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Overlap Target Volume - a new planning structure to aid PTV preservation

Helpful Concepts in Radiotherapy Planning

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Abstract: The overlap of Planning Target Volume (PTV) and Organ At Risk contours (OAR) is a common scenario in Radiotherapy Planning. This paper deals with the method of defining and use in planning of an overlap structure called Overlap Target Volume.

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Keywords: Radiotherapy Planning • Volumes • Contours • Overlap • OTV

1. Introduction

Accurate radiation therapy relies on the proper definition of the treatment volume. Based on internationally accepted recommendations of ICRU reports 50[1], 62[2] and 83[3], planning volumes are created in a step-wise process that start with visible abnormalities and move through estimation of clinical risk to an 3D motion-conscious envelope requiring a particular dose.

The process starts with the gross tumour volume (GTV) which defines a non-anatomical structure on an image which corresponds to the visible tumour. Following this, a second volume is constructed around the GTV by adding a margin to an anatomical plane (or occasionally a distance) to account for expected but unseen microscopic extension creating the clinical target volume (CTV). Since the CTV moves, inter- and intra-fraction motion must be quantified.

A margin, that accounts for internal physiological movement (or "Internal Margin") in size, shape, and position of the CTV relative to anatomical reference points, can be added leading to an increased 'Internal Tumour Volume' (ITV).

$$ITV = CTV + IM$$

Examples of Internal Margins include movements resulting from bladder filling and respiratory motion. Uncertainties in treatment delivery also include repeated patient positioning variation which are quantified by adding a "set-up margin" (SM) to create the Planning Target Volume.

$$PTV = ITV + SM$$

The ICRU approach using GTV-CTV-ITV-PTV paradigm is extremely useful and logical, however there are circumstances where it fails to capture the granularity of the radiotherapy planning process. For example, in H&N planning, definition of GTV for primary and nodes is routine, but there is no accepted method that identifies each one. A plan may use GTV alone; or add GTVp, GTVn and GTVm depending on the type of GTV [4]; or GTVn_1/GTVn_2 or GTVn_2a/GTVn_2b depending on nodal variation. Furthermore there is no help in the designation of the 'node-negative neck', though attempts have been published [5–7]. Modifications to the ICRU approach are common, few are standardised but usually based on the use of suffixes to the ICRU terms.

The GTV is a manually defined region of interest differentiating the gross visible tumour from normal anatomy. Since each modality uses different signals by which to differentiate tissues, the same tumour will display different characteristics with each anatomical imaging modality such as magnetic resonance imaging (MRI) [8], ultrasound (US) or computed tomography (CT), and functional imaging modality such as Technetium-99 bone scan or positron emission tomography (PET). Additional clinical information derived from endoscopic or clinical visual and manual examination may lead to even wider interpretations of tumour location.

The GTV is a visual concept [9]. The profusion of ways to view the GTV makes it appear as it the GTV is 'uncertain', although in each individual imaging modality the visual definition is often quite clear. The fact that GTVs, such as GTVp_CT, GTVp_MRI, GTVp_PET and GTVp_scope, will be of different size does not prevent the oncologist from accurately visually delineating the GTVp in each modality based on what is seen [10, 11]. Multiple GTVp volumes could be summated [4], a process supported by modern planning systems.

The images used may vary depending upon the table shape (flat, round), the positioning of the patient (prone/supine, chin up/down, pillows) and their appendages (arms crossed/by sides). Even if standardised, the imaging modality (CT, MRI), movement and technique, e.g., window level, sequence and use of contrast [12], as well as image reconstruction and plane of view may still influence GTV definition.

The incorrect alignment of multimodality image fusion can also impact on GTV delineation [13–16], and the timing of a scan may reveal changes caused by treatment (tumour response) or side effects (weight loss). Deformable registration based on anatomic segmentation, "regmentation" [17] offers some hope to compensate for these deviations.

There is an extensive literature on the variability of GTV delineation [18, 19] showing that hand drawing is common, variability is marked and reproducibility low even when voluming simple scenarios. Other image examples also demonstrate variability in clinical thinking. The use of Hounsfield thresholding to produce volumes should reduce variability.

