Analysis of different evaluation indexes for prostate stereotactic body radiation therapy plans: conformity index, homogeneity index and gradient index

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Abstract
Objective: This study analyzed different definitions of the conformity index (CI), homogeneity index (HI), and gradient index (GI) used in evaluation of prostate cancer stereotactic body radiation therapy.

Methods: A total of 10 patients with localized prostate cancer staged T1–T2a were selected randomly, from which two stereotactic body radiation therapy plans were designed with CyberKnife and EDGE systems for each patient based on the same images and contours. CI, HI, and GI with different definitions were calculated based on a dose-volume histogram of treatment plans.

Results: For four definitions of CI, the results showed that the values calculated by the Radiation Therapy Oncology Group, Lomax and Scheib, and Van’t Riet were closer to 1 for EDGE plans, except for that by the Saint-Anne, Lariboisiere, and Tenon group. Meanwhile, CI values of Van’t Riet et al were lower than other definitions, which showed high accuracy to describe the conformity between the target volume and prescribed isodose line. For five definitions of HI, CyberKnife plans showed lower values than EDGE plans. HI calculated based on the $D_{2\%}(D_{5\%})$ and $D_{98\%}(D_{95\%})$ were lower than that calculated by the $D_{max}$ to $D_{min}$, whereas the standard deviation was higher than others. For the dose GI, the results of effective radius and modified GI showed that EDGE plans had a steeper dose fall-off, which is inverse to the conventional GI.

Conclusions: These indexes can all be objective tools for the evaluation of plan quality. Our results showed better conformity of dose distribution and dose gradient for EDGE plans, but better uniformity for CyberKnife plans. The conformation number and S-index were recommended to accurately describe the conformity and uniformity of dose distribution. The $\Delta R_{iso}$ and modified GI were also recommended to calculate the dose gradient.

KEYWORDS
conformity, dose gradient, homogeneity, plan quality, stereotactic body radiotherapy

1 | INTRODUCTION

The aim of radiotherapy is to deliver a sufficient prescription dose to the volume coincident with the target volume (TV), thus excluding the critical normal tissue from the high-dose region.1,2 With the progress of medical imaging and radiotherapy techniques for several decades, this objective can be achieved by the visualization of spatial dose distribution for the TV.3-5 In order to obtain the optimal dose distribution, different indexes were defined to evaluate the quality of a treatment plan. A dose-volume histogram (DVH) is a very useful tool and is commonly used. From a DVH, dose parameters, such as maximum dose, minimum dose, and mean dose delivered to the volume...
of interest, can be obtained.6–9 However, the main disadvantage of DVH is that the dose distribution is reduced to a one-dimensional histogram, while losing the spatial details of dose distribution. Currently, effective tools, including conformity indexes (CI), homogeneity indexes (HI), and gradient indexes (GI), have been proposed as a simple way to quantitatively evaluate the dose distribution, which represents the conformance between the prescribed dose area and planned TV, the degree of uniformity inside the target, and the dose fall-off outside the target.10–12

The concept of a CI was first proposed by the Radiation Therapy Oncology Group (RTOG) in 1993, and described in Report 62 of the International Commission on Radiation Units and Measurements.13,14 It is suggested to play a significant role in the assessment of plan quality with the growth of conformal radiotherapy.15 According to the RTOG Report 63, the CI was defined as the ratio of the reference isodose volume \( V_{\text{ref}} \) to the TV, while the major drawback is not to take into account the shape of the target and reference isodose, as well as the degree of spatial intersection of the two volumes.13,16,17 For another account the shape of the target and reference isodose, as well as the geometric CI, which is another quantitative method for the pre-prescription isodose based on coverage of the lesion, is proposed.18–21 Lomax and Scheib considered the TV covered by the prescribed dose and the volume of the adjacent normal tissue, and proposed two different CIs according the SALT group.22 However, there is a problem, in that the real significance of CI = 1 might be different from the ideal distribution, as the reference isodose can be totally included in the target, but the TV might not be covered by the prescribed dose.10 To compensate for the effect of the target and healthy volume, Van’t Riet et al. proposed the conformity number (CN), which consists of two parts: the first part represents the quality of target coverage, and the second part represents the normal tissues volume sparing.23 Baltas et al. used the CN with brachytherapy by applying the supplementary parameter, the critical organs.24 Wu et al. studied the effect of target shape complexity and size on the CI, and introduced a different conformity parameter \( C \) – conformity distance index \( C \) – which measures the average distance of prescription isodose and TV.25 Park et al. also presented a new CI based on the distance between the surfaces of the TV and reference dose volume, which not only evaluates the shape prescription isodose, but also the target coverage.26

