

A quantitative analysis of intensity-modulated radiation therapy plans and comparison of homogeneity indices for the treatment of gynecological cancers

Pushpraj Pathak, Sanjeev Vashisht

Department of Medical Physics, Jawaharlal Nehru Cancer Hospital and Research Centre, Bhopal, Madhya Pradesh, India

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ABSTRACT

The aim of present study was to evaluate the intensity-modulated radiation therapy (IMRT) plans using different homogeneity and conformity indices in gynecological cancers, as well as to compare and find out the most reliable and accurate measure of the dose homogeneity among the available indices. In this study, a cohort of 12 patients were registered for evaluation, those receiving dynamic IMRT treatment on Clinac-2300C/D linear accelerator with 15-Mega Voltage (MV) photon beam. Dynamic IMRT plans were created on Eclipse treatment planning system with Helios dose volume optimization software. Homogeneity indices (HI) such as H index, modified H index, HI index, modified HI index, and S-index (sigma-index) proposed by M Yoon *et al.* (2007) were calculated and compared. The values of S-index vary from 1.63 to 2.99. The results indicate that the H and HI indices and their modified versions may not provide the correct dose homogeneity information, but the S-index provides accurate information about the dose homogeneity in the Planning Target Volume (PTV). Each plan was compared with 6-MV photon energy on the basis of S-index and conformity index (CI). Organs at risk (OAR) doses with 6-MV and 15-MV beams were also reported.

Key words: Intensity-modulated radiation therapy, homogeneity, Conformity index, gynecological cancer, dose, organ at risk

Introduction

The basic requirement of radiotherapy treatment is to deliver maximum dose to the target volume (tumor) and as low as possible to the surrounding normal tissue. This requirement could be easily fulfilled if the separation between tumor control probability (TCP)^[1] and normal tissue complication probability (NTCP) plot would be wide enough, but unfortunately both curves overlap at higher doses. The aim of the new technique in radiotherapy is to widen the separation between the TCP

and NTCP, and at the same time, uniform distribution of the dose throughout the tumor. Intensity-modulated radiation therapy (IMRT)^[2] is one modality by which the reduction of NTCP and escalation of target dose is possible, but may produce less homogeneous dose distribution within the planning target volume (PTV) as compared to three-dimensional conformal radiation therapy (3D-CRT) and conventional technique. In modern radiation therapy, specification of absorbed dose to the relevant volumes rather than some points is critical to communicate the treatment intent. The reported absorbed dose should be descriptive of the absorbed dose in the volume. The radiobiological effects and dose homogeneity are interrelated. The concept of equivalent uniform dose (EUD) for tumors as proposed by Niemierko^[3] is one of the methods used to show the relationship between the dose homogeneity and radiobiological effects.^[4-6] The equivalent uniform dose is defined as the biologically equivalent dose that, if delivered uniformly, would lead to the same reduction in the tumor volume as the actual dose that has an inhomogeneous distribution. Therefore, if the homogeneity indices are properly calculated, then it may be closely related to the EUD. Yoon *et al.*^[7] have evaluated the relationship between EUD and homogeneity index (S-index) for brain tumor and reported highly linear distribution. The dose-volume histogram (DVH)^[8] is the key tool of the 3D-treatment planning system, which

Address for correspondence:

Mr. Pushpraj Pathak,
Jawaharlal Nehru Cancer Hospital and Research Centre,
Idgah-Hills, Bhopal, Madhya Pradesh, India.
E-mail: pushprajkumar@yahoo.co.in

