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Metrics to evaluate the performance of auto-segmentation for radiation treatment planning: A critical review

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Abstract

Advances in artificial intelligence-based methods have led to the development and publication of numerous systems for auto-segmentation in radiotherapy. These systems have the potential to decrease contour variability, which has been associated with poor clinical outcomes and increased efficiency in the treatment planning workflow. However, there are no uniform standards for evaluating auto-segmentation platforms to assess their efficacy at meeting these goals. Here, we review the most frequently used evaluation techniques which include geometric overlap, dosimetric parameters, time spent contouring, and clinical rating scales. These data suggest that many of the most commonly used geometric indices, such as the Dice Similarity Coefficient, are not well correlated with clinically meaningful endpoints. As such, a multi-domain evaluation, including composite geometric and/or dosimetric metrics with physician-reported assessment, is necessary to gauge the clinical readiness of auto-segmentation for radiation treatment planning.

Keywords

Auto-segmentation; Contouring; Treatment planning; Quality assurance

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Contouring target volumes and surrounding organs-at-risk (OARs), also referred to as segmentation or delineation, is a critical step in radiation treatment planning. It is often performed manually by trained radiation oncology professionals (e.g. radiation oncologists/ trainees, physicists, dosimetrists, therapists) and is a time-consuming and subjective process. Variation among providers is common and likely driven by numerous underlying factors including experience [1] as well as the availability, quality, and interpretation of diagnostic imaging used to assist in delineation [2]. This variation impacts plan quality and patient outcomes, with studies across multiple disease sites associating inadequate contouring with worse disease control and increased toxicity [3–5]. In cooperative group trials, radiation protocol deviations have been associated with inferior survival in head and neck [6] and gastrointestinal [7] cancers, with an increasing number of deviations due to contouring errors [3]. This has led to the publication of numerous contouring guidelines designed to assist practitioners with consistent delineation on clinical trials and in routine practice [8,9].

Auto-segmentation, broadly defined as the generation of contours reflecting the boundary of normal structures and/or target volumes on a digital image by a computer algorithm, has the potential to improve dosimetric consistency and clinical outcomes. While the general concept of automated contouring has been under investigation for more than 20 years [10–12], new approaches such as artificial intelligence-based algorithms [13–15] continue to emerge with improved capabilities. The methodologies used to generate auto-segmented contours have been recently reviewed [13]. In this article, we focus on methods to assess the clinical utility and consistency of the resulting contours to guide implementation for the purposes of radiation therapy treatment planning. Auto-segmentation also has potential applications for diagnostic imaging and radiomics [16–18], which are outside the scope of this review.

To decide on a strategy for evaluating the performance of auto-segmentation, it is useful to consider the *goals* of auto-segmentation. These include reducing contouring time, decreasing interobserver variability, and improving dose consistency and accuracy [19–22]. We have classified evaluation metrics into four domains that can be used to assess these goals (Fig. 1): Geometric, dosimetric, time-based, and qualitative scoring. Measures of geometric overlap are useful to assess contour variability, dosimetric calculations can assess the impact of contouring on the treatment plan, and measurement of time saving is important for understanding impact on clinical workflow. Qualitative scoring of contours by end-users (e.g. physicians) provides an overall assessment of clinical acceptability.

Herein we discuss the benefits and limitations of each evaluation strategy, and investigate which metrics, or combinations thereof, may be best suited to evaluate the performance of auto-segmentation. This topic is both clinically relevant and contemporary: automation in radiotherapy is rapidly gathering pace, not only in contouring, but in the development of online adaptive workflows [23,24], treatment planning, and quality assurance [25]. It is important that technologies are robustly evaluated to ensure they are both fit for purpose and that they do what they claim to.

Methodology

This is a narrative review in which articles were identified through a selective literature search of the PubMed database alongside bibliography searches of relevant articles. Searches focused on identifying publications that address the performance of measures used to evaluate auto-segmentation. Abstracts were screened and if deemed to be relevant, the full text was reviewed by multiple authors (MVS, DL, EFG).

