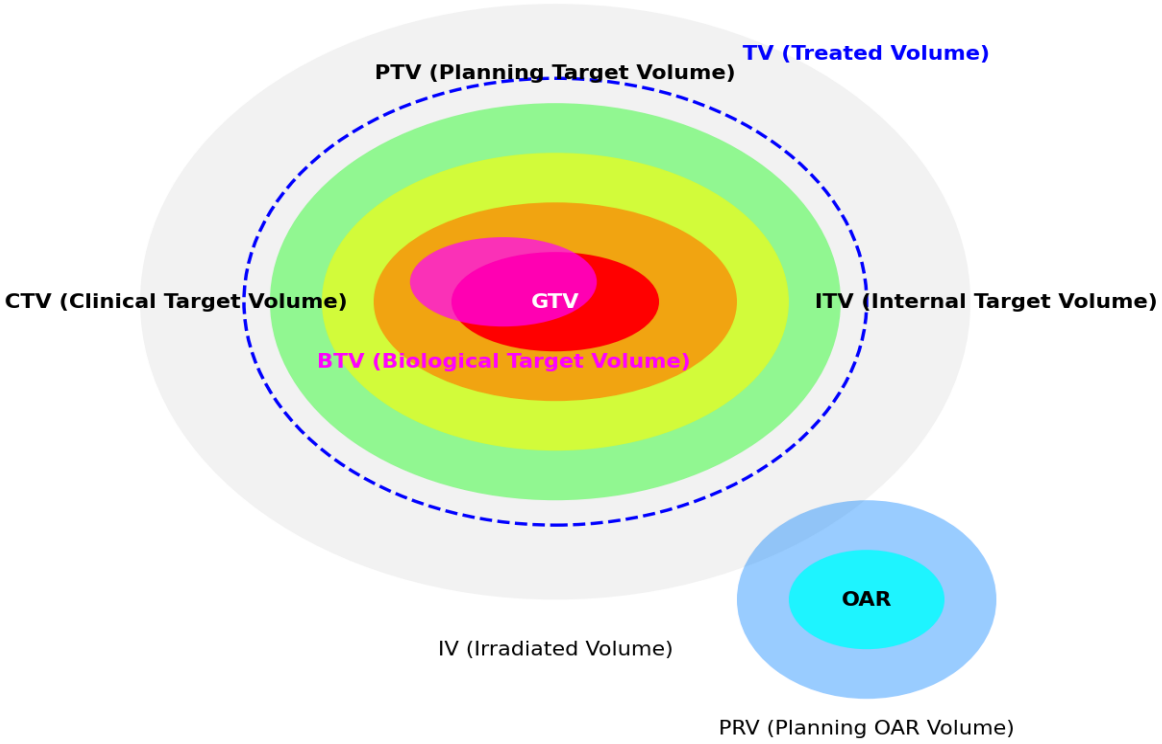
Radiotherapy Volume Relationships (Platy Graph)



Volume Type	Definition
GTV (Gross Tumor Volume)	Demonstrable tumor - what can be seen, palpated, or imaged
CTV (Clinical Target Volume)	GTV plus margin for subclinical microscopic disease spread
ITV (Internal Target Volume)	CTV plus internal margin (IM) for physiological variations
PTV (Planning Target Volume)	CTV/ITV plus margins for all geometrical variations to ensure dose delivery
BTV (Biological Target Volume)	Tumor volume delineated using functional/metabolic imaging (e.g., PET)
TV (Treated Volume)	Volume enclosed by isodose receiving prescribed dose
IV (Irradiated Volume)	Volume receiving significant dose relative to normal tissue tolerance
OAR (Organs at Risk)	Normal tissues whose radiation sensitivity influences treatment planning
PRV (Planning Organ at Risk Volum	OAR plus margin for geometric uncertainties

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Radiotherapy Target Volume Definitions

A Comprehensive Guide Based on ICRU Protocols

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1 Introduction

The precise definition of target volumes in radiotherapy represents one of the most critical steps in radiation treatment planning, directly impacting treatment efficacy and patient safety. The International Commission on Radiation Units and Measurements (ICRU) has established standardized terminology and protocols through a series of reports (ICRU 50, 62, 71, and 83) to ensure consistency across radiotherapy centers worldwide. This comprehensive guide examines the different types of volumes used in radiotherapy planning, their definitions according to ICRU protocols, the roles of medical physicists and oncologists, and the clinical application of these concepts.

Key Concept

The hierarchical relationship between different radiotherapy volumes shows how margins are progressively added from GTV to final treatment volumes according to ICRU protocols.