The CTV is a concept combining clinical risk and anatomy. Normal anatomy may be assigned to a volume based on suspicion of tumour involvement which is below the resolution of the imaging modality where the CTV drawn matches the clinician's knowledge of surrounding anatomical structures and planes which form a barrier to tumour growth, remote tissues that contain microscopically involved lymph nodes. However the CTV may just include a margin of apparently normal tissue[20].
Either way, the CTV should not include anatomic structures or tissues where infiltration is deemed unlikely, which typically includes anatomical barriers such as bones, muscle fasciae, vessel walls or lumina and air at epidermal/mucosal interfaces. The CTV is a large source of uncertainty in volume definition [21] because it is based on an individual clinician's appreciation of and tolerance for risk. As a result of multiple studies showing these deviations among experts, many *anatomical* CTV definition [**?**]atlases for various diseases have been developed to minimise variability [22, 23].

The ITV should compensate for physiological CTV motion and deformation and various approaches deal with this [1, 24–27]. Without patient-specific information, the ITV is generated as a best guess. Four-dimensional CT (4D-CT) may provide better information on rapid tumour motion, especially thoracic targets which move

rhythmically on respiration. The ITV may be defined from a 4D-CT by binning CT slices into respiratory phases or by maximum intensity projections (MIP) [28]. Slow physiological organ change e.g., bladder filling, can be assessed by acquiring consecutive planning CT scans and calculating coverage probability [29] for the target volume and the organs at risk.

The PTV is a geometric construct, an expansion of the CTV by a magnitude and direction dependent on the site-specific and reliability (reproducibility) parameters of daily patient positioning. The ability to easily and repeatedly measure positioning precision using portal imaging, fiducial markers, electromagnetic transponders and cone beam CT each day enables the confident use of very small set-up margins. Nonetheless individual patient factors have to be taken into account when defining the Set up Margin (SM) around the ITV.

Contours of organs at risk (OAR) are the remaining regions of interest marked onto planning datasets. These contours can be expected to undergo the same physiological and positioning variation already discussed for volumes. The Planning Risk Volume (PRV) is a second geometric construct – an expansion of an anatomical entity in a process mirroring the formation of the PTV.

The four volumes typically used (GTV-CTV-ITV-PTV) encompass many treatment-related uncertainties, but takes no account of the proximity of OAR/PRV contours and how they might interact at the time of planning. As recently pointed out [30], there are scenarios where the PTV and PRV volumes overlap, necessitating a clinical decision ordering the importance of overlapping structures. This frequently occurs in situations of prior irradiation and proximity of critical PRVs for the brainstem and spinal cord. It is common to find that PTVs are altered when overlap occurs, contravening the dictates of the ICRU reports.

Following completion of the GTV-CTV-ITV-PTV complex, planning is undertaken. While the quality of the achieved plan will be affected by the dosimetrist's experience and time, it will also be affected by instructions concerning what doses are acceptable. Overlapping OARs and PTVs are one such circumstance. However IMRT plan preparation is often an exercise in constraint relaxation and balancing objective which might not be explicit. The instruction "Parotid dose less than a mean of 26Gy" will achieve a dramatically different dose distribution to "Parotid dose less than a mean of 19Gy" or "Parotid dose ALARA please".[31] Indicating these requirements in a systematic fashion will improve communication, save time and produce more acceptable plans.

As often happens in radiotherapy, previous attempts to achieve this outcome have excluded oncologists. The overlap volume histogram (OVH) to describe the spatial configuration of an OAR with respect to a target was one such attempt, hypothesising that dose conformality around an OAR is related to the proximity of the OAR-PTV pair[31, 32]. The process used concentric rings to investigate what had been achieved in the past. The OVH measurement was able to differentiate plans which could be made much better (average parotid dose reduction of 6.6Gy, n=17) without PTV compromise[31]. Clearly, more informative delineation produces better plans[33].

Clinical compromises affect the dose distribution of a radiation plan [34, 35], but no specific structure has been proposed for oncologists to indicate the exact position and nature of the compromise, and no specific way for this to affect planning. The manual methods of manufacturing anisotropic margins based on the desire to spare OARs [36] and altering the PTV are unacceptable [30].

To assist in this circumstance, we propose the **Overlap Target Volume (OTV)** definition, a novel radiotherapy planning structure assigned by the radiation oncologist to help deal with specific issues of structure sparing without interfering with the formal correctness of the GTV-CTV-ITV-PTV chain.

