

# Derivative based sensitivity analysis of gamma index

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## ABSTRACT

Originally developed as a tool for patient-specific quality assurance in advanced treatment delivery methods to compare between measured and calculated dose distributions, the gamma index ( $\gamma$ ) concept was later extended to compare between any two dose distributions. It takes into effect both the dose difference (DD) and distance-to-agreement (DTA) measurements in the comparison. Its strength lies in its capability to give a quantitative value for the analysis, unlike other methods. For every point on the reference curve, if there is at least one point in the evaluated curve that satisfies the pass criteria (e.g.,  $\delta DD = 1\%$ ,  $\delta DTA = 1$  mm), the point is included in the quantitative score as "pass." Gamma analysis does not account for the gradient of the evaluated curve - it looks at only the minimum gamma value, and if it is  $< 1$ , then the point passes, no matter what the gradient of evaluated curve is. In this work, an attempt has been made to present a derivative-based method for the identification of dose gradient. A mathematically derived reference profile (RP) representing the penumbral region of 6 MV 10 cm  $\times$  10 cm field was generated from an error function. A general test profile (GTP) was created from this RP by introducing 1 mm distance error and 1% dose error at each point. This was considered as the first of the two evaluated curves. By its nature, this curve is a smooth curve and would satisfy the pass criteria for all points in it. The second evaluated profile was generated as a sawtooth test profile (STTP) which again would satisfy the pass criteria for every point on the RP. However, being a sawtooth curve, it is not a smooth one and would be obviously poor when compared with the smooth profile. Considering the smooth GTP as an acceptable profile when it passed the gamma pass criteria (1% DD and 1 mm DTA) against the RP, the first and second order derivatives of the DDs ( $\delta D'$ ,  $\delta D''$ ) between these two curves were derived and used as the boundary values for evaluating the STTP against the RP. Even though the STTP passed the simple gamma pass criteria, it was found failing at many locations when the derivatives were used as the boundary values. The proposed derivative-based method can identify a noisy curve and can prove to be a useful tool for improving the sensitivity of the gamma index.

**Key words:** Derivative, dose distribution comparison, gamma index, radiotherapy, sensitivity, sensitivity analysis

## Introduction

Modern day radiation treatment delivery often involves highly complex dose distributions coupled with a large number of monitoring units from the linear accelerator. This necessitates patient specific quality assurance (QA) tests for every treatment plan before its execution. Planar dose verification in the form of comparison between measured dose distribution using a planar detector

and calculated dose distribution from the treatment planning system (TPS) is the highly preferred method for patient-specific QA. Although there are several ways of comparing the two dose distributions such as simple visual inspection, superpositioning of isodose lines, the gamma index method has become the most popular comparison method since it incorporates the quantitative element in the analysis besides the qualitative aspect. The method, initially introduced to compare measured and calculated dose distributions, has been extended to make a comparison between any two dose distributions - measured versus measured, measured versus calculated, and calculated versus calculated. Thus, its application has extended beyond simple patient specific QA in intensity modulated radiation therapy, volumetric modulated arc

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therapy (VMAT) to the commission of TPSs and beam matching between linear accelerators.<sup>[1]</sup>

