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Tumor heterogeneity in clinical interpretation of PET/CT imaging: evaluation of metabolic tumor volume, total lesion glycolysis, and standardized uptake value

Abstract

Tumor heterogeneity, defined as the biological variability within a single tumor or across different lesions in a patient, is a critical challenge in oncology due to its influence on prognosis and treatment response. This variability encompasses genetic, epigenetic, and phenotypic differences, enabling tumors to adapt and resist conventional therapeutic interventions. Understanding this internal variability is fundamental to designing effective treatment strategies, and advanced imaging studies, such as positron emission tomography combined with computed tomography (PET/CT), provide an indispensable tool to map these differences and guide treatment planning. In the assessment of PET/CT images, quantitative parameters such as Metabolic Tumor Volume (MTV), Total Lesion Glycolysis (TLG), and Standardized Uptake Value (SUV) play a key role in interpreting tumor heterogeneity. These parameters not only allow for a precise quantification of tumor burden but also aid in identifying subpopulations of cells within the tumor with varying levels of aggressiveness or resistance to treatment. These parameters are essential for imaging specialists to understand the tumor's complexity and to develop a more accurate clinical interpretation tailored to each patient's unique tumor biology. The integration of MTV, TLG, and SUV in PET/CT clinical evaluations facilitates the adaptation of treatments to the tumor's metabolic profile, optimizing therapeutic effectiveness and enabling the identification of tumors with a high potential for resistance and progression.

Keywords: cancer heterogeneity, genetics, epigenetics, mutations

Volume 7 Issue 1 - 2024

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Received: October 28, 2024 | **Published:** November 04, 2024

Introduction

Tumor heterogeneity, which encompasses genetic, epigenetic, and phenotypic variations within a single tumor or across different lesions in a patient, presents a crucial challenge in oncology. These differences allow tumor subpopulations to develop adaptations that facilitate progression, treatment resistance, and immune evasion, complicating cancer diagnosis and management.[1,2] In this context, advanced imaging techniques, such as PET/CT (Positron Emission Tomography with Computed Tomography) and PET/MRI (Positron Emission Tomography with Magnetic Resonance Imaging), have gained prominence for offering an in-depth view of tumor biology and internal functionality. These tools enable not only visualization of the tumor but also quantification of its metabolic activity and extent using specific parameters like MTV, SUV, and TLG. Interpreting these values facilitates the identification of tumor subregions with distinct biological behaviors, which is essential for personalizing each patient's treatment strategy.[3] Accurate interpretation of these parameters allows the radiologist to tailor conclusions to each tumor's specific characteristics.[4] With a deep understanding of MTV, SUV, and TLG values, radiologists can identify areas of high aggressiveness or resistance, guide real-time clinical decisions, and collaborate with the oncology team in planning targeted therapies. This approach enables a comprehensive assessment that goes beyond structural imaging, optimizing treatment response monitoring and patient prognosis. The ability to interpret these metrics based on tumor heterogeneity makes the radiologist a key figure in modern oncology, where precise detection and analysis of tumor behavior are essential for successful treatment.[1,2]

Tumor heterogeneity in oncology

Tumor heterogeneity refers to the biological variability in the composition and activity of cells within a single tumor or across different lesions in a patient. This characteristic has become a central focus in oncology as it significantly impacts cancer progression and treatment response.

Clinical analysis

From a clinical perspective, tumor heterogeneity influences patient prognosis and therapeutic strategy. Tumors with a high degree of heterogeneity exhibit variability in treatment response, as different cellular subpopulations within the tumor may react differently to chemotherapy, radiotherapy, or targeted therapies. This phenomenon increases the risk of relapse and treatment resistance since the more resistant cells may survive initial treatment, proliferate, and contribute to disease progression. Additionally, this heterogeneity affects the effectiveness of imaging studies such as PET/CT, as the uptake of metabolic tracers varies across different tumor regions. This variation can indicate areas of high aggressiveness or treatment resistance. Identifying these sub-regions is crucial for planning localized or combined treatments that can effectively target the most active areas and reduce the risk of metastasis.