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summarizes the entire plan into a single 2D graph, though unable to show the spatial distribution of doses. Hence, it is an excellent tool for evaluating as well as comparing the competing plans. Other than evaluation of the dose coverage, cumulative and differential DVH are used to quantify the degree of homogeneity in the plans. Several definitions of the homogeneity index have been proposed and used depending upon the radiotherapy modality. A perfectly homogeneous dose to the planning target volume (PTV) would be characterized by a spike in the differential DVH (dDVH) and the vertical drop of the cumulative DVH (cDVH) line at the prescribed absorbed dose. In practice, the dDVH for PTV in a treatment plan has near Gaussian shaped distribution around the mean absorbed dose. Measure of such a distribution is nothing but the standard deviation of the mean dose (D_{sd}), which directly reflects the degree of dose homogeneity in PTV, and this number is called the sigma-index (S-index). Therefore, as recommended by the International Commission on Radiation Units and Measurements (ICRU) Report 83,^[9] in best circumstances, both mean absorbed dose to PTV and standard deviation of the mean dose would be reported. In the present study, we evaluated different dose homogeneity indices^[7-11] and conformity index^[12-17] for the IMRT plans using 15MV photon energy in cervical cancer and effectiveness of different proposed indices were explored. Each plan was compared with 6MV photon energy. S-index, conformity-index, and organs at risk (OAR) doses were also reported for both photon energies.

Materials and Methods

In the present study, different-dose homogeneity indices were evaluated for 12 patients receiving dynamic IMRT treatment on Clinac 2300C/D linear accelerator (Varian Medical Systems, Palo Alto, USA) with 15MV photon energy. The IMRT plans were generated on Eclipse (Varian Medical Systems, USA) treatment planning system with Helios™ dose volume optimization (DVO) software and pencil beam convolution (PBC) algorithm for dose calculation. Each plan consisted of nine co-planar non-opposing fields with equally spaced gantry at 40-degree interval. Computed tomography (CT) scan data sets were used for the delineation of target (PTV) and OAR volumes. To compare the plan with 6MV photons, all planning parameters and constraints were kept same, except energy. The different indices used for evaluating the plans are defined as under:

H-index = D_{max}/D_p , where H-index is the conventionally used homogeneity index, D_{max} is the maximum dose and D_p is the prescribed dose.

mH-index = D_5/D_p is the modified homogeneity index. Where D_5 is the dose received by the 5% volume of PTV.

HI = $(D_2 - D_{98})/D_p$ is another homogeneity index proposed in ICRU-83, where D_2 and D_{98} represent the doses received by 2% and 98% volumes of PTV, respectively.

mHI = $(D_5 - D_{95})/D_p$ is the modified HI, where D_5 and D_{95} represent the doses received by the 5% and 95% volumes of PTV, respectively.

S-index (D_{sd}) = $\sum \text{SQRT}[(D_i - D_{mean})^2] \times v_i / V$, where D_{sd} is the standard deviation of mean dose, D_{mean} is the mean dose of PTV, v_i is the i th volume element receiving at least D_i dose, and V is the total volume. In contrast to the other homogeneity indices, S-index uses the dDVH curve instead of cDVH curve.

CI^[12] is defined as ratio of volume of the body receiving the prescribed dose (V_p) to the volume of the PTV receiving the same dose (PTV_p), i.e., $CI = V_p/PTV_p$.

Doses received by the OARs as maximum dose, mean dose, and other dose levels according to the department protocol have been evaluated and tabulated for both 16MV and 6MV photon energies.

