Proposal of A New Conformal Factor and Normal Tissue Penalty Factor for the Radiosurgery Treatments

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Abstract

The quality of a treatment plan is evaluated by the conformality of the prescribed isodose around the target and the homogeneity of dose distribution inside the target. Presently, to check the target volume conformality, a number of published conformity indices are in use. Most of these indices are based on the target volume coverage by prescribed isodose, with respect to the total volume of the target. Some take into account the normal tissue covered by the prescribed isodose and suitably weight the target coverage to evaluate the conformity. In this study, for the irradiation of normal tissue by the prescription isodose, a normal tissue penalty factor is proposed and for the target conformality, a new conformal factor is proposed by applying this normal tissue penalty factor to the target coverage. The proposed conformal factor is evaluated for a few samples analytical cases and the results are compared with the those obtained using the published conformity indices.

Categories: Medical Physics, Radiation Oncology
Keywords: ntpf, conf, ci, reference isodose, normal tissue, target volume

Introduction

The basic principle behind the external beam therapy is to maximize the dose to the target and minimize the dose to the surrounding normal tissue. This is valid more so in the case of stereotactic radiosurgery (SRS), where a large dose of radiation is delivered to the target in a single fraction, and in the case of stereotactic radiotherapy (SRT)/ stereotactic body radiotherapy (SBRT) where hypo fractionated doses are delivered. To assess the conformity of the treated target volume (TV) by the reference isodose (RI) used for prescription, a number of formulae [1-5] are available and are in use currently. In 1993, the Radiation Therapy Oncology Group (RTOG) proposed a conformity index (CI) [1], which is a ratio of the volume of the reference isodose (VRI) to TV:

CI(RTOG) = VRI / TV ........ (1)

Paddick [2] proposed a CI, in which the proportion of the target coverage by the RI, is balanced by the proportion of the VRI inside the TV

CI(Paddick) = (TVRI / TV) x (TVRI / VRI) ........(2)

where TVRI is the volume of the target covered by RI.

In 2003, Lomax and Scheib [3], proposed a CI which is a ratio of TVRI to VRI. This is also termed as healthy tissue CI [3]

CI(Lomax) = TVRI / VRI ........ (3)

As most of the published formulae to estimate the CI, are aimed to assess the coverage of the target by the RI, the inclusion of the normal tissue within the RI is not explicitly expressed.

Materials And Methods

Wagner TH, Bova FJ, Friedman WA, Buatti JM, Bouchet LG, Meeks SL [6] have published an index for the SRS plans. This is an average of conformity and gradient scores and is termed as conformity/gradient index (CGI). This CGI is computed based on the TV, TVRI, effective radius of the VRI and the effective radius of the isodose line, which is equal to 50% of the VRI. Jackie Wu QR, Wessels BW, Einstein DB, Maciunas JR, Kim EY and Kinsella TJ [7] have published a different index in 2003, namely conformity distance index (CDI). It is defined as the average distance between the TV and RI. Accordingly, a CDI value of 1 means, the average
distance of the RI from the TV is about 1 mm [7]. The CDI takes into the volume of normal tissue which receives the RI and above, TV, the surface areas of TV and \( V_{RI} \). In 2014, Park JM, Park S-Y, Ye S-J, Kim JH, Carlson J, Wu H-G [8], proposed a distance-based conformity index, called \( CI_{\text{distance}} \). In this method, equiangular lines at one-degree intervals are drawn from the centroid of the TV, three dimensionally. The distances of these lines from the centroid to the point of intersections at the surfaces of TV and \( V_{RI} \) are measured and the difference is calculated. The average difference is analyzed, which is the \( CI_{\text{distance}} \). The authors themselves have concluded that since \( CI_{\text{distance}} \) is an average value, it doesn’t always provide the exact information on the irradiation of normal tissue. As has been mentioned earlier in the introduction part, the amount of normal tissue included within the RI is not clearly expressed. The aim of this article is not to review the indices published so far and bring out the pros and cons associated with each CI, but to propose a factor which is read along with the estimation of normal tissue irradiation in the RI. To estimate the inclusion of the normal tissue within the RI, a normal tissue penalty factor (NTPF) is proposed in this study and is shown in equation (4). This is the ratio of the volume of normal tissue included in the RI (\( NT_{RI} \)) to the \( V_{RI} \). When it is attempted to increase the TV coverage by the RI, it is mostly associated with a possibility of including more of normal tissue around the TV. This scenario happens especially when the TV is close to a dose limiting critical organ on one side. The presence of critical organ on one side of TV impacts the dose distribution and makes it shift to the opposite side. The result is that adequate TV coverage might be achieved, but at the cost of including more normal tissue. Hence, a new conformal factor (CONF) is proposed, which takes into account the \( NT_{RI} \). The CONF is evaluated by subtracting the NTPF from \( TC_{RI} \), which is the target coverage index shown in equation (5). The CONF is clearly expressed in equation (6). In other words, the actual target coverage is penalized due to the inclusion of normal tissue. The basic intention behind this proposal is to evaluate the target conformity in conjunction with the normal tissue irradiation, especially in high precision treatments like SRS and SBRT.