Earlier evaluation of the dose distribution for TPS was calculated by superimposing the isodose distributions, either manually with the isodose distributions on a light box or by software tools. This method was purely qualitative rather than quantitative. van Dyk *et al.* in 1993, proposed a system wherein the isodose distribution was subdivided into regions of high- and low-dose gradients, each with a different acceptance criterion.<sup>[2]</sup> Venselaar *et al.* described another way of qualitative evaluation of a dose distribution and proposed acceptance criteria along the lines proposed by van Dyk *et al.*<sup>[3]</sup> In both the above-mentioned methods, the doses are compared directly in the low-gradient regions, with a specified limit of the difference between the measured and calculated doses.<sup>[2,3]</sup> In the high-gradient region such as penumbra, Venselaar *et al.* proposed that the acceptable deviation in the dose could be as high as 30–50% depending upon the complexity of the geometry.<sup>[3]</sup> Comparison of dose difference (DD) is avoided in the high-gradient region since a small spatial error between test and reference distribution will lead to a large difference in dose. The concept of distance-to-agreement (DTA) was introduced to determine the acceptability of the dose distribution in these regions.<sup>[4]</sup> DTA is the distance between a reference data point and the nearest point in the test dose distribution which exhibits dose specified by %DD. It is meaningful to specify DTA for the high-gradient region and percentage %DD for the low-gradient region. Therefore, when used concurrently, DTA and %DD are complementary to each other in the high- and low-gradient region, respectively. The composite analysis using DTA and %DD was developed by Harms *et al.*<sup>[5]</sup> which had its roots on the methodology proposed by Shiu *et al.*<sup>[6]</sup> Cheng *et al.* applied this concept of using a pass-fail criterion incorporating both the DTA and DD.<sup>[7]</sup> Each test point was investigated to establish if both the DTA and DD exceeded the specified tolerances. The inadequacy of this methodology was that it gave a binary distribution only. It did not give any unique numerical index which represented the degree of accuracy between the reference and evaluated distributions. In 1998, Low *et al.* proposed the gamma index ( $\gamma$ ) method.<sup>[1]</sup> This method still uses the concepts of %DD and DTA, but additionally it gives a quantitative value for each point in the evaluated distribution that is computed from the %DD, DTA, and the selected acceptance criteria. To date, it has remained as the most often used methodology for comparing two dose distributions. The techniques of one-dimensional (1998) and two-dimensional gamma analysis (2003) are well-studied areas and have been studied in depth by several investigators.<sup>[1,8,9]</sup> However, one known disadvantage of the gamma index method is that it is sensitive to normalization and does not recognize dose gradient, if at least a single point from test curve falls within the ellipsoid created by %DD and DTA around the reference point. Li *et al.* proposed a

surface-based method to recognize the dose gradient which the gamma index could not detect.<sup>[10]</sup>

In radiotherapy use of derivatives is commonly employed and can be found in different applications: For example, a technique such as gradient search method is frequently used in inverse plan optimization during the treatment planning. Similarly, dose gradient concept is used in beam matching between two or more linear accelerators.<sup>[11]</sup> In general, any gradient can be recognized and quantified using different order derivatives. Therefore, different order derivatives are useful tools to handle the short comings of the gamma index in terms of dose gradient.

The choice of the order of derivative (first order, second order, etc.) for evaluation of dose distribution depends on the dose gradient in the specific case. In a flat beam geometry, derivative up to second order is sufficient for the evaluation of dose distribution.<sup>[11]</sup>

In this article, we present a theoretical formulation based on the first and second order dose derivatives that can help to distinguish between smooth curves and highly irregular noisy curves. While both the curves satisfy the gamma tolerance criteria, the derivatives show up unacceptable differences in the noisy curve. The method is limited to the one-dimensional gamma analysis only.

## Materials and Methods

The method of obtaining the functional form of the penumbral region from the error function has been described by Low *et al.*<sup>[1]</sup> In this work, we applied the same method using the fitting co-efficient for our machine profile and the matched data.

$$D(x_i) = t + (1-t) \{ a \operatorname{erf}[b_1 \times x] + (1-a) \operatorname{erf}[b_2 \times x] \} \quad (i)$$

Where,  $D(x_i)$  is the dose at any arbitrary position  $x_i$ ;  $b_1$ ,  $b_2$ , and  $a$  are the fitting coefficients,  $t$  is the collimator transmission,  $\operatorname{erf}(x)$  is error function having value ranging between  $-1$  and  $+1$  at  $-\infty$  and  $+\infty$ , respectively. Using the value  $a = 0.22$ ,  $t = 0.02$ ,  $b_1 = 0.456 \text{ cm}^{-1}$ ,  $b_2 = 5 \text{ cm}^{-1}$ , the calculated profile from equation (i) and measured profile matched within 0.3 mm DTA and 0.3% DD. All the dose profiles used in this work were such calculated profiles or their derivatives. Throughout this work, a gamma pass criteria of  $\delta\text{DTA} = 1 \text{ mm}$  and  $\delta\text{DD} = 1\%$  was followed.

The method presented here uses a comparison between reference and evaluated (test) profile through their DDs and the first and second derivatives of dose in space. The reference profile (RP) was generated using equation (i), representing a typical profile of a 10 cm  $\times$  10 cm photon beam field from a linear accelerator. The profile has two distinct regions, a low-gradient region (the flat portion)

and a high-gradient region (the penumbral region). In the low-gradient region, DD between the reference and the evaluated (test) profile is important. Since dose derivatives barely have any role to play in this region, this region was not considered in this study. After removing the low-gradient region, midpoint on the high-gradient part of the curve was chosen as the origin of a new coordinate system, and the entire curve was normalized at this point in such a way to have all other points in the curve within  $\pm 1$ .<sup>[11]</sup> The chosen point divided the curve into a positive half and a negative half while perfectly preserving the functional nature of the curve.