Results

The planning data of 12 patients were analyzed and values of H-index, mH-index, HI-index, mHI-index, S-index, and CI were computed and tabulated. The H-index values vary from 1.05 (highly homogeneous) to 1.17 (less homogeneous). Values of H-index as shown in Table 1 indicate that for patients 1 and 5, these were same, but the cDVH of patient 1 was better than that of patient 5, as shown in [Figure 1], and their corresponding differential DVH with S-index values [Figure 2]. There is about 19% variation between their corresponding S-index values as shown in Table 1. The mH-index values vary from 1.004 (highly homogeneous) to 1.113 (less homogeneous). The mH-index values of patients 1 and 7 were same, but their corresponding cDVH as shown in [Figure 3] and dDVH in [Figure 4] were not matching, because in calculation of mH-index, only the ratio of doses at two points on the cDVH curve as defined above is taken into consideration and not the entire curve. The S-index values show difference of about 20%. The values of HI-index vary from 0.065 (highly homogeneous) to 0.143 (less homogeneous). The values of HI-index of patients 3 and 8 are nearly same (0.092 and 0.091, respectively), but their corresponding cDVH values as shown in [Figure 5] and dDVH with S-index in [Figure 6] show much difference. The S-index values differ by 10%, which can be seen from Table 1. HI-index values, which are less than or close to 0.1 give better dose homogeneity to the PTV. The mHI-index values vary from 0.050 (highly homogeneous) to 0.097 (less homogeneous). The values of mHI-index of patients 1 and 4 are same, but their corresponding cDVH and dDVH values [Figures 7 and 8] show much variation, as shown in Table 1.

S-index values show a difference of about 8%. The values of S-index vary from 1.63 to 2.99. Also, their

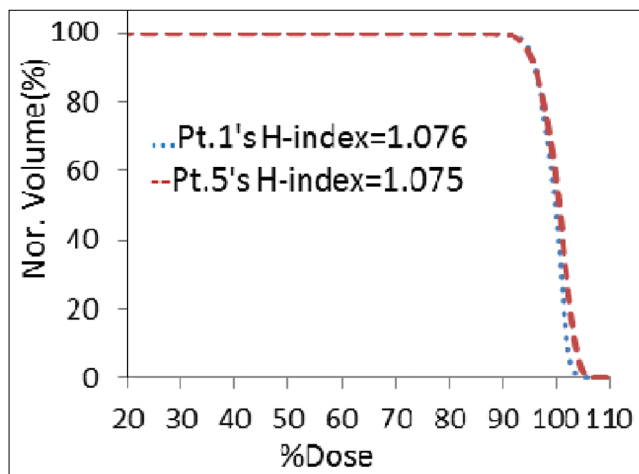


Figure 1: Cumulative dose-volume histogram of patients 1 and 5 with their corresponding H-index values

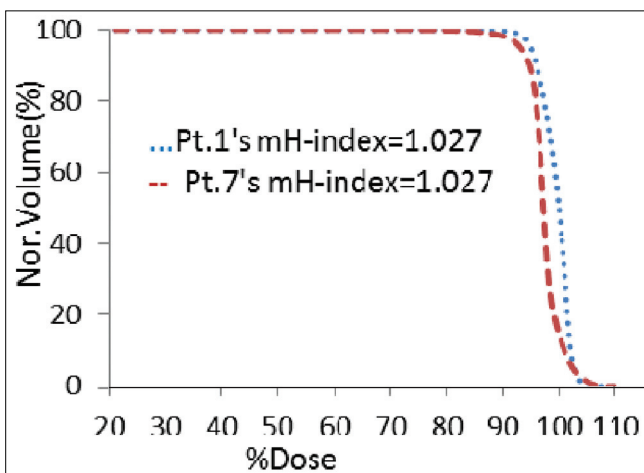


Figure 3: Cumulative dose-volume histogram of patients 1 and 7 with their corresponding mH-index values

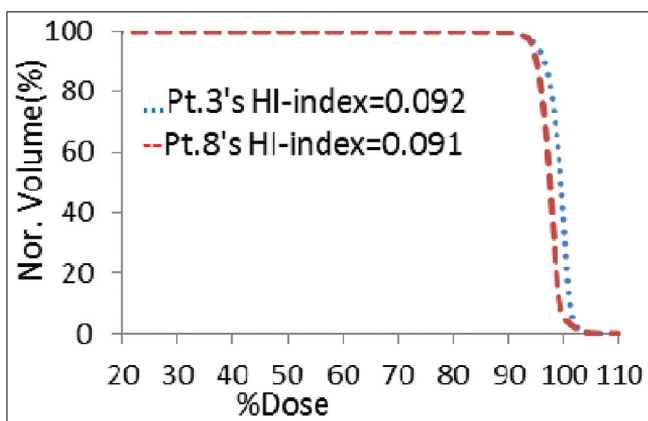


Figure 5: Cumulative dose-volume histogram of patients 3 and 8 with their corresponding HI-index values

corresponding conformity index (CI) values were tabulated, which vary from 1.0 (highly conformal) to 1.092 (less conformal). The value close to 1 gives better conformity of dose to PTV. All homogeneity indices and

