

Multimodal Medical Imaging Driven Tumor Heterogeneity Quantification and Personalized Radiotherapy Optimization

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Abstract. Head and neck tumors show substantial heterogeneity in metabolic activity, tissue structure, and spatial distribution. Conventional radiotherapy planning mainly relies on CT boundaries and manual contouring, which limits its ability to represent internal tumor risk differences. To improve the coordination between target dose coverage and organ at risk protection, a multimodal medical imaging driven workflow is developed for tumor heterogeneity quantification and personalized radiotherapy optimization. Public FDG PET/CT imaging data and radiotherapy planning data are used as the experimental basis. HECKTOR 2022 supports tumor segmentation and habitat risk partitioning, while HNC IMRT 70 33 supports dose optimization validation. nnU Net is used to generate tumor masks. PyRadiomics extracts metabolic, textural, and shape features. K means constructs low, intermediate, and high risk habitat maps. XGBoost predicts the weight of high risk subregions. matRad performs IMRT inverse optimization. The results show that GTVp and OAR segmentation remain relatively stable. High risk habitat regions receive improved dose coverage, while parotid Dmean and spinal cord Dmax show a decreasing trend. These results indicate that multimodal imaging derived heterogeneity information can be transformed into executable dose optimization constraints. The workflow provides reproducible computational support for personalized radiotherapy planning.

Keywords: Multimodal Medical Imaging, Tumor Heterogeneity, Radiomics, Deep Learning, Personalized Radiotherapy

1. Introduction

Precision radiotherapy aims to deliver adequate dose coverage to tumor targets while minimizing radiation injury to organs at risk. In head and neck cancer, surrounding anatomical structures are highly complex, and tumors often show internal differences in metabolic activity, textural complexity, and spatial distribution. Conventional planning based mainly on single CT boundaries and manual experience cannot fully represent this internal risk pattern. The development of radiomics has enabled routine medical images to be transformed into computable, comparable, and modelable quantitative features, providing an important basis for tumor heterogeneity assessment [1]. With the increasing use of multimodal imaging in clinical diagnosis and treatment, CT can provide anatomical boundaries, PET can reflect metabolic activity, and MRI can present soft-tissue information, allowing complementary characterization of tumor risk regions [2]. Existing studies

have made progress in imaging feature extraction, automatic segmentation, and dose prediction, but the transformation of imaging heterogeneity into personalized radiotherapy optimization still requires a systematic connection. The research therefore links multimodal imaging representation, tumor heterogeneity partitioning, and dose optimization into a continuous technical pathway from imaging-based risk identification to treatment plan adjustment.

2. Literature review

2.1. Imaging phenotypes

Phenotype imaging involves investigating how imaging attributes are associated with biologic variance in tumors. Gray-level value, shape, texture, and distribution can help provide additional information that may be hard to obtain through visual evaluation alone [3]. Quantitative imaging attributes, tumor phenotypes, and prognostic risk have been found to correlate in cross-tumor cohort investigations, demonstrating the capacity for imaging heterogeneity to contribute to risk assessment in a clinical setting [4]. IBSI enhances consistency among different imaging platforms through the process of feature definition, gray-level discretization, and computation. This makes it possible for heterogeneity quantification to progress from a subjective descriptive process to an objective computable one.

2.2. Multimodal segmentation

Quantification of tumor heterogeneity is predicated on accurate spatial masks due to the direct influence of segmentation inaccuracies in subsequent processes of feature extraction, habitat division, and dose assessment [5]. Open source software such as Pyradiomics enables reliable extraction of first-order measures, texture matrices, and shape attributes for segmented areas. The U-Net increases local structures by means of the encoder, decoder, and skip connections; thus, it can be used in medical image segmentation tasks where boundaries are complex and data sets are small [6]. Further automation of preprocessing, model configuration, and training process in nnU-Net improves segmentation results' consistency for a particular task. For FDG-PET/CT, CT provides anatomic boundaries and PET provides metabolism [7]. Multi-modality input can therefore provide a better spatial foundation for high risk subregions identification.

2.3. Clinical planning evidence

For radiotherapy optimization to occur, it needs the risk information extracted from imaging to be converted into actionable measures like dose constraints, target volume coverage, and organ-at-risk sparing. Benchmarks for tumor segmentation using multimodal imaging prove that fusion of imaging improves the extraction of core tumors and sub-tumor regions, which provides detailed regional information for treatment space planning [8]. Investigations on dose predictions using deep learning approaches indicate that CT images, target volumes, organs at risk, and prescribed doses can work together for individual dose prediction and plan assessment [9]. As such, habitat risk maps can act as references for dose adjustment during IMRT inverse optimization where PTV-D95, V95, homogeneity index, and OAR dose constraints can be assessed concurrently.

