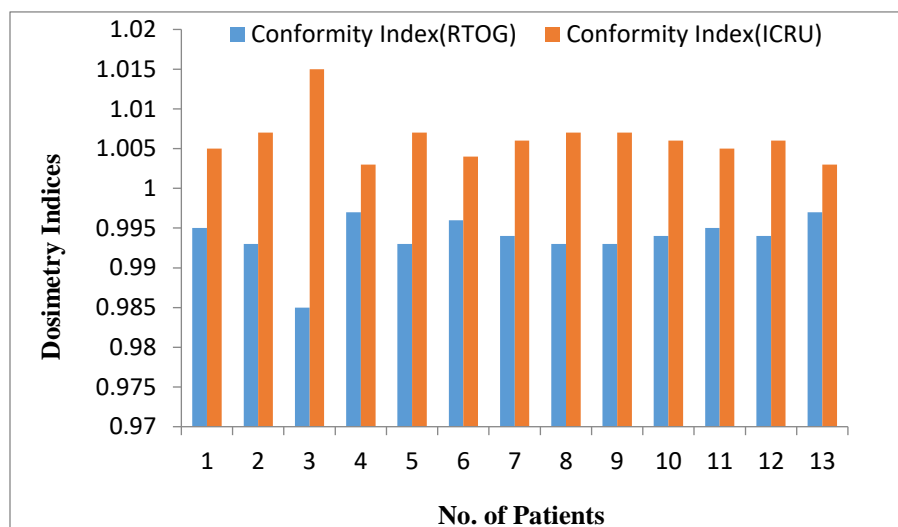
#### Dose to Planning Target volume (PTV)

The dosimetric index of PTV calculated from the DVH of 13 gynecological cancer patients. The mean, median, modal, standard deviation and coefficient of variation are enlisted below. Rapid arc plans achieved for PTV the homogeneity index ( $H=1.08\pm 1.02$ ), thus all values are limited. All of the homogeneity indices are within the RTOG's recommended range, with no value showing a deviation greater than two. Radical dose homogeneity index varies from minimum 0.57 to maximum 0.75 values. Similarly, moderate dose homogeneity index varies between the ranges from  $0.93\pm 0.88$  in Figure-1.



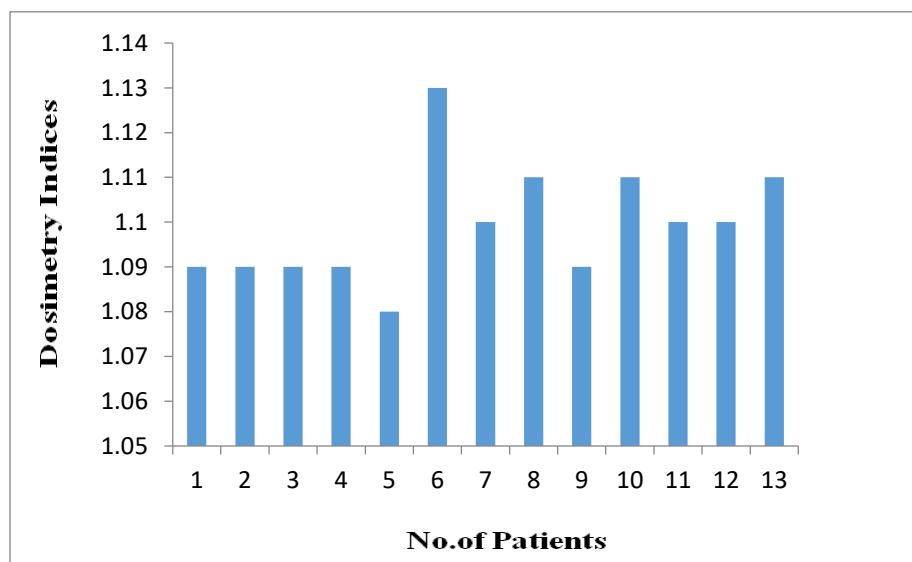
**Figure 1: Comparison of homogeneity index, radical dose homogeneity index and moderate dose homogeneity index in patients**

According to the guidelines proposed by RTOG in 1993, conformity index is determined by the isodose volume and target value. All the values lie between the  $0.985\pm 0.997$ , thus the treatment plan is considered to be acceptable. According to the guidelines proposed by ICRU in 1993, conformation quality is determined by the size of the conformity index (CI) value. The values in ICRU lies in  $1.005\pm 1.003$  in Figure-2.