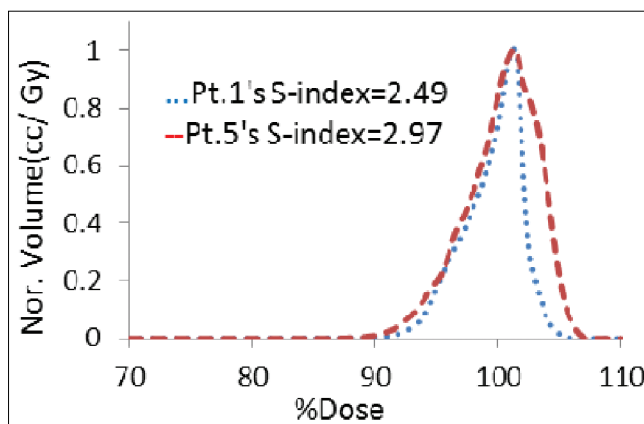


Figure 2: Differential dose-volume histogram of patients 1 and 5 with their corresponding S-index values

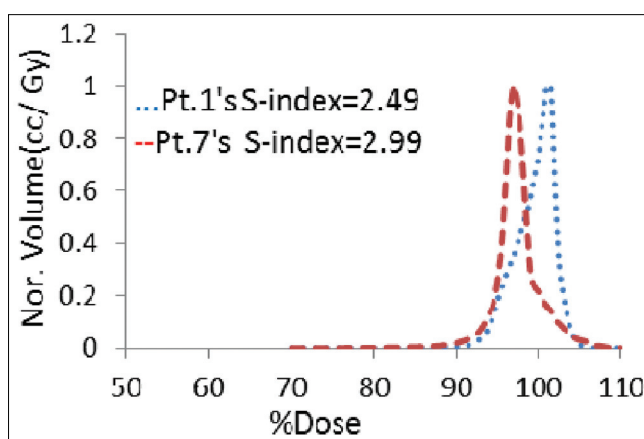


Figure 4: Differential dose-volume histograms of patients 1 and 7 with their corresponding S-index values

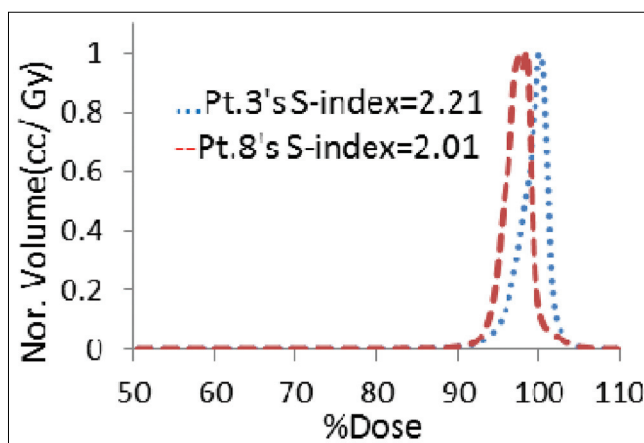


Figure 6: Differential dose-volume histogram of patients 3 and 8 with their corresponding S-index values

their modified versions mentioned above, except S-index, based on the limited point's ratio on the cDVH curve, may not give the correct information about the dose homogeneity. Hence, the S-index, which is based on the entire dDVH curve, gives the correct information about dose homogeneity in the target volume. It can be seen