2. Methods

Prospective and retrospective cases were identified where overlap occurred between a PTV and a PRV. A standard protocol was used to produce an Overlap Target Volume (OTV) without alteration to the PTV or PRV contour. Using Set Theory notation, this is represented:

$$OTV = PTV \cap PRV$$

Subsequently a dose was added to the name (e.g., OTV4500) to indicate the maximum dose permitted within this volume. The additional constraint applied for planning is that the minimum dose in OTV4500 should be 100cGy less, i.e., the OTV4500 volume should not contain more than 4500cGy and no less than 4400cGy.

2.1. Case 1

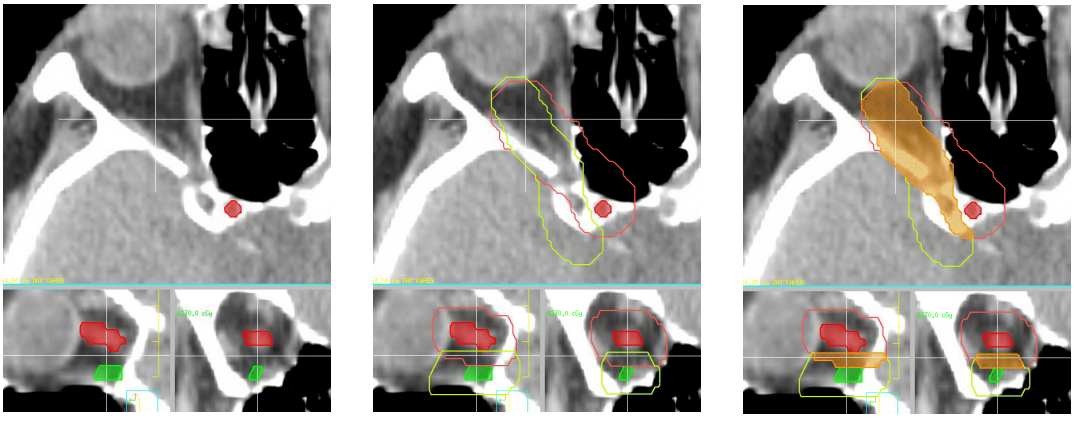
2.1.1. SCC of R cheek with PNI

Patient 1 was a 72 year old woman presented for an opinion about adjuvant radiotherapy following the complete resection of a moderately differentiated (G2) squamous cell carcinoma (SCC) of the right cheek overlying the infraorbital foramen (pT2 cN0 cM0) with extra-tumoral perineural infiltration 0.2mm from the deep margin. While the likelihood of perineural recurrence was low, any clinical perineural recurrence would be catastrophic and poorly salvaged even with heroic measures [37–39]. The radiation oncologist recommended treatment of the operative bed and course of CN V_2, while restricting CN II (OPTICN_R) to a tolerance dose of 45Gy.

The following figure 2 describes the process of definition the two cranial nerves and the overlap. One cranial nerve (CN V_2; GREEN) is at risk of perineural infiltration along its length stopping at the inferior orbital foramen at the posterior orbital cavity (Figure 1a). The CN V_2 is therefore a CTV.

The other cranial nerve (CN II; RED) is nearby, and the risk of blindness in the eye was designated as 'unacceptable'. The CN II is therefore a PRV (Figure 1b).

CN V_2 is expanded by a movement margin of 3mm to form the PTV6000, while CN II is expanded by the same movement margin of 3mm to form the OPTICN_R_PRV (Figure 2). Clearly the two expanded volumes overlap, and since blindness has been judged unacceptable, restriction of the PTV6000 dose coverage is required to meet the lower constraint of the OPTICN_R_PTV, and is visualised as the orange shaded OTV4500 (Figure 1c).



a. CTV (CN V_2); OAR (CN II) b. PTV6000; OPTICN_R_PRV c. OTV4500 (PTV6000∩OPTICN_R_PRV)

Figure 2: *Case 1*: Generation of CTV, OAR, PTV, PRV & OTV

2.1.2. Results

An IMRT plan was produced and assessed (Table 1 & 2), and illustrated with an axial view and the DVH below.