**Figure 2: Comparison of conformity index (RTOG) and conformity index (ICRU) in patients**

The uniformity index lie in  $1.13 \pm 1.05$ , so it means that the high dose volume presence inside the prescription in Figure-3.



**Figure 3: Uniformity index in patients**

The coefficient of variances was 3.24%, 8.38%, 1.65%, 0.29%, 0.29% and 1.47% for homogeneity, rDHI, mDHI and conformity index (in RTOG), conformity index (in ICRU) and uniformity index respectively.

#### **4. Discussion**

The new method of Image Guided Intensity Modulated Radiotherapy radiation therapy is RapidArc radiotherapy, which handles accurate treatment in less time than traditional IMRT. RapidArc therapy performance on uterine cervix tumor has been evaluated Target coverage is almost the same as IMRT. RapidArc may reduce the risk of radiation-induced cancer. RapidArc treatment is more comfortable for patients because they spend less time and can treat on a daily basis (Cozzi et al., 2008).

Tejinder Kataria identified the homogeneity Index: An objective tool for evaluating conformal radiation treatment is considered to be consistent with the treatment protocol if the homogeneous index is  $\leq 2$ , if the index is between 2 and 2.5 it is considered a slight violation, but if the index is outside 2.5 the violation protocol is major (Kataria et al., 2012). In the present work homogeneity index is between 1.08 and 1.20 which is  $\leq 2$  it means that treatment is considered to conform to the protocol for PTV.

Brennan SM identified the factors influencing conformity index in radiotherapy in ICRU conformity index range is 1.06 to 3.8 and the mean value is 2.01 (Brennan, Thirion, Buckney, Shea, & Armstrong, 2010). In the latest research conformity index value lies in 1.003 to 1.015 for PTV.

In RTOG If the conformity index lies between 1 and 2, the treatment is considered to conform with the treatment plan, if the index between 2 and 2.5, is considered to be a minor violation, and when the index value is  $> 0.9$  or  $< 2.5$ , the protocol violation is considered to be major but may be considered to be acceptable (Feuvret, L., Noël, G., Mazon, J. J., & Bey, P. (2006). In our observation conformity index in RTOG is 0.985 to 0.997 for PTV.

Ramachandran Prabhakar identified in Dose-volume uniformity index: a simple tool for treatment plan evaluation in brachytherapy a uniform dose inside the prescription, the DVUI is 1. DVUI  $> 1$  shows the presence of a relatively high dose volume inside the prescription (Prabhakar, R. (2010). In the cited research article uniformity index is 1.05 to 1.13 for PTV.

Qurat-ul-ainShamsi told us in analysis of Dosimetric Indices for Evaluating Intensity Modulated Radiotherapy Plans of Head and Neck Cancer Patients radical dose homogeneity index has a minimum value 0.18 and the maximum value is 0.61 (Brennan et al., 2010). In the present work of radical dose homogeneity index varies from minimum 0.57 to maximum 0.75 values for PTV.

Qurat-ul-ainShamsi told us in Analysis of Dosimetric Indices for Evaluating Intensity Modulated Radiotherapy Plans of Head and Neck Cancer Patients moderate dose homogeneity index varied from the minimum value 0.84 to maximum value 0.92 (Shamsi, Atiq, Atiq, Buzdar, & Iqbal, 2017).