Benchmarking

Most metrics used to evaluate contours require comparison to a benchmark "gold standard" [26]. The importance of gold standard contour selection is highlighted in a recent analysis of cervical cancer brachytherapy planning [27]. In this study, multiple treatment plans were applied to two different gold standard contour sets, which resulted in different estimates of both the mean dose and dose variability to the clinical target volume depending on the benchmark. While the simplest version of a benchmark is a single contour that has been approved for clinical use [28–31], this is most subject to variability given known intra- and inter-observer variations in contour quality seen in clinical practice. To circumvent this, benchmarks incorporating multiple ("expert") contours have been proposed, such as a consensus contour derived by an interdisciplinary expert panel using the simultaneous truth and performance level estimation (STAPLE) [20,32–34]. Another approach is to assess the variation in (edited) auto-segmentation volumes against the variation in manual contours from multiple experts, which eliminates the need for a single "gold standard" contour [19,35]. Use of either of these approaches is recommended to avoid reliance on a single set of contours for benchmarking.

Geometric analysis

The geometric measures used in contour assessment can be subdivided into several classes: volumetric overlap metrics, average or maximal boundary distances, and newer methods based on path length or surface agreement [11,36]. These are illustrated in Fig. 1. Among the most frequently used overlap metrics is the Dice Similarity Coefficient (DSC; or Sørensen–Dice coefficient) [37], which evaluates the intersection of more than one delineated volume over the sum of their total volume, and is scored from zero to one, with one suggesting a perfect overlap:

$$Dice\ Similarity\ Coefficient = \frac{2|\mathrm{A} \cap \mathrm{B}|}{|\mathrm{A}| + |\mathrm{B}|}$$

The DSC is one of the simplest metrics for the assessment of auto-segmented volumes and has been frequently used in the literature [15,37,38]. Despite its popularity, volumetric DSC may not predict the clinical adequacy of contours, as demonstrated in a recent evaluation of the clinical utility of auto-segmentation for prostate cancer [39]. Specifically, it cannot differentiate between systematic and random errors [26] and does not take into account proximity to critical structures [40]. This is also the case for the Jaccard Similarity Coefficient (JSC), a related metric which is defined by the ratio of the intersection of two volumes over their union [41]:

$$Jaccard\ Similarity\ Coefficient = \frac{|A \cap B|}{|A \cup B|}$$

A recent study by Duke et al. reported a significant discordance between the JSC and clinician-rated acceptability scores [42]. Although the contours in this study were manually generated, the findings illustrate the relationship (or lack thereof) between a geometric index and expert evaluation. Using a JSC cut-off of 0.7, only 45% of all contoured volumes considered adequate by experts would have passed (true-positive) while 55% would have failed (false-negative). In addition, 13% of the delineations that failed expert assessment would have passed (false-positive).

Likewise, an analysis of prostate cancer plans found that acceptance rates for manual contours of the bladder and rectum were significantly higher than for automatically generated contours using qualitative clinical evaluation, while surface distance and DSC indicated no difference [43]. Similar results have also been demonstrated in brachytherapy planning for cervical cancer, where a geometric concordance index (which may be described as a generalized version of the DSC/JSC used when comparing more than two volumes [44]) was not predictive of important dosimetric parameters [27]. Together, these studies indicate that conventional volumetric overlap indices, such as JSC and volumetric DSC, provide limited clinical context and correlation with clinical or dosimetric quality.

To overcome the limitations of volume-based metrics, some authors suggest the use of spatial distance-based metrics, which are more sensitive to boundary errors [11,41]. These are generated by calculating the closest distance from each point in the reference contour to the experimental contour. The largest of these distances is the maximum surface distance, also called the Hausdorff distance (HD) [45]. The average distance between the two contours can also calculated. Both metrics are calculated as a distance with zero indicating perfect overlap [46]. It is worth noting that volumetric overlap and distance metrics are often not highly correlated, and therefore, potentially complementary [11].

Evaluations of surface distance metrics as a predictor for clinical acceptability, dosimetric consistency, or time saved in the clinical workflow are limited and demonstrate mixed results. For example, Vassen et al. showed only moderate correlation between the maximum HD and time savings in contours of thoracic organs [36], although this was better than the volumetric DSC, which was poorly correlated. Other studies have also failed to demonstrate significant association between surface distances and qualitative contour scoring or time needed to manually adjust contours [43,47].