2 Historical Development and Evolution of Volume Definitions

The standardization of volume definitions in radiotherapy began in 1978 with the first ICRU report, which distinguished between target and treated volumes. However, significant evolution occurred in 1993 with **ICRU Report 50**, which introduced the foundational concepts of:

- **Gross Tumor Volume (GTV)**
- **Clinical Target Volume (CTV)**
- **Planning Target Volume (PTV)**

These definitions arose from the need to address confusion in radiotherapy reporting, as studies from the early 1990s revealed that only **42%** and **30%** of papers in leading radiotherapy journals provided acceptable and unambiguous information on volumes and dose specification.

The subsequent **ICRU Report 62 (1999)** refined these concepts by introducing the **Internal Target Volume (ITV)** and **Planning Organ at Risk Volume (PRV)**, and providing detailed guidance on margin calculations for both internal motion and setup uncertainties. This report was specifically triggered by the increasing availability of conformal radiotherapy techniques, where margins became more critical to treatment success.

Most recently, **ICRU Report 83 (2010)** addressed the specific needs of intensity-modulated radiation therapy (IMRT), recommending volume-based dose prescription and reporting rather than single-point specifications.

3 Primary Target Volumes: From Visible Tumor to Treatment Planning

3.1 Gross Tumor Volume (GTV)

Critical Definition

The GTV represents the foundation of all target volume definitions and denotes **demonstrable tumor**—what can be seen, palpated, or imaged.

This volume encompasses all clinically evident disease, including the primary tumor and any involved regional lymph nodes. The GTV is typically delineated by radiation oncologists using multiple imaging modalities, with computed tomography (CT) serving as the primary dataset, often supplemented by magnetic resonance imaging (MRI), positron emission tomography (PET), or other advanced imaging techniques.

The accuracy of GTV delineation directly affects all subsequent volumes and is considered **the most important step** in radiotherapy planning. Advances in diagnostic imaging have significantly contributed to improved GTV definition, though inter-observer variability remains a recognized challenge in clinical practice.

Special Case

Not all cases have a GTV—for example, in microscopic disease following complete surgical resection, no gross tumor may be visible, and treatment planning proceeds directly to CTV definition.

3.2 Clinical Target Volume (CTV)

The CTV extends beyond the GTV to encompass regions at risk for **subclinical microscopic disease spread** that cannot be fully imaged. This volume represents the tissue that must be adequately treated to achieve cure and includes the GTV (when present) plus a margin accounting for potential microscopic tumor extension.

The CTV margin varies significantly by tumor type, location, and biological behavior, typically ranging from **5 mm to 20 mm** depending on the clinical situation.

Clinical Examples of CTV Margins:
- Glioblastoma: 20 mm isotropic margin (EORTC recommendation)
- Head and Neck Cancers: 5-10 mm margins

The CTV definition remains one of the most challenging aspects of radiotherapy planning because it cannot be accurately defined for individual patients—radiation oncologists must rely on pathological studies, patterns of failure analyses, and clinical experience to determine appropriate margins.

3.3 Internal Target Volume (ITV)

The ITV concept, introduced in ICRU Report 62, addresses **physiological variations** in the size, shape, and position of the CTV during therapy. This volume encompasses the CTV plus an internal margin (IM) that accounts for:

- Respiratory motion
- Cardiac motion
- Bladder filling variations
- Rectum filling variations
- Peristalsis
- Other physiological processes

Clinical Application

The ITV is particularly critical for thoracic tumors, where respiratory motion can cause tumor displacement of **10-15 mm or more**.

For lung cancer, four-dimensional CT (4DCT) imaging captures tumor motion throughout the breathing cycle, allowing creation of an ITV that encompasses all positions of the CTV during

respiration. The internal margin is physiological in nature and does not depend on external uncertainties in patient setup or beam geometry—it is referenced to the patient's internal coordinate system.

Reporting of ITV is not considered compulsory according to the latest ICRU recommendations, and many centers incorporate the internal margin directly into the PTV expansion rather than contouring a separate ITV structure. However, for sites with significant organ motion, explicitly defining the ITV can improve treatment planning and dose reporting clarity.

3.4 Planning Target Volume (PTV)

Fundamental Concept

The PTV represents a **geometric concept** used for treatment planning to ensure the prescribed dose is actually delivered to the CTV with clinically acceptable probability.

This volume encompasses the CTV or ITV plus additional margins accounting for all geometrical variations and uncertainties, including:

- Setup margins (SM) for patient positioning errors
- Beam alignment uncertainties
- Treatment delivery variations

The PTV is linked to the reference frame of the treatment machine rather than patient anatomy, and as such may extend beyond anatomical barriers or even outside the patient's external contour.