Pathological analysis

Pathologically, tumor heterogeneity manifests as morphological, genetic, and molecular differences among cellular subpopulations. This phenomenon arises from genetic alterations, such as mutations and copy number variations, which create cells with different degrees of proliferation, metabolism, and aggressiveness. There are also epigenetic differences, such as DNA methylation and histone modifications, which influence gene expression without changing the DNA sequence, thus contributing to the tumor's functional diversity. This heterogeneity provides an evolutionary advantage for the tumor, allowing it to adapt and survive in various microenvironments within the body. In oncological pathology, identifying this cellular variability is essential, as it enables the classification of the tumor based on its aggressiveness level and the selection of specific treatments tailored to unique cellular subpopulations (Table 1).[3,5]

Table 1 Challenges in evaluating tumor heterogeneity in imaging.

Challenge	Description
Tumor Internal Variability	Differences in metabolism, cell proliferation, and treatment resistance within a single tumor make it challenging to precisely characterize each cellular subpopulation, affecting the ability to identify regions of high aggressiveness and adjust treatment accordingly.
Genetic and Epigenetic Diversity	Genetic and epigenetic variability within the tumor creates subregions with unique biological characteristics, complicating predictions of disease progression and the effectiveness of therapeutic interventions.
Standardization of Quantification Methods	Differences in imaging techniques and protocols across centers result in inconsistencies in data interpretation, affecting the accuracy and consistency needed for personalized treatment planning.

PET/CT in tumor heterogeneity assessment using MTV, TLG, and SUV

PET/CT enables a detailed assessment of tumor heterogeneity by quantifying essential parameters such as Metabolic Tumor Volume (MTV), Total Lesion Glycolysis (TLG), and Standardized Uptake Value (SUV). These metrics offer precise insights into internal tumor variability, guiding personalized therapeutic decisions (Table 2). Tumor heterogeneity reflects the internal diversity in tumor activity and cellular composition. PET/CT parameters, such as Metabolic Tumor Volume (MTV), Total Lesion Glycolysis (TLG), and Standardized Uptake Value (SUV), are essential for capturing this variability, as each parameter emphasizes distinct aspects of tumor biology. For example, MTV identifies the extent of metabolically active areas, TLG shows the total burden of glycolytic activity, and SUV detects uptake differences among specific subregions. Together, these values provide a comprehensive view of tumor heterogeneity, helping specialists tailor treatments to the unique characteristics of each tumor, thereby improving therapeutic efficacy and prognosisical.[6]

Table 2 Key PET/CT parameters for evaluating tumor heterogeneity.[3,5]

Parameter	Definition and Relevance
Metabolic Tumor Volume (MTV)	MTV measures the volume of metabolically active tumor tissue, crucial for assessing disease extent. High MTV values correlate with significant tumor burden and aggressive prognosis. Clinically, elevated MTV often suggests the need for intensive treatment, reflecting the extent and activity of more aggressive tumor subpopulations.
Total Lesion Glycolysis (TLG)	TLG combines tumor volume with average metabolic activity (SUV), providing an integrated measure of the lesion's glycolytic burden. Particularly useful in tumors with diffuse metabolic activity, high TLG signals significant tumor burden and an aggressive profile, potentially guiding intensified treatment, especially in large, metabolically active tumors.
Standardized Uptake Value (SUV)	SUV measures tracer uptake in specific areas, allowing for the assessment of metabolic activity in different tumor subregions. Though essential for pinpointing highly aggressive areas, SUV has limitations such as dependence on technical factors (e.g., equipment calibration, acquisition time) and variability across lesions. Interpretation is more accurate when supplemented with MTV and TLG for a full understanding of tumor complexity.

Clinical implications of PET/CT in tumor heterogeneity evaluation through MTV, TLG, and SUV

The ability of PET/CT to characterize tumor heterogeneity using parameters such as Metabolic Tumor Volume (MTV), Total Lesion Glycolysis (TLG), and Standardized Uptake Value (SUV) has profound clinical implications, as it allows treatment to be tailored to the specific tumor biology of each patient. These quantitative values assist clinicians in assessing tumor aggressiveness, evaluating treatment response, and determining the need for additional therapeutic interventions or adjustments in treatment strategy.