The first derivative ( $D'$ ) in space with respect to  $x_i$  (called the dose slope) represents the spatial rate of variation of dose, and the second derivative ( $D''$ ), called the curvature, gives the spatial rate of change of dose slope. Figure 1 represents a dose profile, its first and second derivatives in space. For simplicity, only half of the profile is shown. The behavior of the derivative on the other half of the profile will be reciprocal. As shown in Figure 1, the profile is subdivided into the first derivative significant area (slope) and second derivative significant area (curvature). First derivative will be significant around the region where  $x = 0$  and second derivative in the bending parts of the profile where the steep slope region of the profile bends to merge with the plateau region. It is demarcated in Figure 1 as the second derivative significant area. There is no clear demarcation between these first and second derivative significant areas and they overlap with each other. Hence, in the overlap region, both derivatives will be tested. More detailed characteristics of first and second derivatives of dose profile are described elsewhere.<sup>[11]</sup>

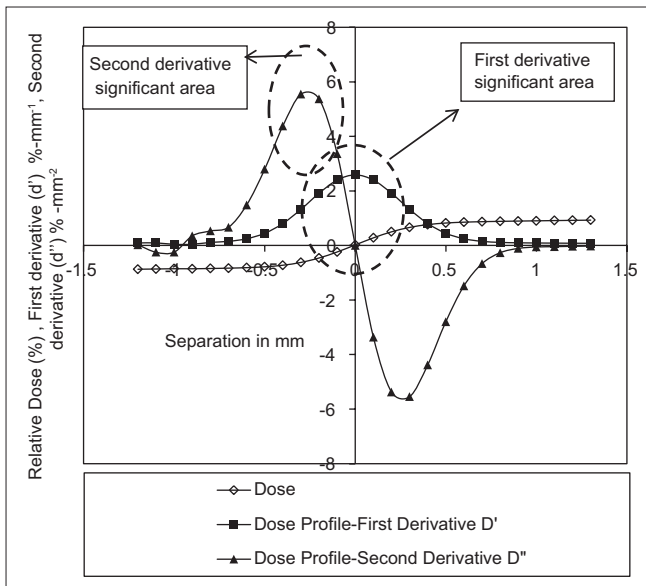


Figure 1: Profile and its first and second derivative in space. In general, mathematics first derivative termed as slope, and the second derivative termed as curvature. The first derivative significant area and second derivative significant area is demarcated in the figure

To investigate, whether the conventional gamma analysis between the RP and a sawtooth test profile (STTP) is an adequate test for quantitative evaluation of the dose matching between the two curves, we first compared the RP with a general test profile (GTP) using the first and second order spatial derivatives. Since the GTP was an acceptable smooth curve that satisfied the 1 mm DTA and 1% DD criteria against the RP, these spatial derivatives were used as boundary conditions for subsequent evaluation of STTP against RP.

The STTP was generated in such a way that it passed the conventional 1% DD and 1 mm DTA gamma criteria for all  $x_i$  as shown in Figure 2a when compared against RP. Figure 2b shows the minimum %DD for 0 mm and  $\pm 1$  mm DTA search yielding  $\gamma \leq \pm 1$  for all points. Thus, the STTP is an acceptable curve when one goes only by the conventional gamma method.<sup>[11,12]</sup> However, it should ideally be not acceptable because of its sawtooth nature. The fact that such an unacceptable profile passes a stringent gamma criteria goes on to prove that the gamma index does not detect the slope of dose or positional changes if these are within certain limits.

### Results

Figure 3a shows the RP and GTP, and the maximum and minimum variation of %DD ( $\delta D$ ) between the two profiles. Similarly, Figure 3b and c show first and second