Volume Name	95% isodose	Volume	Volume covered by 95% isodose (%)
PTV6000	5700cGy	47.09 mLs	94.99%

Table 1: *Case 1*: Assessment of PTV coverage

Name	Volume	Maximum Dose	Minimum Dose	Notes
OPTICN_L	0.51 mLs	4568cGy	1028cGy	mean 3613cGy;
OPTICN_R	0.55 mLs	3242cGy	700cGy	mean 1802cGy
OTV4500	0.50 mLs	4616cGy	4402cGy	mean 4490cGy

Table 2: *Case 1*: Assessment of OAR & OTV coverage

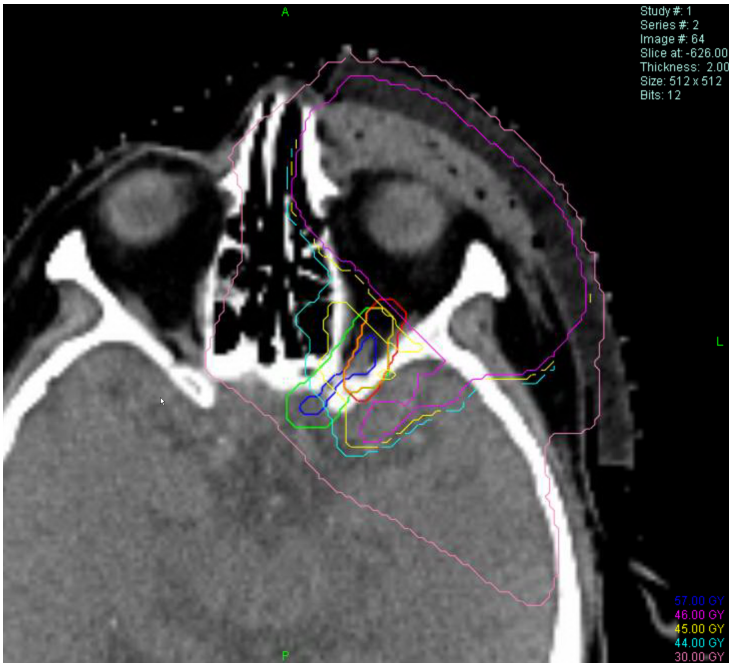


Figure 3: Case 1: the completed Plan (57Gy, 46Gy, 45Gy, 44Gy, 30Gy

2.2. Case 2

2.2.1. Overlapping treatments

Patient 2 was a 78 year old man treated 8 years previously with primary parotidectomy & right neck dissection and adjuvant radiotherapy (R NECK, 66Gy/33Fx) for unknown primary SCC of the neck (ICD10 C77.0).

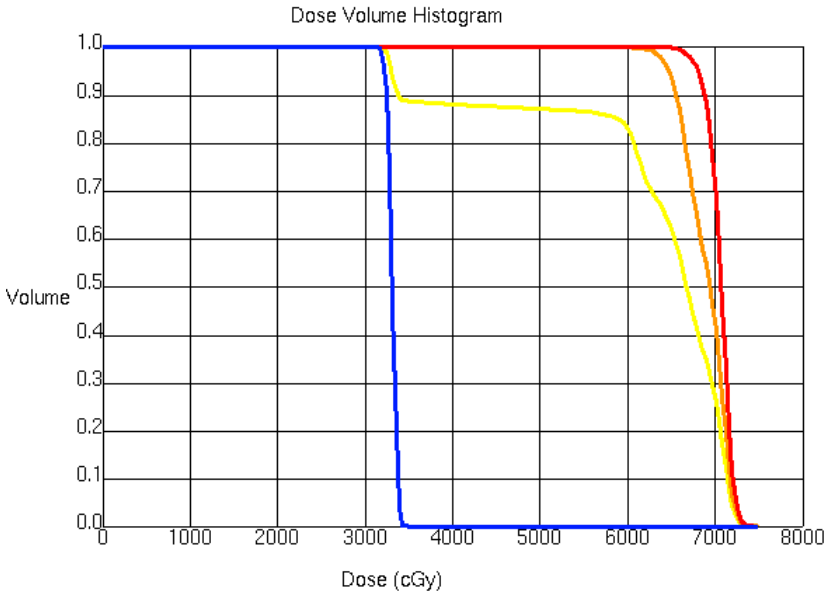


Figure 4: *Case 1*: DVH of completed Plan (PTV7000 - red; PTV6600 - orange; PTV6000 - yellow; OTV3300 - khaki

He subsequently presented after complete excision of two lesions from the right mid-back (27mm, G2 SCC R0; 8mm, G2 R0). At first surgical review, recurrence was clinically evident and at another operation 6 weeks after initial excision, 3 scar-based lesions measuring 47 mm, 17 mm and 10 mm were again completely excised. He was reviewed by a radiation oncologist 6 weeks later, where evidence of recurrence was again found.