The use of PET/CT in this context enables:

Treatment personalization: By evaluating specific metabolic profiles, clinicians can select and adjust intensive or targeted therapies according to areas of higher tumor activity.

Monitoring treatment response: Variation in these parameters across serial studies allows for observation of changes in tumor burden and enables real-time treatment adaptation, optimizing therapeutic efficacy.

Prognosis and follow-up planning: These values also provide insight into the likelihood of disease progression and aid in establishing follow-up intervals, maximizing early detection of recurrences or resistance to therapy.

Below are examples of distinct profiles of MTV, TLG, and SUV and how they guide therapeutic decision-making in clinical practice.[3,6]

Clinical Scenarios with Combinations of MTV, TLG, and SUV

Scenario 1: High MTV, Low TLG, High SUV

Interpretation: A high MTV indicates a significant amount of metabolically active tumor tissue, while a low TLG suggests that the overall metabolic activity is moderate. However, a high SUV in specific regions reflects localized areas of high aggressiveness within a generally low-metabolism tumor.

Citation: Colmenter L, Bernal L, Zuniga S. Tumor heterogeneity in clinical interpretation of PET/CT imaging: evaluation of metabolic tumor volume, total lesion glycolysis, and standardized uptake value. *Int J Mol Biol Open Access*. 2024;7(1):140–143. DOI: 10.15406/ijmboa.2024.07.00184

Clinical Application: This pattern may indicate a heterogeneous tumor where certain regions are highly metabolically active, but the overall activity volume is limited. This finding may guide treatment toward focused therapies in high-uptake areas, with follow-up monitoring of the less active zones.

Scenario 2: High MTV, High TLG, High SUV

Interpretation: In this case, the tumor exhibits a large metabolic volume (MTV), a high total glycolytic load (TLG), and elevated SUV. This combination suggests a tumor that is not only large but also aggressive and metabolically active throughout.

Clinical Application: This profile is typically associated with a highly aggressive, fast-growing tumor, indicating the need for intensive or combined treatments (e.g., chemotherapy, immunotherapy, and possibly radiotherapy). This scenario may also justify prioritizing treatments targeting tumor metabolism.

Scenario 3: Low MTV, Low TLG, Low SUV

Interpretation: A tumor with low MTV, TLG, and SUV reflects a small tumor volume with low metabolic activity, which is common in low-grade or slow-growing tumors.

Clinical Application: The low activity and volume suggest a less intensive treatment approach, with possible options for active surveillance, especially for indolent tumors. However, periodic monitoring of activity is essential to detect any changes in tumor behavior.

Scenario 4: High MTV, High TLG, Low SUV

Interpretation: This combination suggests a large amount of tumor tissue, but with moderate average metabolic activity (high TLG) and low maximum uptake (low SUV). It may indicate a tumor with homogeneous, low-intensity activity.

Clinical Application: This pattern may be associated with tumors of moderate growth, with a risk of progression if uncontrolled. Treatment can focus on strategies to reduce tumor volume (e.g., surgery or radiotherapy), with monitoring of uptake areas to adjust therapy if activity changes.

Scenario 5: Low MTV, High TLG, High SUV

Interpretation: This pattern reflects a small tumor volume but with high glycolytic load and high maximum uptake in specific areas, suggesting a small lesion with focal high aggressiveness.

Clinical Application: This profile may indicate a focal aggressive lesion requiring immediate treatment to prevent progression. The combination of elevated TLG and SUV in a small mass may justify targeted interventions, such as ablation or focal radiotherapy.[7]

Clinical applicability of these scenarios

The variability in MTV, TLG, and SUV values enables a detailed evaluation of tumor heterogeneity and aggressiveness, which is crucial for therapeutic decision-making. Each parameter combination provides a distinct "metabolic signature" of the tumor, assisting clinicians in understanding disease dynamics and tailoring treatment accordingly.