from Table 1 that the values of homogeneity indices were improved by their modified version, but may not reflect the correct dose homogeneity. The S-index is nothing but the measure of the spread of the dDVH curve from their mean dose value, i.e., standard deviation of the mean dose. Also, from Table 1, it can be seen that the S-index values obtained after analyzing the IMRT planning data of 12 patients in the present study is below 2.5, except for patients 5 and 7; for these patients, it is approximately 3. This shows that our plans fall under outstanding and good categories, except two plans, according to Yoon (2007) criteria. The values of S-index less than or close to 2 reflects better dose homogeneity in PTV. The S-index values of patients 2 and 6 are close to each other and the corresponding cDVH value as shown in [Figure 9] has a sharp fall, which reflects that whole target receiving nearly the same prescribed dose, i.e., homogeneous dose in the entire target volume. Further, it can be

explained that if two cDVH curves appear same, their S-indices may not necessarily be close to each other, as shown in [Figures 1 and 2]. But, if two S-indices are close to each other, then their corresponding cDVH curves must be close to each other. From Tables 1 and 2, it can be seen that S-index values are less in the 15MV plan in comparison to the 6MV plan, i.e., 15MV plans have more homogeneous dose distribution. In most cases, the OARs received lower dose in the 15MV plan in comparison to the 6MV plan, but were not clinically significant, as shown in Tables 3-6 for bladder, rectum, femoral heads, and bowel, respectively. Also, it was observed that the integral dose outside the target volume is less in 15MV plans. Hence, two most important benefits of using 15MV beam for IMRT in the pelvic region include better homogeneous dose to the target volume and lower dose to the extra target volume. Figure 10 shows the same level of homogeneity (close S-index values) for the 6MV and

Table 1: Homogeneity indices and conformity index

Pt. no.	H-index	mH-index	HI-index	mHI-index	S-index	CI
1	1.076	1.027	0.098	0.077	2.49	1.00
2	1.091	1.019	0.098	0.067	2.29	1.042
3	1.071	1.025	0.092	0.065	2.21	1.018
4	1.116	1.037	0.108	0.077	2.31	1.092
5	1.075	1.045	0.118	0.097	2.97	1.028
6	1.061	1.015	0.099	0.075	2.28	1.088
7	1.098	1.027	0.143	0.092	2.99	1.092
8	1.091	1.004	0.091	0.058	2.01	1.089
9	1.052	1.008	0.075	0.051	1.67	1.016
10	1.060	1.017	0.065	0.050	1.63	1.021
11	1.174	1.113	0.093	0.063	2.11	1.216
12	1.071	1.024	0.081	0.057	1.76	1.09

H-index: Homogeneity index (D_{max}/D_p), mH-index: Modified homogeneity index (D_5/D_p), HI-index: $(D_2-D_{95})/D_p$, mHI-index: $(D_5-D_{95})/D_p$, S-index: $\text{Sigma-index}(\sum \text{SQRT}[(D_i-D_{mean})^2] \times v_i/V)$, and CI: Conformity index (V_p/PTV_p)

Table 2: Sigma index (S-index) and conformity index (CI) with 6MV intensity-modulated radiation therapy plan

Pt. no.	S-index	CI
1	2.51	1.08
2	2.43	1.13
3	2.22	1.015
4	2.46	1.15
5	2.98	1.026
6	2.43	1.07
7	3.11	1.095
8	2.21	1.13
9	1.72	1.02
10	1.78	1.07
11	2.23	1.17
12	1.92	1.14

CI = Conformity Index (V_p/PTV_p), S-index = Sigma-index ($\text{SQRT}[(D_i-D_{mean})^2]$)

Table 3: Maximum dose (D_{max}) and volume of 45 Gy (V_{45}) for bladder (organ at risk) with 6MV and 16MV plans