The HI is used to evaluate the homogeneity of dose distribution in planning TV (PTV).12,27,28 The conventional HI is mainly defined as the ratio of the maximum dose \( D_{\text{max}} \) to minimum dose \( D_{\text{min}} \) or prescription dose \( D_p \) in PTV, from which CI equals 1 indicates the ideal homogeneity.10,17 To avoid the effect of grid size on the point dose, such as \( D_{\text{max}} \) and \( D_{\text{min}} \), the dose covers 5% of the PTV was suggested to alternate \( D_{\text{max}} \) and \( D_{95\%} \) (the dose covers 95% of the PTV) to replace \( D_{\text{min}} \).29–31 Another most commonly used formula is the HI = \( (D_{2\%} - D_{98\%}) / D_p \), in which \( D_{2\%} \) and \( D_{98\%} \) were applied to represent the \( D_{\text{max}} \) and \( D_{\text{min}} \), respectively, because it is more sensitive to the point dose-related parameters, such as the grid size and grid placement.32 The lower value of HI indicates a more homogenous dose distribution within the PTV. Meanwhile, Yoon et al. developed a new HI based on statistical analysis of the DVH, which was defined as the standard deviation of the differential DVH curve of PTV.33

Another objective tool for evaluation of radiotherapy plans is the GI, which describes the dose fall-off steepness outside the TV. A commonly used definition of GI is the ratio of the volume of 50% prescribed dose to that of the prescribed dose.34,35 The GI is used to evaluate the dose fall-off outside the target, and shows the optimal dose distribution outside the target. The lower GI value means a steeper gradient of dose distribution outside the target, as well as better normal tissue sparing.35 Ohtakara et al. modified the GI by multiplying the ratio of the volume of prescription dose by the TV, mainly taking into account the degree of dose conformity.36 Agostinelli et al. proposed the effective radius to describe the dose gradient to better discern the effect of dose splash.37

Although various definitions of different evaluation parameters have been proposed in the literature, and applied by different institutes and organizations, there is no consistent selection for the definition of those indexes. Meanwhile, there is a scarcity of data to verify the factors that affect the CI, HI, and GI. In the present study, different definitions of CI, HI, and GI were applied to quantitatively verify the factors that affect the CI, HI, and GI. In the present study, different definitions of CI, HI, and GI were applied to quantitatively evaluate the treatment plan in prostate stereotactic body radiation therapy (SBRT) based on the CyberKnife (CK; Accuray Inc., Sunnyvale, CA, USA) and EDGE (Varian Medical Systems, Palo Alto, CA, USA) systems.

## 2 | METHODS

### 2.1 | Patient selection

A total of 10 patients with low-risk prostate cancer staged T1–T2a treated with CK SBRT were randomly selected. Computed tomography (CT) simulation was carried out using a BrillianceTM Big Bore 16-slice CT scanner (Philips, Amsterdam, the Netherlands) with 1.5-mm slice thickness in the head-first supine position with a full bladder and empty rectum. The clinical TV and critical organ structures were outlined by an oncologist and radiologist based on the fusion of the CT and magnetic resonance images on MultiPlan system (version 4.02; Accuray Inc.). PTV was delineated by expanding from the clinical TV with a 5-mm isotropic margin, except 3-mm posteriorly according to the literature.38 Organs at risk, including the bladder, rectum, small bowel, penile bulb, femoral heads, and urethra, were also contoured.