Another concern when using geometric indices, whether based on volume or distance, is the identification of a threshold value for “acceptable” segmentation. As referenced above, the JSC cut-off value of 0.7 used by Duke et al. [42] was selected based on results from a study by Fokas et al. comparing investigator-delineated contours to “gold standard” contours, which showed the median JSC of investigator planning target volume (PTV) to be 0.75 (IQR: 0.71–0.79) [48]. However, there is no evidence that this or any other cut-off value for JSC is correlated with clinical acceptability and should be considered a valid benchmark. As such, we advise against a universal cut-off to indicate clinical acceptability of a particular contour due to (1) the challenge of the variation of “acceptable” cut-offs by disease site and specific contour region of interest, and (2) the weak correlation of geometric indices with dosimetric measures, time savings, and physician ratings.

These results have helped to drive efforts to develop novel geometric performance metrics for auto-segmentation that are also clinically meaningful. For example, Vaassen et al. introduced the APL, which was defined as the absolute cumulative length of a contour that had to be added or removed during editing [36]. The APL accounts for the number of slices an organ encompasses and is *not normalized by volume*, which is particularly helpful for volumetrically small but elongated organs with poorly visualized boundaries, such as the esophagus. This study also evaluated the use of the surface DSC described by Nikolov et al. [49], which provides a measure of the agreement between just the surfaces of two structures above a clinically determined tolerance parameter, **τ**, as shown in the equation below (Fig. 1).

$$Surface\ DSC = \frac{\left|S_1 \cap B_{2,\tau}\right| + \left|S_2 \cap B_{1,\tau}\right|}{\left|S_1\right| + \left|S_2\right|}$$

Vaassen et al. concluded that (1) both the APL and surface DSC were better predictors of relative and absolute time saving than volumetric DSC and HD, and (2) APL and surface DSC provided additional quantifiable surrogates for the assessment of clinical utility and quality of automatically-generated contours. While promising, even these metrics may be limited by the inherent inability of geometric measures to distinguish where the variation is located within a contour. In isolation, we would favor use of the APL or surface DSC given evidence of a correlation with time savings. A composite of multiple geometric indices is hypothesized to further improve utility, though none exists in the current literature to recommend. Importantly, given the limited data available on corresponding clinical utility, incorporation of additional non-geometric assessments appears warranted.

Dosimetric analysis

A clinical limitation of geometric analysis is that spatial variations in contouring may or may not translate to meaningful changes in radiation dose delivered, depending on the relationship between the dose gradient and the structures in question. Some authors have calculated the dose delivered to auto-segmented and manually-segmented structures as a means of assessing clinical validity. However, this strategy introduces another element of variability, namely the treatment planning process used to generate the dosimetric indices. This process is complex and must account for multiple variables, including the geometry of tumor volumes, position of OARs relative to targets, beam arrangements, and clinical dosimetric requirements [50]. Some studies try to overcome this variability using automated knowledge-based planning to minimize subjectivity that could affect dosimetric parameters [50,51]. Alternatively, a previously generated treatment plan can be overlaid on the auto-segmented contours [19].

A recent study by Kaderka et al. used both geometric indices (e.g. DSC) and multiple dosimetric endpoints to analyze the auto-segmentation of cardiac structures in breast cancer patients [52]. In general, they observed a high degree of concordance between the dosimetry of plans based on auto- and manually-generated contours. However, for certain small substructures such as the left anterior descending artery, the DSC was very low and the dosimetric agreement high. Fig. 2 illustrates this scenario as well as the converse, where OAR contours with nearly complete geometric overlap have significant dosimetric variation. This will be influenced by, among other factors, the dose conformality around a given structure.

Dosimetric calculations appear particularly important when evaluating auto-segmented contours of target volumes. For example, one study utilized auto-segmentation to deform a set of initial contours to a CT scan acquired during treatment in head and neck cancer [53]. Plans based on the auto-segmented contours delivered less coverage (defined as D95% and V95%) to both the clinically-approved gross tumor volume (GTV) and clinical target volume (CTV). The DSC was not correlated with target coverage, and the authors warned against its use as a surrogate for plan quality. Another analysis of auto-segmented head and neck plans found large PTV under-dosing [54] with observed reductions in D99% averaging over 14 Gy despite DSCs ≥ 0.8 and mean HD ≤ 1 mm between auto-segmented and manually-generated target contours. Ultimately, such findings highlight the potential negative impact of uncorrected auto-segmentation errors on radiation dosimetry and plan quality. They also emphasize the importance of dose calculations (ideally with measures to reduce planning variability, such as knowledge-based planning) when evaluating the effectiveness of auto-segmentation platforms.