\[
\text{Normal Tissue Penalty Factor, } NTPF = \frac{NT_{RI}}{V_{RI}} \quad (4)
\]

where, \( NT_{RI} = V_{RI} - TV_{RI} \)

\[
\text{Target coverage index, } TC_{RI} = \frac{TV_{RI}}{TV} \quad (5)
\]

\[
\text{Conformal Factor, } CONF = TC_{RI} - NTPF \quad (6)
\]

The equation (4) returns a minimum value of zero, when the \( NT_{RI} \) is zero. This happens when the RI snugly conforms to the TV and when the RI is within the TV. The maximum value would be 1, when the RI is totally out of the TV. The equation (6) returns a maximum value of 1, when \( V_{RI} = TV_{RI} = TV \), a case of perfect conformality and a minimum value of -1 when \( TV_{RI} = 0 \), a case of complete miss of the target and irradiation of normal tissue only. As is seen obviously from equations 4-6, both NTPF and CONF are mere numbers and do not carry any units.

**Results**

The CONF and NTPF are calculated for a few analytical cases in 5 different scenarios, the diagrams of which are shown in Figure 1. Since the proposal of these factors are exclusively for SRS / SBRT, a TV of 5 cc is considered. To portray the scenarios considered very clearly, the TV is so chosen that neither it is regular nor highly irregular. The TV is shown with a solid line, while the RI is with a dotted line. Though some of these cases are not acceptable in clinical situations, only for the sake of study and analysis, they are considered. CI(RTOG, Lomax, Paddick) values are calculated using equations 1 to 3, for these cases and the results are presented in Table 1 for comparison. Since the diagrams shown in the scenarios 1-5 could not be incorporated in the Table 1 itself, the corresponding diagram labels are mentioned in the column 2 of Table 1.
FIGURE 1: Scenarios 1-5 taken for analysis.

Solid Line - Target Volume (TV); Dotted Line- Reference Isodose (RI); In S1(a), the RI conforms to TV hence, only solid line is seen. Figure is for representative purpose only and not drawn to scale.
### TABLE 1: Calculated CI, CONF and NTPF values for 5 different scenarios. TV= 5 cc

Column 1 in the table shows in percentage, the RI volume which overlaps the TV. The CI, CONF, NTPF values are mentioned up to 3 decimals just for comparison only.