The radiation oncology opinion advised salvage high dose radiotherapy in an attempt to eradicate the local disease. At simulation, the CT plan showed visible lymph nodes in the lateral axilla and a PTV was constructed to cover the entire R axilla/supraclavicular fossa (SCF). Overlay and fusion of the previous radiotherapy plan showed that the medial SCF had already received at least 5500cGy.

The previous plan was imported and fused with the contemporary plan. It was decided that the original high dose volume should be restricted to another 33Gy. The previous 5500cGy line was transposed into a current PTV5500_OLD volume. The intersection volume of PTV6000 (new) and PTV5500_OLD was designated OTV3300.

$$\text{OTV3300} = \text{PTV6000} \cap \text{PTV5500\_OLD}$$

The planning constraints were that OTV3300 should not exceed 3300cGy but not be less than 3200cGy.

2.2.2. Case 2

An IMRT plan was produced and assessed, and is illustrated with the DVH below (Figure 4) and an axial view (Figure 5).

The assessed values for the PTVs are provided in the first table 1, and for the OAR and OTV are provided in the second table 2. The dose constraints assigned to OTV3300 have been substantially achieved, as have the target coverage of PTV7000 and PTV6000.

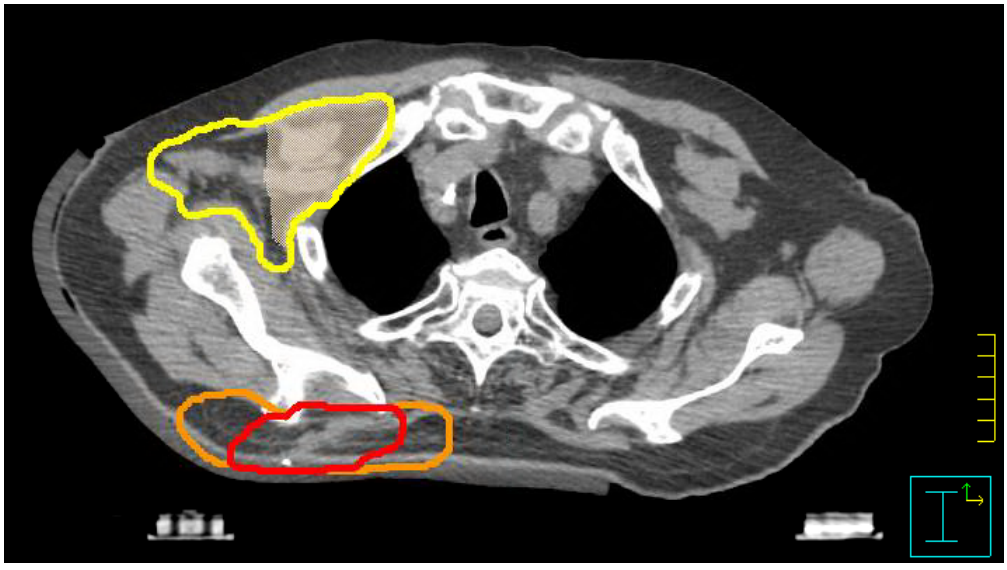


Figure 5: *Case 2*: Planning Targets (PTV7000 - red; PTV6600 - orange; PTV6000 - yellow; OTV3300 - khaki