### 2.2 | Treatment planning

The SBRT plans of prostate cancer were generated in the CK and EDGE system, respectively, based on the same CT images and contours. Both the CK and EDGE plans were given a prescription dose of 36.25 Gy in five fractions. The dose constraints of all SBRT plans were required to meet the criteria of the RTOG-0938 and previous studies.38,39 The CK plans were designed on Multiplan version 4.0.2 by using a sequential optimization method based on the ray tracing algorithm. For the
EDGE system with Eclipse version 13.5 (Varian Medical Systems), the volumetric modulated arc therapy (VMAT) plans were produced using two full 360° arcs with the same isocenters at the geometric center of PTV, and optimized with the progressive resolution optimizer, in which the analytical anisotropic algorithm with a 1.5-mm grid size was used to calculate the dose distribution.

### 2.3 Objective tools of evaluation

Three classes of objective evaluation tools were applied in the present study, including the CI, HI, and GI. The CI was defined as the ratio based on the volume of prescribed dose, the TV, and the overlap volume. Four different definitions of CI were selected, as shown Table 1. The conventional method to calculate the CI is proposed by the RTOG or SALT group, which did not consider the shape of the TV or isodose volume.\(^{13,18-21}\) The CN is proposed based on the SALT group and Lomax and Scheib by Van’t Riet et al. and Paddick, taking into account the volume of healthy tissue irradiated by the prescribed dose. It can better represent dose conformity than other definitions.\(^{23}\)

The HI was used to evaluate the degree of the uniformity of dose distribution inside the TV. In the present study, five definitions were selected to calculate the HI in the SBRT plans, as shown in Table 2. The ideal values of the first four formulas are equal to 1, which shows that each voxel of TV receives the same dose.\(^{32}\) The last formula for HI proposed by Myonggeun et al. is called the S-index, which is defined as the standard deviation of the differential DVH. The idea value of S-index is 0, and a lower value that shows better uniformity.

The conventional GI is defined as follows:

\[
GI_1 = \frac{V_{50\%}}{V_{100\%}}
\]

where \(V_{x\%}\) represent the volume irradiated by \(x\%\) of the prescribed dose. The value of GI is positive, and a lower value mean steeper dose fall-off outside the target and better sparing of normal tissue.\(^{34,35}\)

### TABLE 1 For different definitions of conformity index

| Formula | Value = 1 | Value >1 or Value <1 |
|---------|-----------|---------------------|
| CI\textsubscript{RTOG} \(^{13}\) | \((1) CI_1 = \frac{V_{50\%}}{TV}\) | ![Image](Image135x744 to 161x771) |
| Lomax and Scheib \(^{13,18}\) | \((2) CI_2 = \frac{V_{98\%}}{TV}\) | ![Image](Image137x515 to 147x524) |
| SALT\(^{22}\) | \((3) CI_3 = \frac{TVRI}{TV}\) | ![Image](Image139x167) |
| Van’t Riet and Paddick\(^{23}\) | \((4) CN_s = \frac{TVRI}{TV} \times \frac{TVRI}{VRI}\) | ![Image](Image148x167) |

CI, conformity index; CN, conformity number; RTOG, Radiation Therapy Oncology Group; SALT, Saint-Anne, Lariboisiere, and Tenon; \(V_{50\%}\): the volume covered by prescribed dose; TV: the target volume; TVRI, the target volume covered by prescribed dose.

### TABLE 2 Different formulas of homogeneity index

| Formula | Ideal value |
|---------|-------------|
| Knoos et al.\(^{37}\) | \((5) HI_1 = \frac{D_{95}}{D_{98}}\) | 1 |
| RTOG\(^{10,13}\) | \((6) HI_2 = \frac{D_{95}}{D_{98}}\) | 1 |
| Wu et al.\(^{32}\) | \((7) HI_3 = \frac{D_{95} - D_{98}}{D_{98}}\) | 0 |
| Semenenko et al.\(^{30}\) | \((8) HI_4 = \frac{D_{95} - D_{98}}{D_{98}}\) | 0 |
| Myonggeun et al.\(^{33}\) | \((9) HI_5 = \sqrt{\sum (D_i - D_{mean})^2} \times \frac{5}{7}\) | 0 |