<table>
<thead>
<tr>
<th>Volume of RI overlap-Relative to TV</th>
<th>Representative Diagram</th>
<th>TVRI (cc)</th>
<th>VRI (cc)</th>
<th>NTRI (cc)</th>
<th>CI (RTOG)</th>
<th>CI (Lomax)</th>
<th>CI (Paddick)</th>
<th>CONF</th>
<th>NTPF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario 1 – RI perfectly covers TV</td>
<td>S1(a)</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Scenario 2 - RI over covers TV</td>
<td>S2(a)</td>
<td>5</td>
<td>6</td>
<td>1</td>
<td>1.200</td>
<td>0.833</td>
<td>0.833</td>
<td>0.833</td>
<td>0.167</td>
</tr>
<tr>
<td></td>
<td>S2(b)</td>
<td>5</td>
<td>8</td>
<td>3</td>
<td>1.600</td>
<td>0.625</td>
<td>0.625</td>
<td>0.625</td>
<td>0.375</td>
</tr>
<tr>
<td></td>
<td>S2(c)</td>
<td>5</td>
<td>10</td>
<td>5</td>
<td>2.000</td>
<td>0.500</td>
<td>0.500</td>
<td>0.500</td>
<td>0.500</td>
</tr>
<tr>
<td>Scenario 3 - RI partly covers TV</td>
<td>S3(a)</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>1.000</td>
<td>0.200</td>
<td>0.040</td>
<td>-0.600</td>
<td>0.800</td>
</tr>
<tr>
<td></td>
<td>S3(b)</td>
<td>2.5</td>
<td>5</td>
<td>2.5</td>
<td>1.000</td>
<td>0.500</td>
<td>0.250</td>
<td>0.000</td>
<td>0.500</td>
</tr>
<tr>
<td></td>
<td>S3(c)</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>1.000</td>
<td>0.800</td>
<td>0.640</td>
<td>0.600</td>
<td>0.200</td>
</tr>
<tr>
<td></td>
<td>S3(d)</td>
<td>4.5</td>
<td>5</td>
<td>0.5</td>
<td>1.000</td>
<td>0.900</td>
<td>0.810</td>
<td>0.800</td>
<td>0.100</td>
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<tr>
<td></td>
<td>S3(e)</td>
<td>4.75</td>
<td>5</td>
<td>0.25</td>
<td>1.000</td>
<td>0.950</td>
<td>0.902</td>
<td>0.900</td>
<td>0.050</td>
</tr>
<tr>
<td>Scenario 4 - RI within TV</td>
<td>S4(a)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0.200</td>
<td>1.000</td>
<td>0.200</td>
<td>0.200</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>S4(b)</td>
<td>2.5</td>
<td>2.5</td>
<td>0</td>
<td>0.500</td>
<td>1.000</td>
<td>0.500</td>
<td>0.500</td>
<td>0.000</td>
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<tr>
<td></td>
<td>S4(c)</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0.800</td>
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<td>0.800</td>
<td>0.800</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>S4(d)</td>
<td>4.5</td>
<td>4.5</td>
<td>0</td>
<td>0.900</td>
<td>1.000</td>
<td>0.900</td>
<td>0.900</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>S4(e)</td>
<td>4.75</td>
<td>4.75</td>
<td>0</td>
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<td>1.000</td>
<td>0.950</td>
<td>0.950</td>
<td>0.000</td>
</tr>
<tr>
<td>Scenario 5 - RI outside TV</td>
<td>S5(a)</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td>1.000</td>
<td>0.000</td>
<td>0.000</td>
<td>-1.000</td>
<td>1.000</td>
</tr>
</tbody>
</table>

### Discussion

The proposed CONF computation needs to be checked against computed values of few published CI. Then only the proposal could be validated and justified. Hence CI(RTOG, Lomax, Paddick) are chosen, as these CI computations are very simple and easy. On analyzing the results, it is seen that in scenario 1, for a perfectly covered TV, the CI(RTOG, Lomax, Paddick) and the CONF values are equal to 1. As NTRI is zero, the NTPF is also zero. In scenario 2, where the RI over covers the TV, three different cases are presented with VRI, 120%, 160% and 200% of the TV. The CONF matches well with CI(Lomax, Paddick). As VRI increases, the NTRI also increases, which in turn increases NTPF and decreases CONF. This shows that the CONF estimates the target conformity, applying the penalty for the normal tissue irradiation appropriately. As the VRI increases, the CI(RTOG) also increases. The reason for which is, CI(RTOG) takes into the consideration, only the numerical value of the VRI, rather than its geometric location relative to TV.