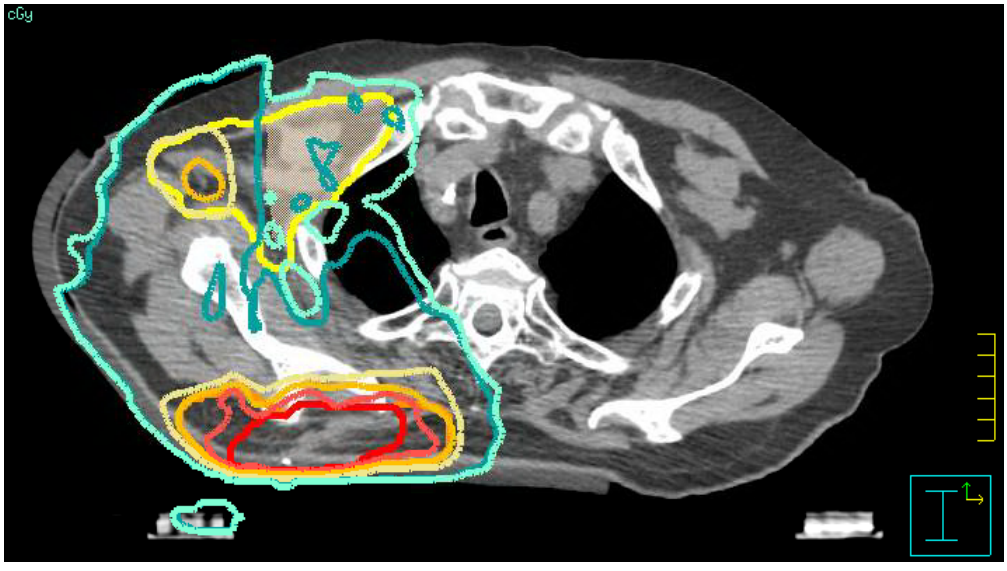


Figure 6: *Case 2*: the completed Plan (PTV7000–red, PTV6000–orange; 66.5Gy–tomato, 57Gy–khaki, 33Gy–teal, 32Gy–sky blue)

3. Discussion

During routine treatment planning, clinics have adapted various methods of dealing with the situation of PTV/PRV overlap, including manual alteration of the PTV. The production of an ancillary volume, the OTV, addresses this issue explicitly. The use of the OTV allows the PTV to remain unchanged, matching the definitions and intentions of all ICRU reports[1, 2]. As previously discussed [30], the PTV is a geometric expansion of clinical risk volumes (CTV). Once drawn, the CTV boundaries should not be altered because the clinical risk is not altered. Similarly, the PTV matches the underlying CTV. The PTV coverage does not need to be perfect for

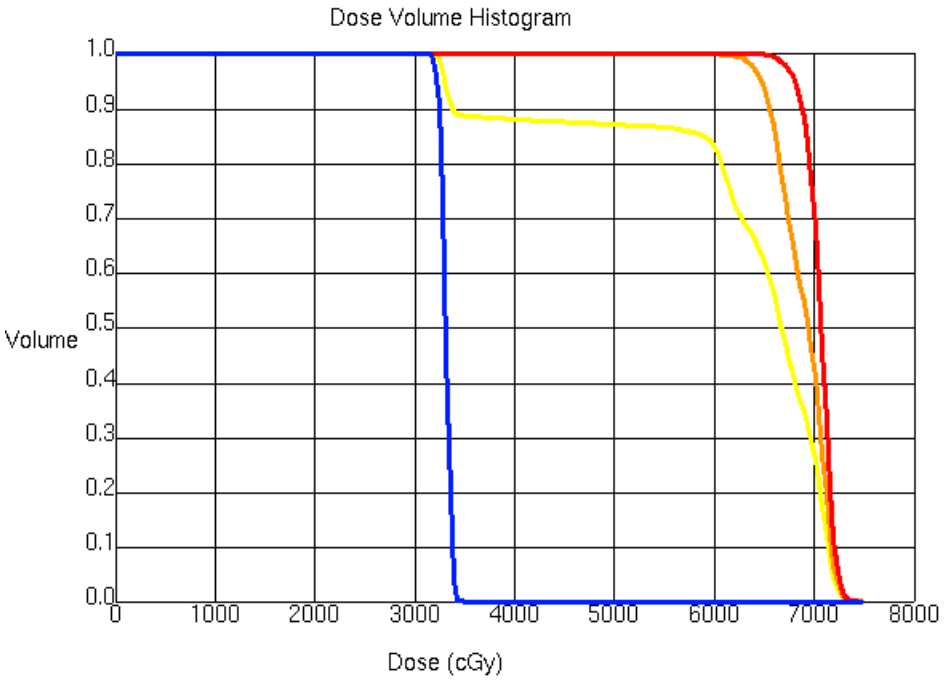


Figure 7: *Case 2*: DVH (PTV7000–red; PTV6600–orange; PTV6000–yellow; OTV3300–blue