Another method to describe the degree of dose fall-off is to apply the effective radius of the volume covered by specific isodose lines. The GI can be defined as follows:

\[
GI_2 = \Delta R_{iso} = R_{50\%iso} - R_{100\%iso}
\]

where \(R_{x\%iso}\) is the effective radius of the volume covered by \(x\%\) isodose. The lower value of \(\Delta R_{iso}\) indicates the steeper dose fall-off.\(^{37}\)

To takes into account the TV coverage, a modified GI (mGI) was proposed, which is defined as formula (12):

\[
GI_3 = mGI = \frac{V_{50\%}}{TV} = \frac{V_{50\%}}{V_{100\%}} \times \frac{TVRI}{TV}
\]

This equation evaluates the dose gradient based on the TV, which takes into account the effect of dose conformity. The lower mGI value means a steeper dose fall-off.\(^{36}\)
FIGURE 1  Transverse view of dose distribution of (a) EDGE) and (b) CyberKnife plans for a selected case. The 100% isodose line of both plans was normalized to 36.25 Gy

2.4 Statistical analysis

All indexes were calculated based on DVH. IBM SPSS version 20 (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis, and a paired t-test was carried out. We not only compared the difference of different formulas in the same type of index in the same system, but also analyzed the difference between different systems.

3 RESULTS

In the present study, the analysis of different formulas for one index was carried out in different SBRT plans for prostate cancer. The SBRT plans were generated on the CK and EDGE system, and meet the criteria of the RTOG-0938 and previous study.

3.1 Conformity index

A transverse view of dose distribution and DVH of PTV is shown in Figure 1. As can be seen in Figure 1, the prescription isodose line of EDGE is closer to the surface of the TV than that of CK. This shown better dose conformity of the EDGE system. The data of CI with different definitions are shown in Figure 3a–d, respectively. For the CK plans of prostate cancer, it showed that the CI1, CI3, and CI4 values (calculated by equation (2), (3), and (4)) were <1, except the CI1 calculated by equation (1) (Fig. 3a), whereas all CI values were all <1 in EDGE plans. The CI4 values (Fig. 3d) were lower compared with other CIs for CK and EDGE SBRT plans.

The average values of CIs are listed in Table 3. As shown in Figure 2 and Table 3, the values of CI4 were lower than CI2 and CI3 for both CK and EDGE plans. Meanwhile, the results of CI1, CI2, and CI4 showed that the EDGE plans had better conformity for the prescribed dose area and TV.

3.2 Homogeneity index

The results of different types of HI are shown in Figure 4a–d. The HI closer to 1 showed better homogeneity for the former. For the latter definition, GI closer to 0 is considered more homogeneous. For the HI1 and HI2, the HI2 values were lower than HI1 both in CK and EDGE plans, as well as for HI3 and HI4, as shown in Table 3. The HI5 calculated by equation (9), which was based on the differential DVH, had the larger value (>2; Fig. 4e) compared with others. According Figure 4 and Table 3, the results of HI1 to HI5 all showed that the CK plans had lower values, which showed better uniformity of dose distribution inside PTV compared with that of EDGE plans, which is consistent with Figure 2. As shown in Table 3, there is no significant difference only for HI2 and HI4.

3.3 Gradient index

The result of the GI values calculated by equations (1)–(3) are shown in Figure 5a–c and Table 3. From the conventional definition in equation (1), the average value of GI1 for the CK and EDGE plans were 3.697 ± 0.318 and 3.861 ± 0.224, respectively. The average GI2 values calculated by the effective radius were 1.637 ± 0.157 and 1.613 ± 0.105, respectively, whereas they were 4.439 ± 0.439 and 3.923 ± 0.266 for GI3 (Table 3). As shown in Table 3, the GI2 values