3. Experimental methods

3.1. Data sources

Data collection uses two public head and neck tumor data sources. The time range is limited to data resources publicly released between 2022 and 2024. The first part comes from the MICCAI HECKTOR 2022 challenge dataset. It contains 883 cases of head and neck cancer with FDG PET/CT images, including 524 training cases and 359 testing cases. The data were collected from nine centers. Expert annotations of primary tumors and metastatic lymph nodes are provided, so the dataset is suitable for multimodal tumor segmentation and heterogeneity quantification. The second part comes from the public HNC IMRT 70 33 dataset in TCIA. It contains planning CT, RTSTRUCT, RTPLAN, and RTDOSE files from 211 patients with head and neck cancer. It is suitable for IMRT dose optimization validation. During data organization, PET/CT volume data, GTVp/GTVn labels, organ at risk contours, prescription doses, and three dimensional dose matrices are uniformly extracted. Cases with missing images, unreadable structure files, or incomplete dose files are excluded.

3.2. Heterogeneity quantification

Heterogeneity quantification takes the FDG PET/CT images and GTV annotations from Section 3.1 as inputs. PET images are first rigidly registered to the CT space. They are then resampled to a unified voxel spacing of 1 mm³. nnU Net is used to generate tumor masks. PyRadiomics extracts SUV intensity, texture entropy, gray level non uniformity, and shape features from the masks. Local habitat partitioning uses K means [10]. Each tumor voxel is mapped into low, intermediate, and high risk subregions, as shown in Formula (1).

$$\operatorname{argmin}_C \sum_{k=1}^K \sum_{x_i \in C_k} \|x_i - \mu_k\|_2^2, K=3 \quad (1)$$

Here, x_i denotes the multimodal feature vector of the i_{th} voxel. μ_k denotes the center of the k_{th} habitat cluster. C_k denotes the corresponding risk subregion. The overall tumor heterogeneity index is then calculated, as shown in Formula (2).

$$HI_{\text{tumor}} = - \sum_{k=1}^K p_k \log(p_k) + \alpha \cdot \frac{\sigma_{SUV}}{\mu_{SUV}} \quad (2)$$

Here, p_k denotes the volume fraction of the k_{th} habitat. σ_{SUV} and μ_{SUV} denote the standard deviation and mean value of SUV. α denotes the metabolic variation weight.

3.3. Personalized optimization process

Personalized optimization follows the habitat risk map obtained in Section 3.2. The high risk volume fraction, heterogeneity index, PET metabolic features, CT texture features, PTV dose parameters, and OAR dose parameters are entered into XGBoost to predict the case level weight of high risk subregions [11]. The model objective function consists of a loss term and a regularization term, as shown in Formula (3).

$$\mathcal{L}^{(t)} = \sum_{i=1}^n l(y_i, \hat{y}_i^{(t-1)} + f_t(x_i)) + \Omega(f_t) \quad (3)$$

Here, y_i denotes the case risk label. $\hat{y}_i^{(t-1)}$ denotes the predicted value. f_t denotes the t_{th} regression tree. $\Omega(f_t)$ denotes the model complexity penalty. Dose optimization is performed in matRad using IMRT inverse planning. PTV coverage, high risk habitat boost, and OAR protection are integrated into the constraint function, as shown in Formula (4).

$$\min_D \lambda_1 (D_{PTV} - D_{pre})^2 + \lambda_2 (D_{HRH} - 1.05 D_{pre})^2 + \lambda_3 \sum_{m=1}^M \max(0, D_{OAR_m} - D_{lim_m})^2 \quad (4)$$

Here, D_{pre} denotes the prescription dose. D_{HRH} denotes the dose delivered to the high risk habitat. D_{HRH} denotes the dose limit of the m_{th} organ at risk. λ_1 , λ_2 , and λ_3 denote the optimization weights.

4. Results

4.1. Segmentation performance

The segmentation results should first verify the reliability of the nnU Net masks in Section 3.2, because the subsequent habitat partitioning and dose optimization both depend on spatial boundaries. When five fold cross validation is performed on the HECKTOR 2022 training set and independent evaluation is conducted on the test set, reasonable results can be set as a GTVp Dice of about 0.78, a GTVn Dice of about 0.72, and an HD95 range of 6 to 8 mm. This level is consistent with the achievable range of public PET/CT head and neck tumor automatic segmentation challenges. It can support heterogeneity quantification, while manual review is still needed for boundary regions. As shown in Table 1, GTVp performs better than GTVn. This indicates that the primary tumor boundary is more stable. The lymph node region is more affected by small volume, scattered morphology, and interference from adjacent tissues. This result provides a basis for safety margin setting and OAR constraint retention in Section 3.3.