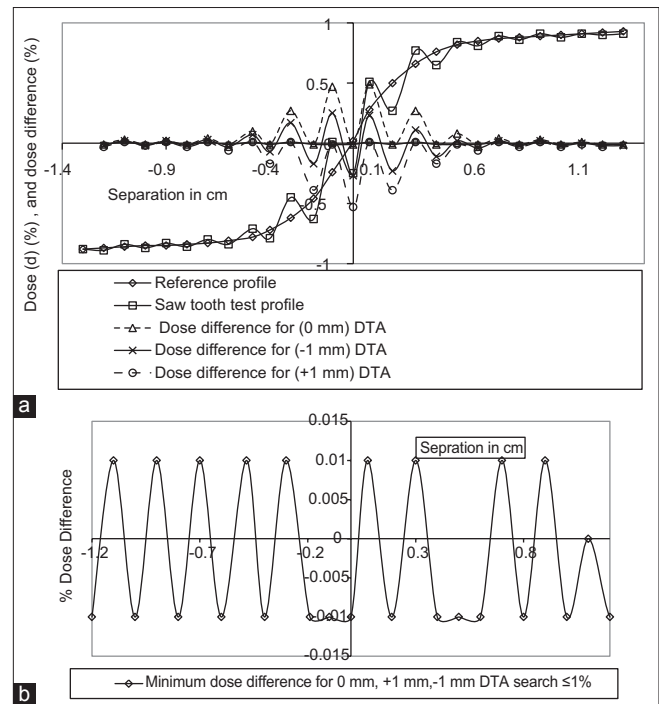
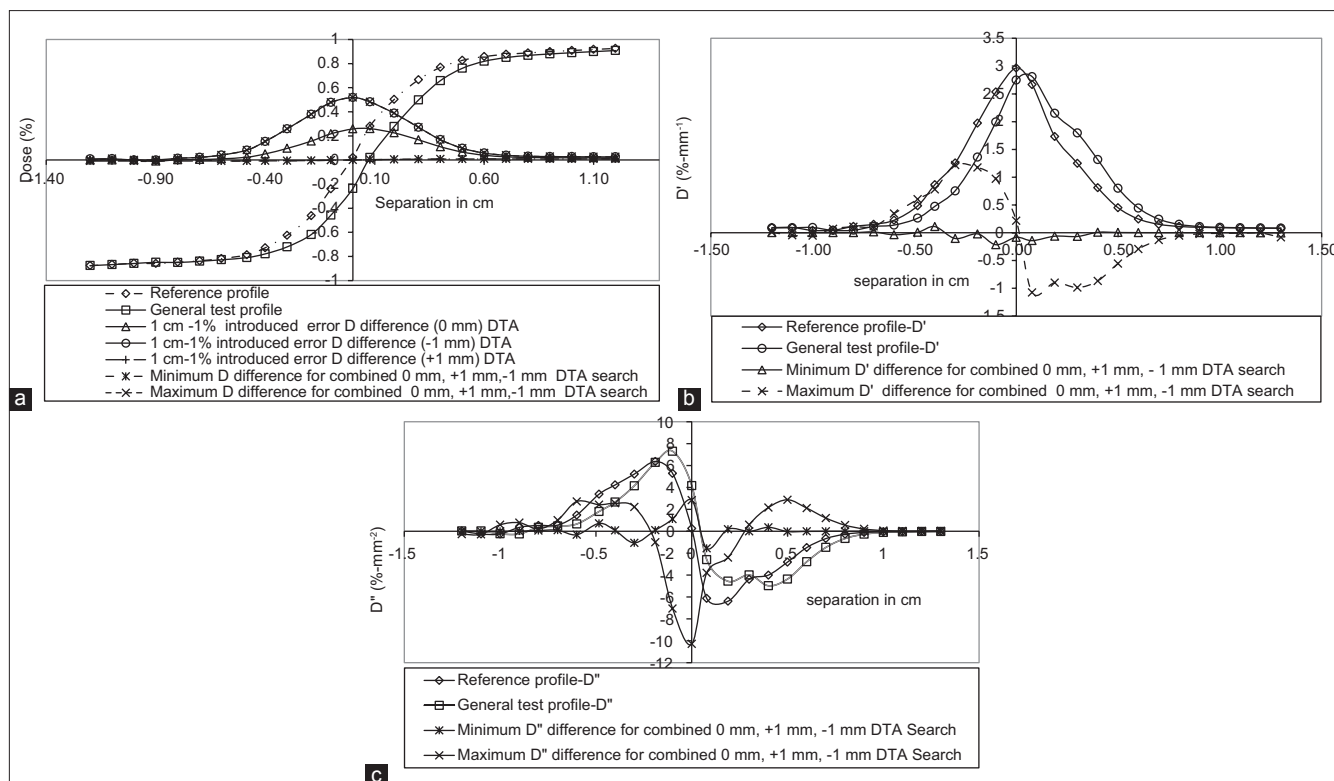


Figure 2: (a) Reference profile and sawtooth test profile and their 0 mm, 1 mm, and -1 mm distance-to-agreement search (b) Minimum dose difference for 0 mm, +1 mm, and -1 mm distance-to-agreement search yielding  $\gamma \leq \pm 1$  for all points