Volume Name	95% isodose	Volume	Volume covered by 95% isodose (%)
PTV6000	5700cGy	993.45 mL	85.80%
PTV6600	6270cGy	629.71 mL	98.76%
PTV7000	6650cGy	363.50 mL	98.29%

Table 3: *Case 2*: Assessment of PTV coverage

Name	volume	Maximum Dose	Minimum Dose	Notes
LUNGS	2945.06 mL	6042 cGy	32 cGy	mean 1185 cGy; V_{20} = 17.91%
SPINALCANAL	75.40 mL	2949.7 cGy	24.9 cGy	mean 756 cGy
OTV3300	97.12 mL	3473 cGy	3027 cGy	3100 cGy covers 99.95% 3200 cGy covers 95.90% 3300 cGy covers 44.07% 3400 cGy covers 0.67%

Table 4: *Case 2*: Assessment of OAR & OTV coverage

a plan to be acceptable. After forming the PTV, clinical decision making and prioritisation during planning can result in reduced doses as overlapping volumes require.

The simplicity of the OTV is that it does not require any complex modification to previous volumes or complex mathematics. The addition of a dose within the OTV nomenclature, e.g., OTV4500, makes it patently clear

what is the intended maximum dose in the overlap area (4500cGy), and what is the minimum dose in the overlap area, e.g., 100cGy less at 4400cGy.

The dose gradients around the OTV are within the PTV (dose increase to target dose) and PRV (dose decrease to minimal). Clearly the width of these penumbral gradients will be in the order of 2-5mm.

The process of determining how to manage overlapping volumes is greatly helped by the analysis of two pieces of data. The first data item is the acceptability of the DVH for the PTV, and the second is the acceptability of the DVH for the OAR. There are four circumstances possible displayed in Table 5.

	PTV coverage ACCEPTABLE	PTV coverage DEFICIENT
OAR coverage ACCEPTABLE	acceptable target, acceptable OAR i.e., "**PERFECT**" plan	*deficient target, acceptable OAR* *i.e., "poor" plan, expect **RECURRENCE***
OAR coverage EXCESSIVE	*acceptable target, excessive OAR* *i.e., "poor" plan, expect **LATE EFFECT***	deficient target, excessive OAR **UNACCEPTABLE**, continue planning

Table 5: Possible Outcomes when planning to cover PTVs & PRVs

When the PTV and PRV overlap, a choice is required between 'deficient target, acceptable OAR' and 'acceptable target, excessive OAR', with the respective consequences of that choice being either an elevated recurrence rate, or an elevated late effects rate.

The 'acceptable target, excessive OAR' plan is easy to identify from the DVH of the OAR, and the rate of late effects determined from the clinical record. However, the 'deficient target, acceptable OAR' can only be identified from the DVH of the PTV **if the PTV has not been altered**. An altered PTV results in a "PERFECT" plan, i.e., acceptable target, acceptable OAR. Detecting an altered PTV could be automated, but would be difficult given the frequency of PTV-PRV overlaps.

Patterns of failure studies are very difficult to perform. Recurrence is one of the predictable outcomes of cancer treatment, and radiation plan construction has been shown to be a factor in ensuring locoregional control [40]. However, meaningful analysis requires that the site of recurrence be analysed with respect to the sites of original disease and sites of elevated risk [20, 41]. These pattern of failure studies need to be undertaken in the cases of PTV-PRV overlap, since it is only recurrences within the OTV and its penumbra which are pertinent to the decision of accepting a plan with a higher recurrence risk.

4. Conclusion

The Overlap Target Volume (OTV) is the volume of overlap between a high dose PTV based on a high risk CTV, and a dose restricted PTV based on a sensitive OAR.

This OTV definition provides a simple, standardised mechanism for adapting clinical treatments plans to common overlap problems that are not currently covered by the ICRU reports, while still maintaining the formal correctness of the anatomical definitions of the GTV and CTV, and the systematic expansion definitions of the ITV and PTV.

Using the OTV, a clear and explicit optimisation of the degree of OAR-sparing could be performed, the acceptability of a plan can be easily assessed, and future patterns of failure studies are enabled to accurately geographically assess the impact of dose sculpting in high risk regions.

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