The specific dosimetric parameter to select for evaluation is dependent on the disease site and clinical scenario. But in contrast to geometric indices, numerous dosimetric parameters (or dose constraints) have been shown to correlate with clinical outcomes – for example, mean dose to the parotid gland affects the risk of xerostomia when treating head and neck cancer [55]. From first principles, maximum doses are typically used for serially arranged OARs (i.e. spinal cord and optic structures), while parallel organs (i.e. lungs, kidneys) and target volume coverage are often evaluated by looking at the percentage of the volume receiving a given fraction of the prescription dose [56]. It is important to recognize that many dosimetric parameters used in both clinical trials and routine practice have *not* been shown to correlate with clinical outcomes. When evaluating the dosimetric impact of auto-segmented contours, priority should be given to evidence-based dose constraints for the disease site in question.

Time analysis

Reduction in contouring time is a clinically meaningful way to evaluate automated delineation. Strategies for measuring time spent contouring include manual timing in a test environment [21], self-reporting by providers [22,29,39,57–59], and automatic measurements using software [29,60,61]. One specific platform called “Big Brother” has been used to analyze variation in human contouring behaviors [60]. This software accounted for user inactivity or distraction by discounting any pauses in input activity longer than a specified time interval (which ranged from 30 s to 5 min). The results showed good correlation between automatically recorded (6.2 min/case) and self-reported (5.5 min/case) time saving. Since manual timing requires a simulated environment that is often not feasible, and access to the "Big Brother" software may be limited, self-reporting is therefore a reliable method to evaluate time spent contouring.

It is important to note that both relative and absolute time savings should be reported as both estimates have value to the audience. One randomized trial compared time spent contouring among residents assigned to (1) automated delineation with editing or (2) manual segmentation, and reported a 30% time reduction with atlas-based auto-segmentation of OARs [22]. However, mean time savings per resident varied from 2.3 to 15.7 min, as senior residents were faster at contouring and thus received a smaller absolute benefit.

Time savings is inherently valuable as it allows radiation oncology professionals to redirect their efforts to other meaningful activities, such as direct patient care or peer review. Data support the importance of peer review for optimizing contour quality in clinical practice, which is currently hampered by a lack of available time [62]. However, speed alone should not be used to declare auto-segmentation successful without a concurrent rigorous validation ensuring that the quality of such contours is not compromised.

Qualitative scoring systems

In clinical practice, the ultimate acceptability of contours, whether automated or manually generated, is determined by physician judgment. While this introduces potential for subjectivity and interrater variability, there is clinical trial quality assurance data that physician-assessed protocol deviations, of which contours are an important component [63], do correlate with patient outcomes. Multiple meta-analyses of cooperative group trials have found that protocol deviations were associated with increased mortality and treatment failure [63,64]. Exact rating systems vary between trials, however amongst the most common is a three-point scale consisting of: (1) Accept/per protocol; (2) Minor deviation, (3) Major deviation [3,63]. The relevance of contour review is also recognized in routine clinical practice, and has led to, for example, implementation of peer review chart rounds in which an inadequate contour is decided by consensus [65,66].

As discussed above, Duke et al. found that geometric overlap was an inadequate predictor of expert-assessed scores on a three-point scale [42]. Given the difficulty in finding surrogates for expert review, several auto-segmentation studies have implemented physician review with similar scoring scales to clinical trials [31,47,57]. Others have expanded this approach by using a broader seven-point categorization system [67]. In a recent evaluation of the three-point system, expert case reviewers noted that a five-point system might have provided greater ability to differentiate contour quality, since no physicians reported "unacceptable/-major edits" [39].