#### **5. Conclusion**

In this work, 13 gynecologic cancer patients were treated with RapidArc and we studied using a linear accelerator and Eclipse treatment plan. The design of this radiation therapy plan involves some dosimetric indices which are homogeneity index, conformity index, uniformity index, radical dose homogeneity index, moderate dose homogeneity index, gradient dose homogeneity index and coverage with 28 fractions of 5040cGy prescribed dose. These dosimetric indices indicate the better results from the RapidArc treatment. RapidArc treatment gives excellent homogeneity index, conformity index, radical dose homogeneity index and moderate dose homogeneity index improve for gynecological cancer. All indices are within the range specified by RTOG; 1993, ICRU and OLIVER; except in rare cases may be due to complex geometry, tumor volume range, and low

radiation dose. The quality of the treatment of patient improves with the RapidArc treatment. RapidArc treatment provides high conformity and uniform dose distribution within the PTV, bladder, and rectum. The risk of radiation-induced cancer may decrease by the RapidArc. RapidArc treatment is more comfortable for the patients because they spend less time to take the daily treatment. In RapidArc treatment, the exact location of the tumor can be observed. RapidArc therapy treats cancer at lower energy. In treatment planning system RapidArc depends on the actual optimization algorithm. To achieve the advantage of the potential of RapidArc only actual optimization algorithm increase degree of freedom. Gynecological cancer treatment is improved by the RapidArc therapy rather than IMRT and 3D-conformal radiotherapy. The arcs and the number of fields are different.

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### **List of Abbreviations**

HI	Homogeneity index
CI	Conformity index
UI	Uniformity index
rDHI	Radical dose homogeneity index
mDHI	Moderate dose homogeneity index
RTOG	Radiation therapy oncology group
ICRU	International Commission on Radiation Units and Measurements
FRT	Female reproductive tract
RT	Radiation therapy
IMRT	Imaging Guided Intensity Modulated Radiotherapy
FFF	Flattering filter free mode
DVH	Dose volume histograms
GTV	Gross target volume
CT	Computed tomography
CTV	Clinical target volume
PTV	Planning target volume
PD	Prescribed dose
MLC	Multi-Leaf Collimator
TV	Target volume
DVUI	Dose-volume uniformity index

## **6. References**

Alexander, A., Wells, D., Berrang, T., Parsons, C., Mydin, A., Shaffer, R., . . . Otto, K. (2008). Volumetric arc therapy (VMAT) reduces treatment time compared to conventional IMRT (cIMRT) while maintaining similar plan quality in whole pelvic gynecologic radiotherapy. *International Journal of Radiation Oncology, Biology, Physics*, 72(1), S366.

Allehyani, S. H., Sharyan, H. A., Tolba, A. R., & Hassan, R. A. (2017). 3DCRT Versus RapidArc in Terms of Iso-Dose Distribution, Dose Volume Histogram (DVH) and

Organs at Risk for Esophageal Cancer (EC) Dosimetric Study. *American Journal of Clinical and Experimental Medicine*, 5(4), 123-133.

Ayana, B. A., Negash, S., Yusuf, L., Tigeneh, W., & Haile, D. (2018). Health related quality of life of gynaecologic cancer patients attending at Tikur Anbesa Specialized Hospital (TASH), Addis Ababa, Ethiopia. *BMC women's health*, 18(1), 1-9.

Brennan, S. M., Thirion, P., Buckney, S., Shea, C. O., & Armstrong, J. (2010). Factors Influencing Conformity Index in Radiotherapy for Non-Small Cell Lung Cancer. *Medical Dosimetry*, 35(1), 38-42.

Cao, T., Dai, Z., Ding, Z., Li, W., & Quan, H. (2019). Analysis of different evaluation indexes for prostate stereotactic body radiation therapy plans: conformity index, homogeneity index and gradient index. *Precision Radiation Oncology*, 3(3), 72-79.

Cao, W., Zhuang, Y., Chen, L., & Liu, X. (2020). Application of dose-volume histogram prediction in biologically related models for nasopharyngeal carcinomas treatment planning. *Radiation Oncology*, 15(1), 1-9.

Cilla, S., Ianiro, A., Romano, C., Deodato, F., Macchia, G., Buwenge, M., . . . Valentini, V. (2020). Template-based automation of treatment planning in advanced radiotherapy: a comprehensive dosimetric and clinical evaluation. *Scientific reports*, 10(1), 1-13.