Pt. no.	D_{max} (Gy)		V_{45} (%)	
	6MV	16MV	6MV	16MV
1	51.5	51.3	69.23	70.95
2	54.2	54.2	67.85	68.0
3	53.4	54.0	80.01	81.36
4	55.0	56.0	69.23	69.62
5	46.3	46.6	0.29	0.39
6	52.0	53.0	23.7	31.2
7	54.3	54.7	36.78	37.62
8	52.2	52.8	35.71	39.26
9	51.1	51.3	70.68	72.54
10	50.3	51.0	88.99	91.7
11	52.2	52.8	86.6	89.9
12	55.1	53.9	62.44	64.6

Table 4: Maximum dose (D_{max}), volume of 30 Gy and 45 Gy (V_{30} , V_{45}) for rectum (organ at risk) with 6MV and 16MV plans

Pt. no.	D_{max} (Gy)		V_{30} (%)		V_{45} (%)	
	6MV	16MV	6MV	16MV	6MV	16MV
1	51.9	52.4	58.3	58.5	20.1	20.8
2	54.2	53.8	67.1	66.9	34.6	35.2
3	50.9	51.6	59.9	60.7	25.6	28.1
4	52.6	53.2	62.6	62.1	27.2	33.9
5	46.2	46.7	42.8	42.9	0.32	0.76
6	50.9	50.8	57.6	57.8	27.2	30.9
7	52.4	52.2	55.5	62.1	18.6	37.6
8	47.3	48.2	54.4	55.4	28.9	32.8
9	50.6	50.4	66.6	68.4	25.0	26.5
10	50.0	50.1	61.8	63.9	25.1	27.2
11	50.5	51.2	46.6	47.4	10.9	14.8
12	50.0	51.4	53.2	54.8	19.9	23.0

Table 5: Maximum dose (D_{max}), volume of 30 Gy (V_{30}) for femoral head (organs at risk) with 6MV and 16MV plan

Pt. no.	D_{max} (Gy)		V_{30} (%)	
	6MV	16MV	6MV	16MV
1	49.4	48.5	12.7	20.0
2	45.8	44.5	16.0	15.5
3	47.5	48.0	19.8	20.6
4	48.1	48.3	14.4	13.3
5	41.4	39.5	12.7	7.60
6	49.3	48.1	17.9	18.5
7	52.0	51.9	35.5	34.8
8	48.7	47.9	24.8	25.7
9	46.9	46.4	18.6	18.5
10	43.3	42.3	30.3	36.2
11	44.1	44.9	23.2	23.7
12	42.8	43.3	9.22	7.35

Table 6: Maximum dose (D_{max}), volume of 45 Gy (V_{45}), and volume of 15 Gy (V_{15}) for bowel with 6MV and 16MV plan

Pt. no.	D_{max} (Gy)		V_{45} (cc)		V_{15} (cc)	
	6MV	16MV	6MV	16MV	6MV	16MV
1	49.4	48.7	19.0	9.87	618	600
2	53.5	53.6	173	183	935	932
3	49.3	50.0	23.0	31.7	631	632
4	54.2	53.3	171	172	1559	1519
5	44.6	45.0	-	-	629	607
6	47.5	48.9	14.5	23.1	1460	1373
7	50.8	50.7	104	168	1078	1075
8	48.7	49.8	30.7	37.9	901	895
9	48.2	49.4	11.9	15.5	1011	982
10	49.3	50.1	114	167	746	732
11	46.7	47.5	3.20	8.00	944	916
12	48.0	49.9	2.73	7.50	482	481

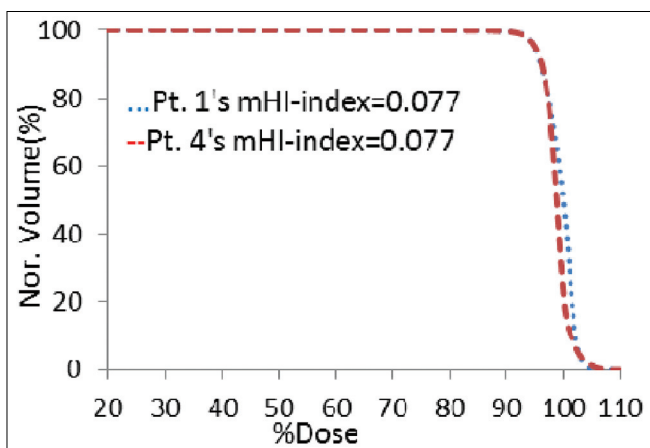


Figure 7: Cumulative dose-volume histogram of patients 1 and 4 with their corresponding mHI-index values