3.4.1 Margin Calculation Formulas

The classic margin recipe developed by **van Herk and colleagues** provides a mathematical framework for PTV margin calculation:

$$M = 2.5\Sigma + 0.7\sigma$$

where:

- Σ = standard deviation of systematic errors
- σ = standard deviation of random errors

This formula is designed to ensure that **90% of patients** receive at least **95% of the prescribed dose** to the CTV.

Alternative Margin Formulas:

- Stroom formula: $M = 2\Sigma + 0.7\sigma$
- ICRU 62 recommendation: $M = 2\Sigma + 0.7{-}1.0\sigma$

These margins must account for both systematic errors (preparation errors that affect all fractions equally) and random errors (execution errors that vary fraction-to-fraction).

3.4.2 Clinical PTV Margins by Anatomical Site

The magnitude of PTV margins varies substantially by anatomical site and image guidance capabilities:

Anatomical Site	Margin Range	Conditions
Prostate	10-15 mm	Skin marks/bony anatomy
Prostate	5-8 mm	Daily CBCT imaging
Prostate	3 mm	Fiducial markers + real-time tracking
Brain tumors	3-5 mm	Thermoplastic mask immobilization
Lung SBRT	3-5 mm	Respiratory gating + 4DCT

3.5 Biological Target Volume (BTV)

Emerging Concept

While not part of the standard ICRU framework, the BTV has emerged as an important concept for incorporating functional and metabolic imaging into radiotherapy planning.

The BTV is delineated using positron emission tomography (PET), particularly with fluorodeoxyglucose (FDG-PET), which takes advantage of enhanced glucose metabolism in cancer cells to distinguish malignant from normal tissues.

3.5.1 BTV Delineation Methods

Various methods exist for BTV delineation:

1. **Fixed SUV thresholds** (e.g., SUV 2.0 or 2.5)
2. **Percentage of maximum SUV** (e.g., 40-50% of SUV_{max})
3. **Sophisticated algorithms** like PERCIST (PET Response Criteria in Solid Tumors)

However, significant controversy exists regarding optimal BTV definition methods, as different techniques can yield widely varying volume estimations.

Research Findings

Studies have demonstrated spatial mismatches between BTV and conventional CT-based volumes (ITV or GTV), with conformity indices often **less than 60%**.

For non-small cell lung cancer, researchers have proposed an **Internal Biological Target Volume (IBTV)** concept that combines ITV and BTV information, though this requires margins of approximately 13 mm to encompass 95% of the combined volume.

Despite these challenges, FDG-PET/CT has been shown to:

- ✔ Improve target definition accuracy
- ✔ Reduce inter-observer variability
- ✔ Potentially allow dose escalation to metabolically active regions

4 Dose-Related Volumes: Treated and Irradiated Volumes

4.1 Treated Volume (TV)

The treated volume is defined when the treatment planning procedure is complete and represents the tissue volume planned to receive **at least the dose selected and specified** by the radiation oncologist as appropriate to achieve the treatment purpose (tumor eradication or palliation).

This volume is enclosed by an isodose surface, typically the **95% isodose line**, corresponding to the minimum acceptable dose.

Ideally, the treated volume should conform closely to the PTV—a concept known as **conformal radiotherapy**. However, due to limitations in radiation delivery techniques and clinical compromises necessary to spare organs at risk, the treated volume often exceeds the PTV.

4.1.1 Conformity Index

The relationship between the treated volume and PTV is quantified using the conformity index (CI):

$$CI = \frac{TV}{PTV}$$

Interpretation:

- CI = 1.0: Ideal conformity
- $CI > 1.0$: TV exceeds PTV (excess normal tissue exposure)
- $CI < 1.0$: Inadequate PTV coverage

Typical Conformity Index Values:

- 3D Conformal RT (lung): 1.5 to 2.5
- IMRT/VMAT: 1.0 to 1.2

4.2 Irradiated Volume (IV)

The irradiated volume represents the tissue volume receiving a dose considered **significant in relation to normal tissue tolerance**. This volume is larger than the treated volume and depends on the treatment technique employed.

The definition of "significant dose" must be specified either in absolute values (Gray) or relative to the prescribed PTV dose, and varies by tissue type—for example, lung tissue has lower tolerance than muscle and therefore a lower threshold for defining the irradiated volume.

Important Paradox

Techniques using many beams (such as IMRT) can make the treated volume **smaller and more conformal** to the PTV while simultaneously making the irradiated volume **larger**, increasing the integral dose to surrounding normal tissues.

This trade-off between conformity and integral dose represents a fundamental consideration in treatment planning optimization.

5 Organs at Risk and Planning Organ at Risk Volume

5.1 Organs at Risk (OAR)

Organs at risk are normal tissues whose radiation sensitivity may significantly influence treatment planning and dose prescription. These structures, if irradiated, could suffer significant morbidity and thus must be carefully considered during treatment optimization.

