AN *IN-SILICO* COMPARISON OF CLINICAL TARGET VOLUME AND CLINICAL TARGET DISTRIBUTION FOR SKULL BASE CHORDOMA

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Abstract – Clinical target volume (CTV) is a traditional target delineation method used in radiotherapy. The concept has several limitations (such as binary conceptualisation, variability and uncertainty). More recently a continuous probabilistic concept - Clinical Target Distribution (CTD) has come into prominence, which addresses the above mentioned limitations. In this paper, we implemented CTD in the treatment planning system and compared CTV and CTD in the cases of skull base chordomas. Under the CTD concept we infer tumoral prescription dose, observe maximal OAR dose constraints and highlight the dose distribution advantages.

INTRODUCTION

Accurate delineation of target volumes in proton therapy is an important challenge. The traditionally defined in radiotherapy clinical target volume (CTV) has a number of limitations that may negatively impact treatment outcomes. Firstly, CTV is a binary concept. It means that there are tumor cells inside the area selected by the physician, but not outside. However, the distribution of the tumor occurs differently: the further the point is from the gross tumor volume (GTV), the less likely it is that it is tumorous. Moreover, the CTV may require redrawing or modification if it intersects with the Organs at Risk (OAR) to limit exposure to normal tissues. Finally, traditional CTV has a high interobserver variability [1,2].

In contrast to this the clinical target distribution (CTD) is a continuous probabilistic concept that allows to describe closer to the real tumor distribution: the probability of having tumor cells decreases from 100% near the GTV to 0% away from it. The CTD was introduced by Shusharina et. al. [3], and represents probabilistic delineation of regions by several shells, each of which is assigned the probability *r* of having a tumor outside this shell (the outer shell implies the absence of tumor cells). The probability *p* that the voxel is tumorous:

$$p_h = 1 - \left(\frac{1 - r_h}{1 - r_{h+1}}\right)^{\frac{1}{N_h}},$$

where N - number of voxels in layer h, h – layer (area between two contiguous shells).

The concept was developed by Buti et. al. [4]. It was proposed to exclude treatment of 1% of voxels near OAR (the dose of which is farthest from the prescribed one and the probability of the presence of a tumor is minimal) with minimal change in the tumor control probability (TCP). This attitude let us find more suitable tradeoff between target coverage and sparing of OAR.

In this paper, we implemented CTD in treatment planning system and compared CTV and CTD in the five cases of skull base chordomas, exploring the benefits and limitations of the new concept.

MATERIALS AND METHODS

We created treatment plans for five cases of skull base chordomas (one CTV plan and one CTD plan for each case). CT and MRI images were obtained from an open database [5]. GTV, CTV, OAR and five probability shells of CTD were defined under the guidance of oncologist.

Method described by Shusharina et. al. [3] and Buti et. al. [4] was introduced in OpenTPS (open-source treatment planning system for proton therapy), which has MCsquare (Monte Carlo simulation) integrated in it [6]. Treatment plans were created with pencil beam scanning (PBS) technique. We chose to use four beams (2 anterior oblique and 2 posterior oblique), as this is standard clinical practice for this type of tumor and offers a good balance between efficiency and optimization time. The dose goal for chordoma is more than 60-70 Gy [7]. Spot spacing and layer spacing were 5 mm.

The optimization was done with the limited-memory Broyden–Fletcher–Goldfarb–Shanno (LM-BFGS). OAR optimization parameters satisfy the European Particle Therapy Network consensus on OAR dose constraints (Table 1) [8]. Each plan was evaluated by calculating TCP and by acceptance criteria of treatment goals [9] and DVH (dose-volume histogram) parameters [10].

Table 1: Optimization parameters for OAR

Target	Function	Dose level, Gy	Weight
Brainstem surface	Max dose	65	Constraint
Brainstem center	Max dose	50	Constraint
Optic Chiasm	Max dose	55	Constraint
Hippocampi	Max dose	7.3	Constraint

Due to the small sample (n=5), statistical significance of differences between groups was determined using the sign test and the Wilcoxon signed-rank test. Differences were considered statistically significant at a significance level of less than 0.05.

RESULTS

For our cases of skull base chordomas in both CTV and CTD plans we received prescription dose in GTV (Table 2). Moreover, the maximal dose constraints for the OAR were satisfied for all plans, and we observed a statistically significant decrease in the values for CTD plans (Fig. 1). The mean dose reduction to the optic chiasm was 4.02 Gy and to the brainstem was 2.98 Gy. Meanwhile, TCP reduction was lower than 1%. In one case, we were able to change the brainstem risk acceptance criterion from "Minor Deviation" to "Acceptable" [10].

Table 2: Treatment characteristics

	Mean dose level, Gy	
	CTV	**CTD**
GTV (D98)	70.83 (67.70 – 74.21)	70.77 (67.34 – 73.93)
Brainstem (Dmax)	53.44 (48.55 – 58.33)	50.47 (46.85 – 54.33)
Optic Chiasm (Dmax)	52.75 (50.90 – 54.99)	48.74 (45.54 – 50.42)