In scenario 3, where the RI partly covers the TV, five cases are shown. There is a shift of the RI to one side of the target, keeping VRI – TV. The CI(RTOG) for all the five cases is equal to 1, as VRI=TV. When the RI covers 20%, 50%, 80%, 90% and 95% of the TV, CI(Lomax) respectively is 0.2, 0.5, 0.8, 0.9 and 0.95 which is obviously the fraction of TV coverage. CI(Paddick) for the same cases, yields lesser values compared to CI(Lomax), as TV coverage is proportionately weighted for the RI inside TV. The NTPF yields values proportionate to the NTRI. Since the NTPF is applied as a penalty to TCRI, the CONF is still less compared to the corresponding CI(Paddick). As per the equation (6), the CONF will be equal to zero, when the
In other words, the target conformity is nullified, if TVRI is 50% of TV and NTRI is 50% of VRI. In scenario 4, again five cases are shown, where the RI covers 20%, 50%, 80%, 90% and 95% of the TV as in scenario 3, but the difference is that the RI is within the TV and NTRI is zero. While, CI(RTOG) estimates values corresponding to the coverage of TV, the CI (Lomax) yields a value of 1 for all the cases, as TVRI=VRI. CI(Paddick) and CONF both yield similar values, corresponding to the coverage of the TV. Since NTRI is zero, the NTPF is zero and hence it has nil impact on the CONF. Interestingly, it is observed that the CI (RTOG, Lomax) values are getting swapped in scenarios 3 and 4 for the same TVRI. In scenario 5, as the RI is outside the TV, the TVRI is zero hence CI (Lomax, Paddick) is also zero. CI(RTOG) is 1, as this index is not a function of TVRI. The CONF returns a value of -1 as NTPF is 1, indicating a complete miss of the target and irradiation of normal tissue only.

In scenarios 1 and 4, the NTRI is zero and hence NTPF has no impact on the CONF. In scenario 2, though the TV is fully covered, since the normal tissue is also irradiated to the same level or more of RI, the NTPF plays its role. As the NTRI increases, so the NTPF, which brings down the CONF for a TV, which is otherwise fully covered by the RI. The same trend is seen in scenario 3, where the TV is partly covered. As a matter of fact, the CONV turns negative when the NTRI exceeds 50% of VRI. Of course, this depends on the VRI, TVRI and TV. In the Table 1, line 2 of scenario 3, the case is presented with TV=VRI=5 cc; TVRI=2.5 cc (50% of VRI) and hence CONV is zero. The scenario 5 is only for the sake of analysis and not clinically relevant. It is seen that the proposed NTPF and CONF, definitely would be useful in the scenarios 2 and 3 to assess the conformity along with the normal tissue irradiation, when planning for an irregular target. An example for this is the planning for an arteriovenous malformation (AVM). Along with a nidus drawn, healthy blood vessels also get into the RI. The proposed NTPF and CONF would enable the planning physicist to generate multiple plans, by bringing down the value of NTPF close to zero and increasing the value of CONF towards 1. The radiation oncologist would have the advantage of choosing an appropriate isodose for prescription, based on the NTPF and CONF values. In this study, only analytical data from the simulated scenarios could be presented and discussed. At the time writing this article, there was no access to get patient data. Otherwise results of retrospective analysis would have also been included to substantiate the proposal of NTPF and CONF. This study is limited only to target dose conformity and normal tissue irradiation. Moreover, since this study is on the simulated models, the impact of reducing the NTPF on the dose homogeneity of the TV or the dose gradient outside the TV is not known. Multiple treatment plans need to be generated on the real patient data by varying the NTPF and evaluated.

Conclusions

In high precision radiation treatments like SRS and SBRT, as very high doses are delivered, sub milli-meter accuracy in targeting is aimed using image guidance. During planning process, while delineating the target on CT images, additional modalities of imaging like MR, PET etc. are utilized. The basic idea is that the target needs to be perfectly delineated and treated without including much of the normal tissue. Similarly, while planning it needs to be aimed at covering the TV as much as possible, minimizing the irradiation of the normal tissue. Though, it is always desirable to have the RI just covering only the TV and achieve a perfect conformity, it may not be always possible in practice. Normal tissue does get irradiated, while trying to improve the coverage. Hence there is a need to estimate the NTRI and evaluate the conformity. The CONF takes into account the NTRI and estimates the conformity of the TV, as it is clearly evident from results given for the scenarios 3 and 4, for the same TVRI. The NTPF clearly indicates the inclusion of normal tissue as a fraction of VRI. This would help the treatment planning physicists to keep the NTPF tending towards zero, while trying to achieve a reasonably good coverage of the TV.

Two major points need to be mentioned here. One is that the NTPF and CONF directly convey the quality of a plan without requiring any interpretation. The other one is that the computation of NTPF and CONF doesn’t involve complex mathematical operations for the treatment planning computers to handle. Institutions can set their own policy of NTPF and CONF to evaluate the plans. Recording of NTPF along with CONF, in the treatment plan dose statistics, would enable the radiation oncologists to compare different plans and choose a better one.

Additional Information

Disclosures

Human subjects: All authors have confirmed that this study did not involve human participants or tissue. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.
References