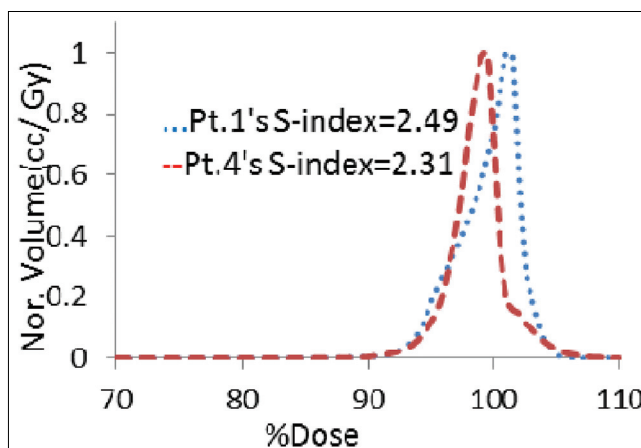


Figure 8: Differential dose-volume histogram of patients 1 and 4 with their corresponding S-index values

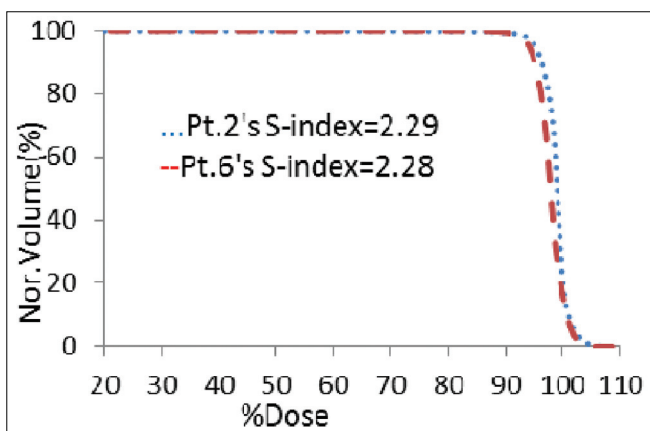


Figure 9: Cumulative dose-volume histogram of patients 2 and 6 with their corresponding S-index values

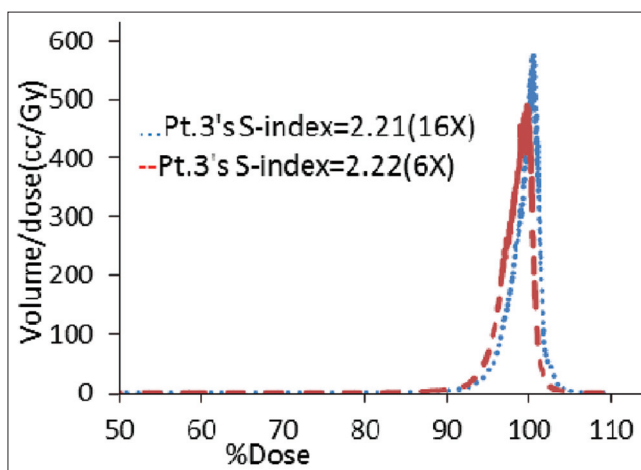


Figure 10: Differential histogram of patient 3 with the corresponding S-index values for 6X and 16X energy

15MV plans, but the peak position is at a slightly lower dose level than the prescribed one in case of the 6MV plan. It has been observed that for underweight patients, there is not much difference in S-index values in either

the 6MV or 15MV IMRT plan for pelvic regions, but a high level of difference has been observed, especially in overweight patients.