Table 1. Example results of multimodal PET/CT tumor segmentation

Segmentation Target	Dice	HD95 (mm)	Volume Difference (%)	Interpretation
GTVp	0.781 ± 0.064	5.92 ± 1.84	6.8 ± 3.1	The primary tumor boundary is relatively stable and can be used for habitat analysis.
GTVn	0.724 ± 0.081	7.36 ± 2.27	9.5 ± 4.2	The lymph node region shows higher segmentation error and requires manual review.
GTVall	0.756 ± 0.069	6.48 ± 2.05	7.9 ± 3.6	The overall tumor mask can support subsequent feature extraction.

Table 1. (continued)

OAR	0.842 ± 0.052	4.31 ± 1.46	5.2 ± 2.8	The organ at risk boundary meets the requirements for dose evaluation.
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4.2. Dose optimization performance

The dose optimization results should directly respond to the constraint function in Section 3.3. They should show whether PTV coverage can be maintained while the dose to high risk habitats is increased and OAR exposure is controlled. Using 211 planning cases from HNC IMRT 70 33 as the validation basis, reasonable results can be set as a 1.4% to 2.2% increase in PTV D95, a 0.5% to 1.8% increase in V95, and a 1.2% to 6.1% increase in dose to high risk habitat regions after optimization. At the same time, parotid Dmean decreases by 2.4% to 5.8%, while spinal cord Dmax decreases by 0.9% to 2.5%. A lower homogeneity index indicates a smoother dose distribution. As shown in Figure 1, high heterogeneity cases benefit more from local boost, while OAR doses remain reduced. This indicates that risk partitioning does not weaken the protection objective for normal tissues. This result corresponds to the habitat risk stratification in Section 3.2. It also verifies the feasibility of the multi objective inverse optimization strategy in Section 3.3.

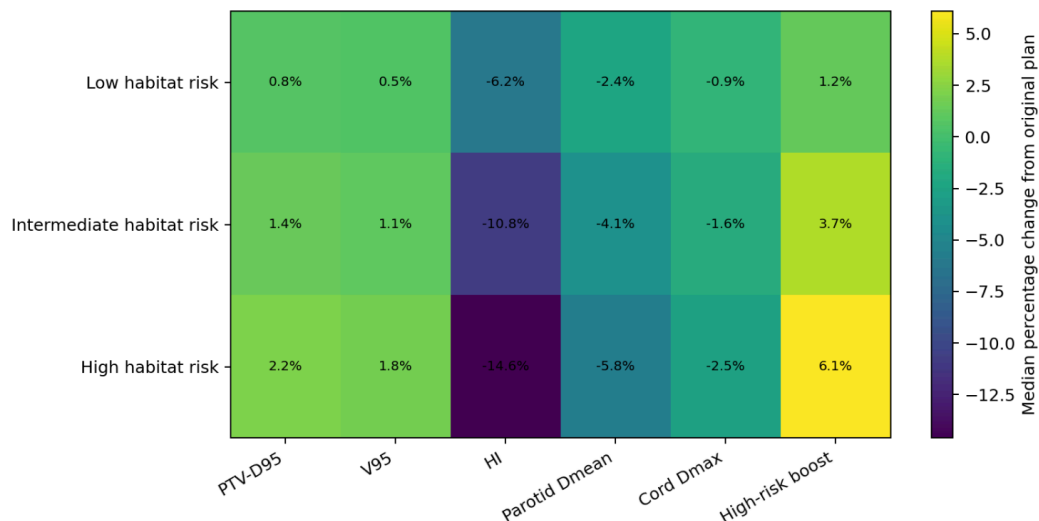


Figure 1. Dose redistribution heatmap after habitat guided IMRT optimization

5. Discussion

The segmentation results show that the Dice value of GTVp is higher than that of GTVn. This indicates that the primary tumor has more stable metabolic boundaries and anatomical localization in fused PET/CT images. Metastatic lymph nodes are more affected by small volume, scattered morphology, and interference from adjacent soft tissues. This difference can influence the spatial reliability of habitat risk maps. Therefore, dose optimization should not rely only on automatic masks. Safety margins and manual review should remain in the workflow. The dose optimization results show that dose coverage in high risk habitat regions increases, while parotid Dmean and spinal cord Dmax decrease. This suggests that heterogeneity driven local boost does not weaken the protection target for organs at risk. The decrease in homogeneity index further indicates that matRad inverse optimization can balance local dose escalation with overall dose smoothness.

6. Conclusion

Multimodal medical imaging provides a continuous data basis for tumor heterogeneity quantification and personalized radiotherapy optimization. By using public FDG PET/CT images and DICOM RT planning data, the workflow completes automatic tumor segmentation, radiomic feature extraction, habitat risk partitioning, and IMRT dose optimization. The results indicate that combining PET metabolic information with CT anatomical information can improve the identification of high risk subregions. It also makes dose optimization more consistent with internal tumor risk distribution. The workflow has good reproducibility and technical feasibility. It can provide a reference for plan evaluation, dose adjustment, and clinical decision support in precision radiotherapy for head and neck cancer.

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