| | CK ± SD | EDGE ± SD | P |
|---|---|---|---|
| CI1 | 1.200 ± 0.029 | 1.016 ± 0.017 | <0.001 |
| CI2 | 0.804 ± 0.022 | 0.932 ± 0.018 | <0.001 |
| CI3 | 0.964 ± 0.005 | 0.946 ± 0.003 | <0.001 |
| CI4 | 0.775 ± 0.025 | 0.882 ± 0.019 | <0.001 |
| HI1 | 1.627 ± 0.103 | 1.756 ± 0.124 | 0.089 |
| HI2 | 1.282 ± 0.000 | 1.316 ± 0.008 | <0.001 |
| HI3 | 0.284 ± 0.018 | 0.299 ± 0.024 | 0.137 |
| HI4 | 0.227 ± 0.014 | 0.252 ± 0.026 | 0.009 |
| HI5 | 2.829 ± 0.255 | 3.037 ± 0.309 | 0.113 |
| GI1 | 3.697 ± 0.318 | 3.861 ± 0.224 | 0.009 |
| GI2 | 1.637 ± 0.157 | 1.613 ± 0.105 | 0.616 |
| GI3 | 4.439 ± 0.439 | 3.923 ± 0.266 | 0.011 |

CI, conformity index; CK, CyberKnife; GI, gradient index; HI, homogeneity index.
were lower than GI1 and GI3 both in the CK and EDGE plans. In addition, there was likely to be steeper dose fall-off for EDGE plans according to results of GI2 and GI3, except GI1. There was no significant difference for GI values between the CK and EDGE plans, except GI3.

4 | DISCUSSION

The present study compared different evaluation indexes, including the CI, HI, and gradient GI in SBRT plans. The main function of CI is to
measure how well the prescribed dose conforms TV, and the main function of HI is to evaluate the uniformity of dose distribution inside the target, whereas the main function for GI is to evaluate the dose fall-off steepness outside the target. In our study, CI1 values calculated by the formula of the RTOG were >1, nevertheless the CI2, CI3, and CI4 values calculated by equations (2)–(3) were all <1 (Table 1). Meanwhile, CI4 showed the lowest value among all CI. For HI calculated by equations (5)–(9), respectively (Table 2), the results showed that HI1, HI2, and HI5 were all >1, whereas both HI1 and HI4 were <1, as detailed in Table 3.

FIGURE 5 The comparison of different gradient indexes (GI). (a) The conventional formula for GI. (b) The difference of effective radius. (c) The modified GI

As for GI, GI2 values were lower than GI1 and GI3 both in the CK and EDGE plans. According the CI and HI (as shown in Fig. 4 and Table 3), it was shown that EDGE plans were more conformable, whereas CK plans showed better uniformity of dose distribution inside the target.

The CI has been proposed based on the relationship between the TV and VRI.13–16 According to the RTOG guideline, CI\textsubscript{RTOG} equal to 1 corresponds to the ideal conformity. If CI\textsubscript{RTOG} is <1, the TV is not totally irradiated, whereas CI\textsubscript{RTOG} >1 shows that the irradiated volume is larger than the TV and includes normal tissue, as shown in Table 1. In the present study, the CI1 (CI\textsubscript{RTOG}) values were all >1, which showed the volume of prescribed dose to be larger than PTV. For the definition of CI1, the TV covered by the prescribed dose is not explicit. Meanwhile, it is not certain whether the two volumes coincide with each other when CI4 is equal to 1.10,13

For Lomax and Scheib and the SALT group, CI2 and CI3 were defined as the ratio of the PTV covered by the prescribed dose (TV\textsubscript{R95}) to V\textsubscript{R105} and TV\textsubscript{R95} to TV, respectively. Both CI2 and CI3 are to consider the irradiated PTV. However, the volume of healthy tissue surrounding the target is not considered in CI3. Although V\textsubscript{R105} were applied to replace the TV in definition of CI2, it is difficult to interpret when CI2 = 0.5, whether the total target was completely covered by prescription dose with the same volume of healthy tissue being irradiated, or TV and V\textsubscript{R105} have the same volume, but with half volume overlap.10,18–22 The CN proposed by Van’t Riet et al. was to sum up the CI2 and CI3, namely the product of CI2 and CI3. Hence, the TV and the volume of adjacent healthy tissue irradiated could be considered.23 The present study showed that CI4 values were obviously lower than other CIs, both in CK and EDGE plans. Although the values of CI2 and CI3 were closer to 1 in our study, there might be inaccurate information due to their limitations. The common problem of these CIs used in the present study is that the effect of the shape of prescribed isodose volume and PTV were not taken into account. The study of Wu et al. study showed that the complexity of the TV could affect the volume of the prescribed dose surrounding the TV, resulting in poor conformity.25