Cozzi, L., Dinshaw, K. A., Shrivastava, S. K., Mahantshetty, U., Engineer, R., Deshpande, D. D., . . . Nicolini, G. (2008). A treatment planning study comparing volumetric arc modulation with RapidArc and fixed field IMRT for cervix uteri radiotherapy. *Radiotherapy and oncology*, 89(2), 180-191.

Govindan, R. (2008). *The Washington manual of oncology*: Lippincott Williams & Wilkins.

Grégoire, V., & Mackie, T. (2011). State of the art on dose prescription, reporting and recording in Intensity-Modulated Radiation Therapy (ICRU report No. 83). *Cancer/Radiothérapie*, 15(6-7), 555-559.

Ji, S., Hu, Q., Zhu, J., Chen, J., Chen, Q., Liu, Z., . . . Wu, J. (2018). Combined pretreatment with 18 F-FDG PET/CT and Comet assay guides the concurrent chemoradiotherapy of locally advanced cervical cancer: study protocol for a randomized controlled trial. *Trials*, 19(1), 1-10.

Kataria, T., Sharma, K., Subramani, V., Karrthick, K., & Bisht, S. S. (2012). Homogeneity Index: An objective tool for assessment of conformal radiation treatments. *Journal of medical physics/Association of Medical Physicists of India*, 37(4), 207.

Khan, F. M., & Gibbons, J. P. (2014). *Khan's the physics of radiation therapy*: Lippincott Williams & Wilkins.

Löhmussaar, K., Boretto, M., & Clevers, H. (2020). Human-derived model systems in gynecological cancer research. *Trends in Cancer*.



Manikandan, P., Supe, S., & Katke, A. (2012). Comparison of homogeneity indices for quantitative evaluation of dose homogeneity for IMRT treatments of head and neck cancers. *Gulf J Oncolog*, 11, 25-30.

Oliver, M., Chen, J., Wong, E., Van Dyk, J., & Perera, F. (2007). A treatment planning study comparing whole breast radiation therapy against conformal, IMRT and tomotherapy for accelerated partial breast irradiation. *Radiotherapy and oncology*, 82(3), 317-323.

Otto, K. (2008). Volumetric modulated arc therapy: IMRT in a single gantry arc. *Medical physics*, 35(1), 310-317.

Perez, C. A., & Brady, L. W. (2011). *Radiation oncology: management decisions*: Lippincott Williams & Wilkins.

Rotman, M., Sedlis, A., Piedmonte, M. R., Bundy, B., Lentz, S. S., Muderspach, L. I., & Zaino, R. J. (2006). A phase III randomized trial of postoperative pelvic irradiation in Stage IB cervical carcinoma with poor prognostic features: follow-up of a gynecologic oncology group study. *International Journal of Radiation Oncology\* Biology\* Physics*, 65(1), 169-176.

Shamsi, Q., Atiq, M., Atiq, A., Buzdar, S., & Iqbal, K. (2017). Analysis of dosimetric indices for evaluating intensity modulated radiotherapy plans of head and neck cancer patients. *J Radiol Radiat Ther*, 5(1), 1065-1070.

Sharyan, H., Allehyani, S., & Tolba, A. (2015). Dosimetric comparison of 3DCRT versus RapidArc in terms of iso-dose distribution, dose volume histogram (DVH) and dosimetric results for the PTV and critical organs for glioblastoma (GBM). *Am J Med Med Sci*, 5(5), 208-219.

Treutwein, M., Hipp, M., Koelbl, O., & Dobler, B. (2017). Volumetric-modulated arc therapy and intensity-modulated radiation therapy treatment planning for prostate cancer with flattened beam and flattening filter free linear accelerators. *Journal of applied clinical medical physics*, 18(5), 307-314.

Yoon, M., Park, S. Y., Shin, D., Lee, S. B., Pyo, H. R., Kim, D. Y., & Cho, K. H. (2007). A new homogeneity index based on statistical analysis of the dose-volume histogram. *Journal of applied clinical medical physics*, 8(2), 9-17.