Instead of asking end users to rate the quality of auto-segmented volumes, an alternative approach is to ask users to distinguish the origin of a contour (auto-segmented or manual). A study by Gooding et al. [47] used this approach, inspired by Turing's Imitation Game [68], to analyze segmentation of six thoracic OARs. Their data confirmed that the "misclassification rate" (user inability to judge the source of contour) appeared to be a better predictor of the time needed for contouring edits than the DSC, suggesting this strategy could be incorporated into the evaluation of auto-segmentation platforms.

Given concerns regarding the potential subjectivity and reproducibility of qualitative scoring systems, some studies have proposed multiple rounds of reviews by panels of experts [69]. McCarroll et al. conducted a study where multiple physicians reviewed the same automated contours for eight OARs on a three-point scale (no edit, minor edit, major edit) [70]. They found that only a small minority of automated contours generated substantial disagreement, suggesting reasonable interobserver variability in clinical qualitative scoring. Quality assurance programs for clinical trials are variable [71] but some protocols include review by at least two experts [72]. At present, an optimal contour scoring system likely involves at minimum a blinded physician qualitative review. Our recommendations align with those proposed in a recently published framework for evaluation of treatment planning studies [73], which also noted the importance of clinician evaluation.

While physician scoring may be a reliable approach, it is time-consuming and may be difficult to implement in some settings. Centralized quality assurance programs for clinical trials face similar logistical challenges. Proposed solutions have included review of only the first ten cases from a given center, as this is when the majority of improvement is reported [74], or the use of a benchmark case [75]. Such approaches could similarly be applied to the clinical implementation of auto-segmentation [39]. Regardless, physician feedback and participation in the process of implementation is as important as, in the authors' experience, algorithms that are often implemented without providing definite utility. These challenges highlight the ongoing need to develop and validate appropriate surrogate measures for clinician assessment to facilitate a thorough evaluation and comparison of auto-segmentation platforms.

Conclusion

Auto-segmentation algorithms offer the potential to improve the consistency and speed of delineation in radiation oncology. As the methods for generating auto-segmented contours continue to evolve, new approaches and algorithms will emerge, and it is critical for these to be evaluated by metrics that reflect clinically meaningful outcomes. Recent studies question the correlation of commonly used measures of geometric overlap such as the DSC and HD, with dose delivered, clinical acceptability, and time saved. As such, these measures should preferably not be utilized as the sole determinant of contour quality. If clinically relevant contour quality is the endpoint, then the gold standard remains physician evaluation, which is supported by the strongest evidence for correlation with clinical outcomes. Since this is a time-consuming and labor-intensive approach, there is an unmet need for the development and validation of adequate surrogate measures to allow for more efficient evaluation of automated platforms. The approach to evaluation also needs to consider the purpose of the evaluation, such as anatomical "correctness", suitability for segmentation of non-critical or critical structures in routine clinical practice, or time savings. If the goal of the auto-segmentation is more limited, then a specific geometric, dosimetric or time-based metric may be adequate to address the particular question being posed.

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Conflict of interest

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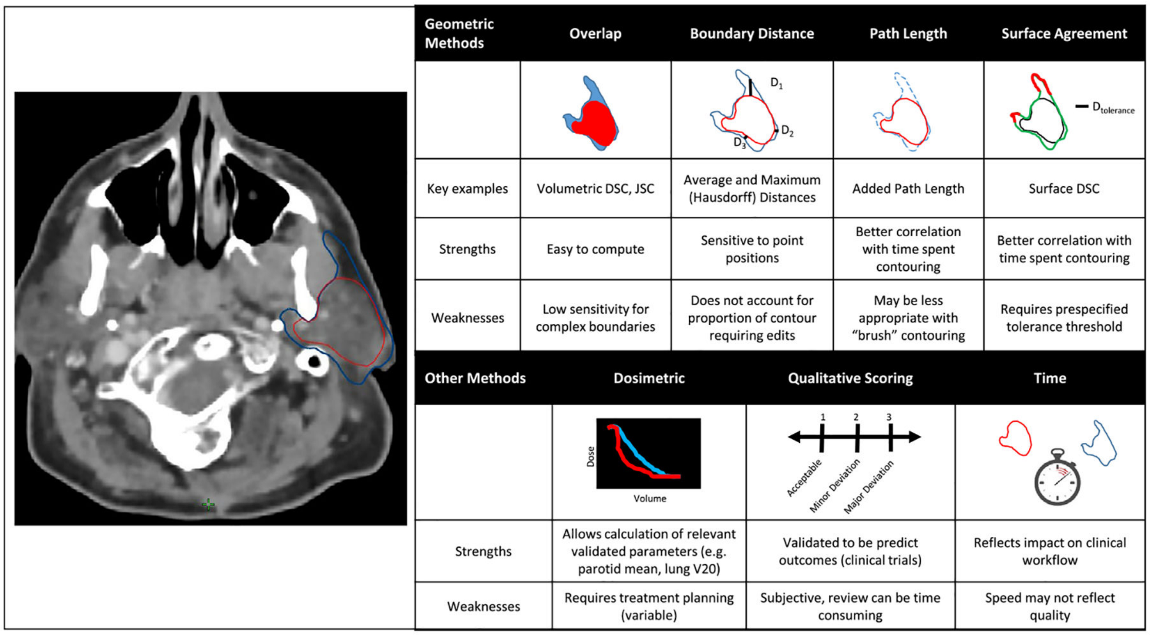
D1
D2
D3
Dtolerance
Dose
Volume
1
2
3
Acceptable
Minor Deviation
Major Deviation