Discussion

The selection of dose reporting points lying within a high or low-absorbed dose-gradient region could then significantly misrepresent the absorbed dose throughout the volume concerned. A comparison between homogeneity indices indicate that the indices that are based on the limited points on the DVH curve may not be the actual measurement of the dose homogeneity. S-index may be the actual measure of the dose homogeneity. The modified homogeneity indices give some improved results, but still not matching with their cDVH curves and S-index for the two closed modified index values. Dose homogeneity in the patients at the time of dose delivery can only be assured if leaves are in the correct position at each moment regardless of the multi-leaf collimator (MLC) design and delivery methods. Because the dose delivered throughout the target volume with IMRT is sensitive to leaf positioning errors, 1 mm error in positioning will produce about 5% errors in dose delivery, as reported by Thomas LoSasso *et al.*^[18] Hence, the aim is to maintain the positioning errors below 0.2 mm and to ensure this, proper quality assurance (QA)^[18-21] of the MLC must be carried out regularly; these may include picket fence and garden fence tests with and without intentionally introduced errors. This test is able to detect error in positioning by 0.2 mm as we have observed. Further, Dynalog file viewer (Varian) is the software for position-verification and plays an important role in checking the positional error of the leaves. The minimum physical leaf gap is the closest separation maintained by the opposite leaf without wear and tear, which affects the overall dose delivery; for Varian MLC, this is about 0.5 mm. Dosimetric leaf gap is the most important parameter and attention must be paid to test and quantify the same, defined by the opposing leaf pairs of MLC for each beam. One of the methods used to evaluate the same is sweeping gap output for different slit widths formed by MLC and programmed in the MLC shaper software supplied by Varian Medical Systems, USA. The measured leaf gap values are 1.7 mm for 6 MV and 1.8 mm for 15 MV. Although using 15MV beam for IMRT is a controversial issue but has certain advantages and disadvantages. Although various advantages such as higher homogeneity and less integral dose have been discussed above, it has some disadvantages as it has higher probability to produce neutrons as compared to 10-MV beam, but less probability than 18-MV beam. Kry *et al.*^[22] reported that contribution of neutrons in out-of-field dose equivalent is significant for beam >15 MV. In literature,^[22,23] it has been reported that the calculated risk of second malignancy is 3.4% using Varian 15MV beam for IMRT and 3.7% with Siemens 6MV beam. Hence, the contribution of neutrons is not significant with 15MV IMRT plans. The other concern is dose modulation and transmission. The leaf transmission in 15-MV Varian accelerator may not produce significant effect as total MU and time of delivery is less in comparison to 6-MV beam. The modulation in IMRT

with higher beam is limited by lateral beam degradation due to production of high-energy electrons. However, high modulation and sharp fall in dose distribution is needed to avoid close and sensitive OARs especially those have less tolerance, whereas the pelvic region may not require the highest level of modulation. Also, it has been reported^[24] that there is little difference in volume (closed to target) exposed to dose, regardless of energy and number of fields used, but significant increases in dose for distant volume occur in low energy/few fields (<9) plan as compared to high energy/many field (≥ 9) plan. Also, using high-energy beams in prostate IMRT is beneficial for saving some OARs even in low-dose regions under 50% of prescription dose, but losing benefits in high-dose regions may not be clinically significant.^[25] Hence, the use of 15MV beam with ≥ 9 fields IMRT plan in case of cervical cancer especially in overweight patients are well justified.

Conclusion

In the present article, comparisons between the different homogeneity indices and their modified versions with their DVH and S-index values have been presented for both 6MV and 15MV beams. From the results, it can be seen that the S-index represents the correct dose homogeneity in the target. It can be concluded here that each IMRT plan must be evaluated and compared by using the S-index score because S-index is directly related to the biological effects (equivalent uniform dose).

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