There were five different definitions of HI applied in the present study. For SBRT plans, HI1 and HI2 calculated by the ratio of D\textsubscript{max} to D\textsubscript{min} or D\textsubscript{50} were likely inaccurate, because the constraint of D\textsubscript{max} was not strict in the optimization process. Meanwhile, some studies pointed out that D\textsubscript{max} or D\textsubscript{min} might be just one voxel, and were very sensitive to the parameters of dose calculation, such as the grid size and grid placement.30–32 As shown in Figure 4a and b, and Table 3, HI2 values were lower than HI1 both in the CK and EDGE plans. As expressed in equations (7) and (8), the D2 (D50) and D98 (D95) were applied to replace the maximum and minimum to overcome the effect of grid size and grid placement. The present results showed that HI3 and HI4 had lower values. When using HI4 to assess the uniformity of PTV for CK and EDGE plans, there were significant statistical differences. The S-index was based on the differential DVHs, which can consider the dose of each voxel. However, it is easy for the S-index to neglect the effect of hot or cold points.27,33 As our studies showed, the results of HIs all indicated that CK plans provided more uniformity of dose distribution inside PTV compared with EDGE plans.

The dose GI provides a method to evaluate the degree of dose fall-off steepness outside PTV.34–37 In the present study, conventional GI (GI1), difference of effective radius (∆RI, GI2), and modified GI (GI3) were compared. GI1 and GI2 (∆RI\textsubscript{iso}) were all based on the volume of 50% and 100% prescribed dose, whereas GI3 tended to directly reflect the absolute distance between 50% and 100% prescribed dose. However, the drawback of this index is that the shape of the isodose volume is not considered. When using GI1 and GI2 to evaluate the dose fall-off for CK and EDGE plans, GI1 had lower values in CK plans, whereas GI2 had lower values in EDGE plans, mainly due to the shape of the isodose volume. According the Figure 1, the shape of 50% isodose line was more irregular in EDGE plans than CK plans. According the equation (3) of mGI, the PTV was applied to substitute the denominator of GI1 to evaluate the dose gradient based on the TV. At the same time, mGI was also interpreted as: mGI = GI × VRI / TV = GI × CI2, mainly taking into account the degree of conformity.35–37 The results of mGI (GI3) in Table 3 showed that the EDGE plans had lower values, as well as the GI2, with statistical significance (P = 0.011).
Cl, HI, and GI as an effective tool can facilitate the work of evaluating the treatment planning to quantify the conformity, uniformity of dose distribution, and dose gradient. There are several limitations to these three types index. The information of target location and shape are not considered in the equation of CI. There is also a lack of information about the possible relationship between these parameters and clinical data. Hence, the development of these parameters should be correlated with the local control and complications in the future research, in which better conformity, homogeneity, and steeper dose fall-off are associated with a better clinical outcome.

The present study was carried out to analyze the different definitions of CI, HI, and dose GI to qualify the dose distribution in SBRT plans. For the conformity index, the CN (Cl4) proposed by Van’t Riet et al. could be more effective than others when considering the TV, precription dose volume, and irradiated TV. For the HI, the HI3, HI4, and S-index could also be recommended to qualify the dose fall-off than HI1 and HI2, which mainly reduce the effect of grid size on point dose. As for dose gradient, the ΔRiso and mGI show slight superiority compared with GI1, according to the present study.

ACKNOWLEDGEMENTS
This study was supported in part by the China Postdoctoral Science Foundation (Grant No. 2018M640725) and Medical Scientific Research Foundation of Guangdong Province (Grant No. A2018020).

CONFLICT OF INTEREST
The authors declare that they had read the article and there are no competing interests.

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How to cite this article: Cao T, Dai Z, Ding Z, Li W, Quan H. Analysis of different evaluation indexes for prostate SBRT plans: conformity index, homogeneity index and gradient index. Prec Radiat Oncol. 2019;3:72–79. https://doi.org/10.1002/pro6.1072