Geometric Methods	Overlap	Boundary Distance	Path Length	Surface Agreement
Key examples	Volumetric DSC, JSC	Average and Maximum (Hausdorff) Distances	Added Path Length	Surface DSC
Strengths	Easy to compute	Sensitive to point positions	Better correlation with time spent contouring	Better correlation with time spent contouring
Weaknesses	Low sensitivity for complex boundaries	Does not account for proportion of contour requiring edits	May be less appropriate with "brush" contouring	Requires prespecified tolerance threshold

Other Methods	Dosimetric	Qualitative Scoring	Time
Strengths	Allows calculation of relevant validated parameters (e.g. parotid mean, lung V20)	Validated to be predict outcomes (clinical trials)	Reflects impact on clinical workflow
Weaknesses	Requires treatment planning (variable)	Subjective, review can be time consuming	Speed may not reflect quality

Fig. 1.

Overview of metrics used for contour evaluation.

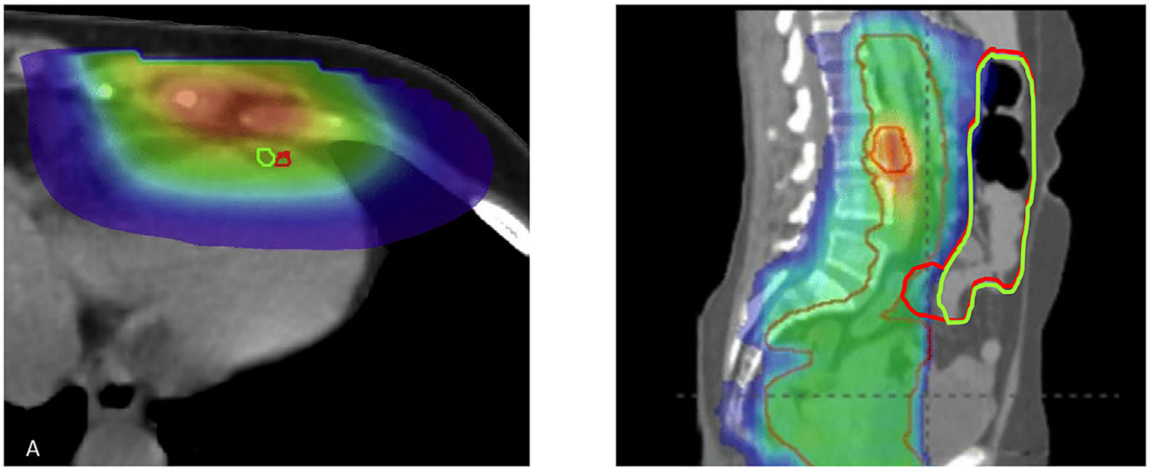

Fig. 2.

Examples of Geometric-Dosimetric discordance. On the left, two contours of the left anterior descending artery have almost no overlap but both structures receive a nearly identical dose (Figure reprinted with permission from reference [52]). On the right, two small bowel contours have excellent geometric agreement but disagreement within a high dose gradient region would result in a higher Dmax for the red contour.