**Figure 3: (a) Maximum and minimum D difference between reference and general test profile for 0 mm, +1 mm, and -1 mm distance-to-agreement (b) Maximum and minimum D' difference between reference and general test profile for 0 mm, +1 mm, and -1 mm distance-to-agreement (c) Maximum and minimum D'' difference between reference and general test profile for 0 mm, 1 mm, and -1 mm distance-to-agreement**

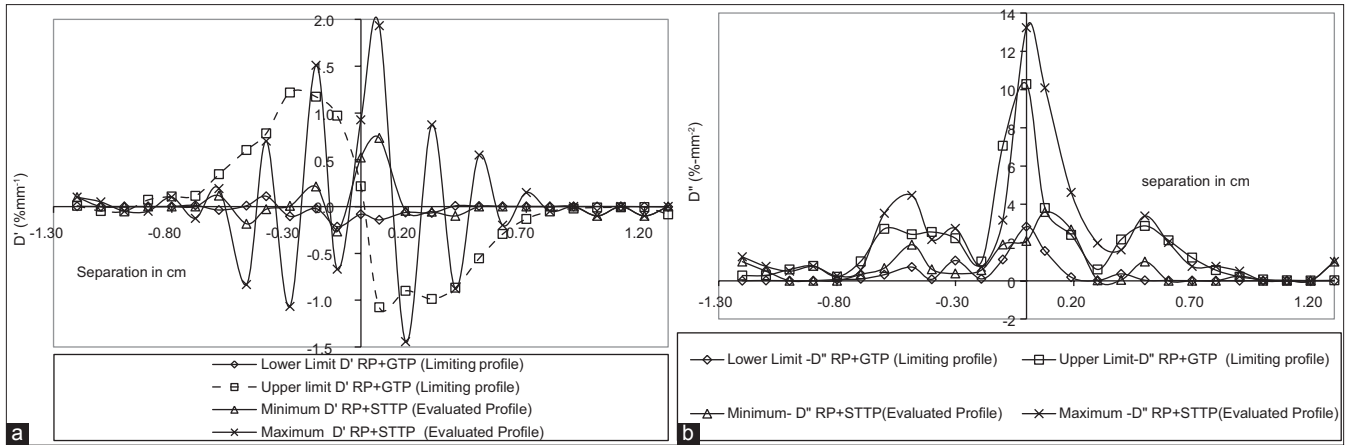
derivative of RP and its maximum and minimum variation of  $D'$  ( $\delta D'$ ) and  $D''$  ( $\delta D''$ ) differences, respectively. The profiles for maximum and minimum difference for  $D$ ,  $D'$ , and  $D''$  obtained by 0 and  $\pm 1$  mm DTA search are shown in Figure 3a-c, respectively. Therefore, the test profile used here (GTP) is acceptable for the 1% DD and 1 mm DTA ( $\gamma \leq 1$ ) search criteria when tested against RP. Consequently, these derivatives can serve as limits for testing derivatives of any other profile satisfying  $\gamma \leq 1$  for limits of 1% DD and 1 mm DTA, the difference in dose profile, its slope and curvature with those of the RP should lie within these limits profiles.

The difference in dose ( $\delta D$ ) and derivatives ( $\delta D'$  and  $\delta D''$ ) between these two curves (GTP and RP) give the upper and lower limits of the differences for dose and its derivatives as shown in Figure 3a-c. If the differences  $\delta D'$ ,  $\delta D''$  between the reference and the evaluated profiles are outside the limits specified in Figure 3b and c, then the evaluated profile is not acceptable even though it may be passing the gamma test as in Figure 3a. To investigate the acceptability of STTP, the curve was examined with the derivatives as the upper and lower boundary limits. For the curve to pass, the first and second order derivatives of the STTP should fall within these limits. The results are shown in Figure 4a and b. These figures clearly indicate the derivatives of RP-STTP combination fall beyond the limits

derived from the RP-GTP combination. From Figure 4a it is evident that the limits are exceeded at the following points: 1 mm, -2 mm, -5 mm, and -3 mm, -4 mm, 2 mm, 3 mm, respectively. Similarly from Figure 4b, it is evident that the limits are exceeded at 0 mm, -5 mm, -6 mm, 5 mm, and -3 mm, 4 mm, respectively. The results demonstrate that it is possible to identify large fluctuations in the evaluated profile by means of derivatives which was not otherwise possible with the simple gamma test based on DTA and %DD.