Definition

In principle, all non-target tissues could be considered OARs, though in practice, the designation typically applies to specific critical structures based on the location of the target volume and the clinical situation.

5.1.1 Classification of OARs

OARs are classified as **serial** or **parallel** organs based on their functional organization:

Type	Examples	Characteristics
Serial Organs	Spinal cord, optic nerve, esophagus	Lose function if critical volume receives excessive dose
Parallel Organs	Lungs, liver, kidneys	Can tolerate higher doses to portions while maintaining function

5.1.2 Dose Reporting Recommendations

According to ICRU 83:

- **Serial organs:** Report near-maximum dose ($D_{2\%}$ or dose to 2% of organ volume)
- **Parallel organs:** Report mean dose and dose-volume metrics (e.g., V_{20} for lung)

5.2 Planning Organ at Risk Volume (PRV)

The PRV concept, analogous to the PTV for target volumes, adds a margin around an OAR to account for **geometric uncertainties** in organ position and shape.

This is particularly important for serial organs where damage to even a small volume could produce severe clinical manifestations, such as spinal cord myelopathy or optic nerve injury.

5.2.1 PRV Margin Formulas

For critical organs with maximum dose constraints:

Spinal Cord: $M = 1.6\Sigma + 0.2\sigma$

Ocular Structures/Optic Pathways: $M = 1.3\Sigma + 0.5\sigma$

5.2.2 Limitations of PRV Concept

Important Limitation

However, the PRV concept has significant limitations and is less universally applicable than the PTV concept.

For organs with dose-volume constraints (e.g., rectum, bladder), the PRV concept becomes problematic because adding a margin changes the organ volume in ways that make dose-volume constraints less meaningful.

For example, expanding the rectum by 5 mm uniformly changes both the volume and the three-dimensional dose distribution relationship, making it unclear how to apply constraints like "no more than 50% of rectum receiving 50 Gy".

Alternative Approaches

Consequently, alternative approaches such as **probabilistic planning** or **robust optimization** may be more appropriate for these structures than simple margin expansion.

6 Conclusion

The standardized definitions of target volumes and organs at risk established by ICRU reports represent the foundation of modern radiotherapy planning. Understanding the hierarchical relationship between GTV, CTV, ITV, PTV, and the various dose-related volumes is essential for:

- ✔ Accurate treatment planning
- ✔ Optimal dose delivery
- ✔ Minimizing toxicity
- ✔ Maximizing tumor control
- ✔ Consistency in reporting
- ✔ Quality assurance

As radiotherapy techniques continue to evolve with advances in imaging, treatment delivery, and motion management, these fundamental concepts remain critical for ensuring safe and effective cancer treatment.

☢

"Precision in definition leads to precision in treatment."

— Fundamental Principle of Radiotherapy Planning

Volume Type	Definition	ICRU Report	Primary User	Key Margins/Considerations
GTV (Gross Tumor Volume)	Demonstrable tumor - what can be seen, palpated, or imaged	ICRU 50, 62, 83	Oncologist	None - direct imaging
CTV (Clinical Target Volume)	GTV plus margin for subclinical microscopic disease spread	ICRU 50, 62, 83	Oncologist	Microscopic spread (typically 5-20mm)
ITV (Internal Target Volume)	CTV plus internal margin (IM) for physiological variations	ICRU 62, 83	Oncologist/Physici	Organ motion (breathing, bladder/rectum filling)
PTV (Planning Target Volume)	CTV/ITV plus margins for all geometrical variations to ensure dose delivery	ICRU 50, 62, 83	Physicist/Dosimetr	Setup errors + internal motion ($2.5\Sigma + 0.7\sigma$)
BTV (Biological Target Volume)	Tumor volume delineated using functional/metabolic imaging (e.g., PET)	Not ICRU standard	Oncologist/Nuclear Medicine	SUV thresholds (e.g., 40-50% SUV_{max})
TV (Treated Volume)	Volume enclosed by isodose receiving prescribed dose	ICRU 50, 62	Physicist	Reference isodose (typically 95%)
IV (Irradiated Volume)	Volume receiving significant dose relative to normal tissue tolerance	ICRU 50, 62	Physicist	Significant dose level (site-specific)
OAR (Organs at Risk)	Normal tissues whose radiation sensitivity influences treatment planning	ICRU 62, 83	Oncologist	Anatomical delineation
PRV (Planning Organ at Risk Volume)	OAR plus margin for geometric uncertainties	ICRU 62, 83	Physicist/Dosimetr	Setup + motion errors (smaller than PTV margins)

Table 1: Radiation Therapy Volume Definitions and Specifications