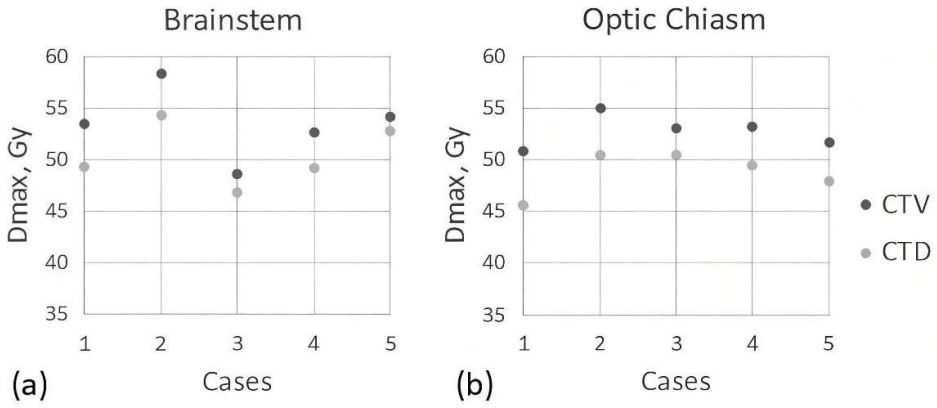

Figure 1 - Plot of maximum dose to the (a) brainstem and (b) optic chiasm. Black – CTV, grey – CTD.

CTD allows better OAR sparing by reducing the high-dose regions (Fig. 2a-b). The CTD plan optimization results in steeper high dose shift which provides us lower dose in most of the OAR (Fig. 2c).

DISCUSSION

CTD is a new concept that should help to eliminate the limitations of CTV (especially binary concept, variability and uncertainty). For our cases of skull base chordomas using CTD let us receive prescription dose in target, satisfied maximal dose constraints for the OAR (we observe an overall lower dose in CTD plans) and had balance between target coverage and OAR sparing. Despite the positive results, the data should be interpreted with caution due to the limited sample size.

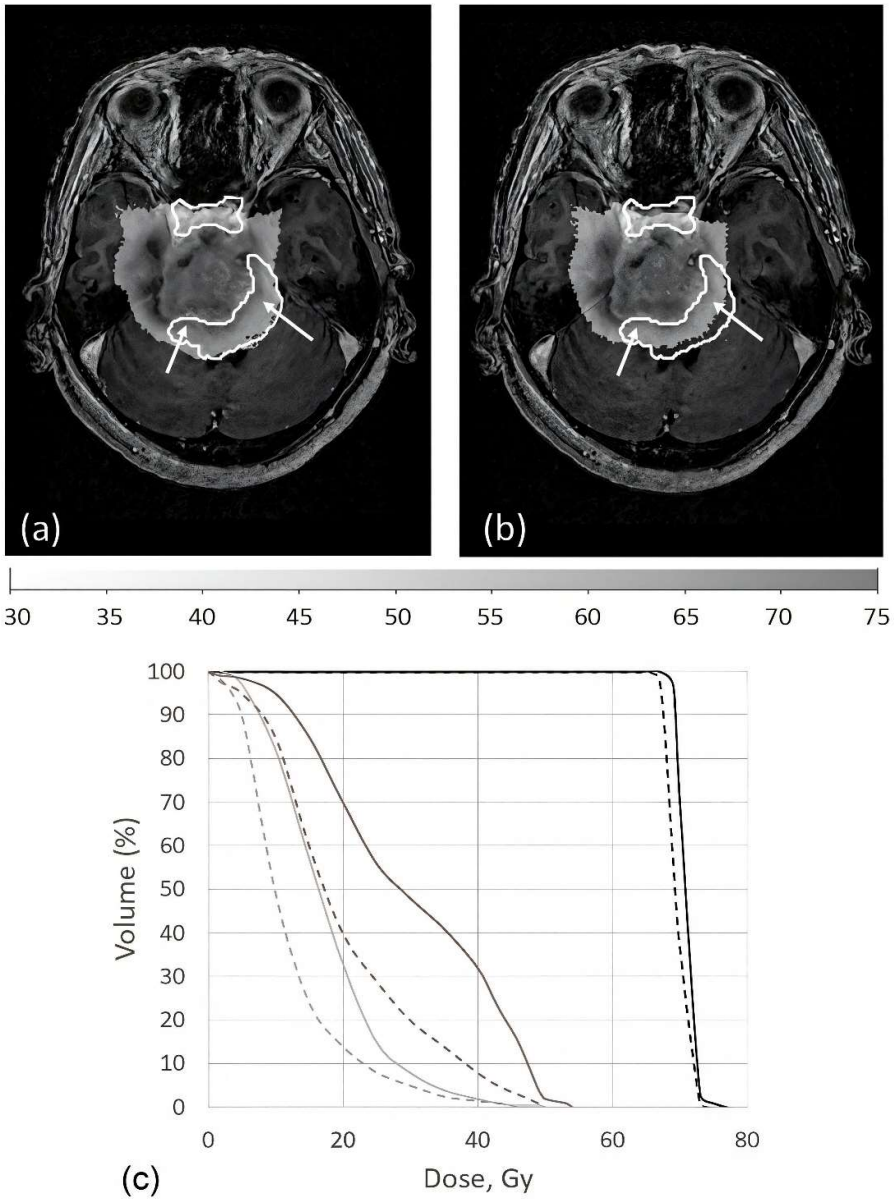

Figure 2 - Dose image for CTV (a) and CTD (b) plans. The most significant dose differences are indicated by the white arrows. DVH (c) of the CTV (black), brainstem (dark grey) and optic chiasm (light grey) for CTV (solid) and CTD (dashed) plans.

CONCLUSION

We implemented CTD in treatment planning system and compared CTV and CTD in the five cases of skull base chordomas. Our results suggest that CTD might be a good alternative to CTV, but further research is needed to overcome number of limitations. For example, determining the planning target volume (PTV) for the CTD plans or moving on to the objective creation of CTD shells (which can be achieved with pathological studies). However, the method is worth further consideration and may be introduced to clinical practice after needed research.

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