## Discussion

Gamma analysis is a mathematically rigorous technique to compare two or more dose distributions in one or more dimensions. Matching of gamma index within a specified value is a necessary boundary condition; nevertheless, it is not the sufficient boundary condition for all situations, especially in evaluating a noisy curve. In our study, gamma analysis of an acceptable profile (the GTP) and an unacceptable profile (STTP) with respect to a mathematically generated RP resulted in a value of  $\gamma = 1$  for both cases indicating both curves passed the test. However, the slope of the STTP suggested that it was not an acceptable dose profile. For steepest part of the test profile, difference in the first derivative indicated whether the dose profile was within the acceptable error limits or not.



**Figure 4: (a)  $D'$  differences for evaluated profile (reference profile + sawtooth test profile) in terms of limiting profile (reference profile + general test profile) for 0 mm, 1 mm, and -1 mm distance-to-agreement (b)  $D''$  differences for evaluated profile (reference profile + sawtooth test profile) in terms of limiting profile (reference profile + general test profile) for 0 mm, 1 mm, and -1 mm distance-to-agreement search**

Similarly, in the bending portions of the profile where the slope changes rapidly, evaluation of  $D''$  at different points helped us to correctly identify whether the evaluated curve is an acceptable one or not.

The other drawback of gamma index is that it underestimates the results against no noise condition.<sup>[1]</sup> Noise in dose distribution has a profound impact on gamma calculation. The impact depends on whether the noise is in the reference or evaluated distribution. If the evaluated distribution has noise, and if the reference distribution has no noise then it will be added to  $\gamma$  distribution in the same ratio to the normalized dose noise.<sup>[1]</sup> It is a known fact that differentiation increases noise, the effect being predominant in the low-gradient region. The mathematical property of the derivative quantifies the gradient, which was exploited in this study. As shown in Figure 2a, the dose profile (signal) gets saturated at  $y = \pm 1$ , whereas the first derivative peaks at  $x = 0$  where the rate of change of dose (dose slope) is the highest. The second derivative peaks at two positions, going up to  $\pm 6$  where the dose curve bends (dose curvature), clearly indicating where the rate of change of slope is at its highest. The true characteristics of the dose curve at the said positions can thus only be determined uniquely by derivatives and not the simple gamma test.

Tremendous advancement in the radiotherapy equipment and delivery technique in recent times such as linear accelerator based stereotactic radiosurgery and radiotherapy using miniature MLC, VMAT, Tomotherapy, and CyberKnife make the dose distributions fall more sharply with a very high-degree of dose and fluence modulation, leading to dose escalation attempts for the tumor volume and better sparing of the normal tissues. It may not always be possible to quantify such high-gradient distribution using the simple gamma pass-fail criteria. Physically, a dose distribution is continuous in character, but because of the limitation of our measuring devices

only a discreet dose distribution can be obtained. Gamma analysis is also discreet in nature, and that is attributed to the inherent character of the dose measurement. It is possible to qualitatively identify a distribution within a specified limit by gamma analysis applied to its dose, first derivative and second derivative differences.

The two components of gamma index DTA and %DD are complementary to each other in high- and low-gradient region, respectively. Derivative gamma index is effective in the high-gradient region where DTA is prominent. The evaluation using a derivative gamma index is more stringent than using DTA. In the recent times, several modifications have been tested on the gamma index methodology.<sup>[10,13]</sup> Li *et al.* described a surface-based distance method for gamma index. They established the relation between DTA and %DD using dose gradient factor, or the reciprocal of the mean dose gradient.<sup>[10]</sup> In our study, we exploited similar characteristic of the dose distribution and gamma index. Li *et al.* also established a minimum detectable error of the gamma index with a given set of parameters using a step function.<sup>[10]</sup> In our study, we used a hypothetical profile (STTP) to establish the insensitivity of the gamma index.

Further studies will be carried out to examine the usefulness of derivative gamma method for two-dimensional cases. A study of the method's reliability and sensitivity to noise will also be investigated and presented in future articles.

### Conclusion

It is known that derivatives are the most suited mathematical functions to detect the slope and curvature. In derivative-based gamma evaluation method presented here, these characteristics were successfully used to identify the unacceptable nature of a noisy curve such as STTP which

otherwise would have passed a routine gamma analysis. Use of derivative increases the minimum detectable error of gamma index.

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### Conflicts of interest

There are no conflicts of interest.

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