Treatment Personalization: By identifying highly active areas within a tumor with either high or low MTV, clinicians can select targeted therapies, such as focused radiotherapy or ablation, for the most active regions. This approach optimizes treatment efficacy while minimizing adverse effects.[8]

Monitoring Treatment Response: Serial studies that track changes in these parameters allow clinicians to assess whether a treatment effectively reduces tumor burden and aggressiveness. Decreases in TLG and SUV in specific areas indicate a favorable response, while increases may signal progression or resistance.[8]

Prognosis and Follow-up Planning: Tumors with high MTV and TLG profiles have a higher likelihood of recurrence and rapid progression, necessitating intensive planning. Conversely, low MTV and TLG profiles may support a less aggressive treatment approach and a monitoring strategy.[8]

Selection of Targeted or Combined Therapies: In cases where a tumor displays metabolic heterogeneity (e.g., high SUV in some regions and low in others), a combination of chemotherapy for less active regions and targeted therapies for high-uptake zones may improve outcomes by addressing resistant tumor subpopulations.[8]

Additional parameters for studying tumor heterogeneity

Within PET/CT imaging for assessing tumor heterogeneity, several additional parameters are in development:

Texture Analysis: Quantifies tumor heterogeneity using metrics such as entropy, which reflects the complexity and dispersion of tumor uptake within the image.

SUV Variability: By measuring SUV fluctuations across the tumor volume, this parameter highlights metabolically active subregions and may correlate with specific treatment responses.

Perfusion Parameters: Evaluating tumor blood flow and vascularization offers insights into nutrient and oxygen distribution, key factors in tumor aggressiveness.

Diffusion in PET-MRI (ADC): Measures cellular density, differentiating viable from necrotic areas, essential for understanding heterogeneous tumors.[1]

Conclusion

Accurate interpretation of quantitative PET/CT parameters, such as Metabolic Tumor Volume (MTV), Total Lesion Glycolysis (TLG), and Standardized Uptake Value (SUV), is essential for clinical applicability in managing tumor heterogeneity. The imaging specialist's ability to analyze these values and understand their implications not only enables personalized treatment but also allows for anticipating tumor progression and adapting monitoring and therapy based on changes observed in serial studies. In this context, the imaging specialist serves as an essential mediator between imaging data and clinical decision-making, providing a detailed evaluation that guides oncologists in selecting specific therapeutic strategies for each active or resistant tumor subpopulation. Correctly interpreting values such as high MTV or TLG in specific regions allows the clinician to prioritize treatments targeting areas with high metabolic uptake, thereby optimizing treatment efficacy and minimizing side effects. Similarly, observing intratumoral heterogeneity-such as SUV variability across different regions-can alert clinicians to more aggressive cell subpopulations, guiding the approach toward combined and personalized therapies that enhance overall therapeutic effectiveness. Thus, the clinical interpretation and application of these advanced PET/CT parameters offer a more precise understanding of tumor biology and support a precision medicine model in oncology.

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Acknowledgments

None.

Conflicts of interest

The authors declared that there are no conflicts of interest.

References

1. Buvat I, Orlhac F, Soussan M. Tumor texture analysis in PET: where do we stand? *J Nucl Med.* 2015;56(11):1642–1644.
2. What is tumor heterogeneity? Memorial Sloan Kettering Cancer Center. 2024.
3. Ottaiano A, Ianniello M, Santorsola M, et al. From chaos to opportunity: decoding cancer heterogeneity for enhanced treatment strategies. *Biology.* 2023;12(9):1183.
4. Zaidi H, Burger IA. PET/MRI: reliability/reproducibility of SUV measurements in oncology. *Cancer Imaging*. 2022. pp. 97–114.
5. Nioche C, Orlhac F, Boughdad S, et al. A freeware for tumor heterogeneity characterization in PET, SPECT, CT, MRI and US to accelerate advances in radiomics. *J Nucl Med*. 2017;58:1316.
6. Proietto M, Crippa M, Damiani C, et al. Tumor heterogeneity: preclinical models, emerging technologies, and future applications. *Front Oncol.* 2023;13:1164535.
7. Sharma A, Mohan A, Bhalla A, et al. Role of metabolic tumor volume (MTV) and standardized uptake value (SUV) based parameters derived from whole body (WB) 18F-FDG PET/CT in interim treatment response assessment of NSCLC. *J Nucl Med*. 2019;60:1326.
8. Hack RI, Becker AS, Bode LB, et al. When SUV matters: FDG PET/CT at baseline correlates with survival in soft tissue and Ewing sarcoma. *Life*. 2021;11(9):869.