Voxel-wise Dose Heterogeneity Following Yttrium-90 Glass Microsphere Radioembolization in HCC: Association with Pretreatment Tc-99m MAA SPECT/CT Tumor-to-Normal Ratio

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Introduction

- Yttrium-90 transarterial radioembolization (Y^{90} TARE) is a form of locoregional therapy for hepatocellular carcinoma (HCC)[1]. However, treatment success depends on achieving optimal radiation dose distribution within the tumor[2].
- Unequal microsphere distribution can lead to cold spots in a large, heterogeneous tumor, while high microsphere density can cause embolic effects and reduce radiation efficacy[3].
- Optimizing tumor microsphere density has thus been hypothesized as a key metric of Y^{90} success.[3]
- Tumor-to-normal ratio (TNR) derived from pretreatment Tc-99m MAA SPECT/CT is widely used as a surrogate marker of perfusion in yttrium-90 (^{90}Y) radioembolization for patients with hepatocellular carcinoma (HCC)[4]. However, the ability of pretreatment TNR to predict voxel-wise absorbed dose distribution following Y^{90} TARE remains unclear.

Objective

The objective of this study was to quantify post-treatment voxel-wise dose homogeneity following Y^{90} microsphere radioembolization and assess its association with pretreatment Tc-99m MAA SPECT/CT-derived TNR as well as to evaluate the utility of pretreatment TNR to reflect intratumoral dose distribution.

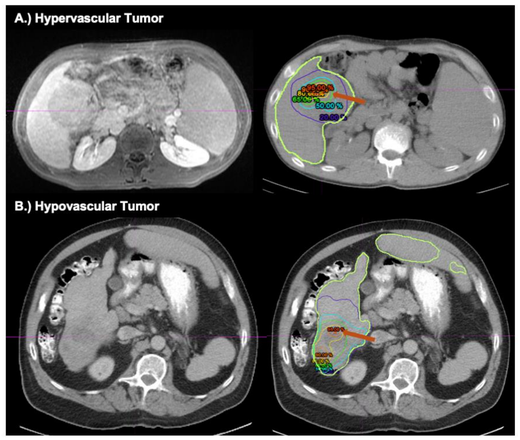

Figure 1: Impact of Tumor Vascularity on Voxel wise Dose Coverage *Representative post-treatment dose maps are shown for two HCC cases. (A) A hypervascular tumor (homogeneity index, HI = 8) demonstrates near-complete target coverage. (B) In contrast, a hypovascular tumor (HI = 2.3) exhibits dose deposition with substantial focal hot spots (arrow), reflecting decreased dose homogeneity. These visual differences underscore the spatial variability of absorbed dose within treated tumors.*

Methods and Materials

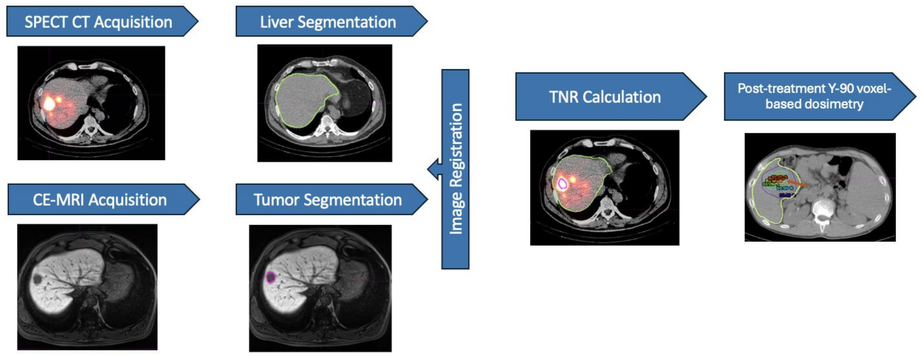

Figure 2. Pretreatment Tc-99m MAA SPECT/CT and contrast-enhanced MRI (CE-MRI) were used for liver/tumor segmentation and TNR calculation. Liver contours were automatically generated and tumor contours were manually segmented and co-registered with Tc-99m MAA as well as post-treatment Y-90 imaging. Voxel-based dosimetry was performed using post-treatment Y-90 SPECT/CT, with tumor dose-volume histograms (DVHs) generated to extract D5, D95, and the homogeneity index (D5/D95). Associations between pretreatment TNR and post-treatment dose heterogeneity were evaluated using nonparametric correlation analysis.

SPECT/CT and CE-MRI Image Acquisition

1. Imaging data from 21 patients treated with initial lobar radioembolization from 2018-2022 using Y^{90} glass microspheres were included. All patients underwent single-photon emission computed tomography/computed tomography (SPECT/CT) and most also had contrast-enhanced magnetic resonance imaging (CE-MRI) available within 3 months prior to treatment. Liver contours and tumor-to-normal ratios (TNR) were derived from SPECT/CT, while CE-MRI was used for tumor segmentation.

Liver and Tumor Segmentation

2. Liver segmentation was performed using MiM SurePlan (MIM software Cleveland, USA) Software's AI-Protégé tool on CT scans. Manual corrections were applied as needed.

3. Tumor segmentation was performed manually using CE-MRI or CT scans. The segmented liver and tumor volumes were then co-registered and then deformably aligned with the 99mTc-MAA (Technetium-99m macroaggregated albumin) mapping scan as well as the Y^{90} microsphere distribution.

TNR Calculation

4. TNR (Tumor-to-Normal ratio) was calculated using a 99mTc-MAA SPECT/CT scan. The TNR is a measure of the relative difference in radiotracer update between the tumor and surrounding tissue and can be calculated by dividing the total activity in the tumor by the total activity in the non-tumor liver parenchyma, standardized by their respective masses.

Tumor Heterogeneity Analysis

5. Utilizing the Y^{90} treatment SPECT/CT scans, Dose–volume histograms (DVHs) were generated for treated tumor volumes, from which D95 and D5 were extracted to quantify intratumoral dose homogeneity (D5/D95). Associations between pretreatment TNR and post-treatment dosimetry metrics were assessed using nonparametric correlation analysis.

Results

- Substantial interpatient variability was observed in both pretreatment TNR and post-treatment voxel-wise dosimetry. Heterogeneity indices ranged from 1.5 to 19.2, demonstrating wide variation in intratumoral dose distribution despite targeted delivery.
- A trend toward greater dose uniformity was observed in tumors with higher pretreatment TNR, suggesting that increased tumor perfusion may facilitate more homogeneous microsphere deposition.
- However, no strong association was identified between TNR and intratumoral dose heterogeneity ($R^2 = 0.07$), indicating that TNR alone may not fully capture voxel-level absorbed dose patterns in HCC tumors.

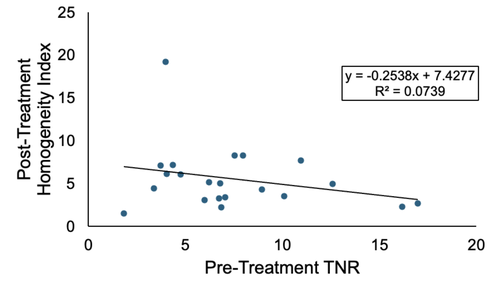

Figure 3. Association between pretreatment tumor-to-normal ratio (TNR) and post-treatment dose heterogeneity. Higher TNR demonstrated a trend toward lower D5/D95 heterogeneity indices, suggesting more uniform intratumoral dose distribution in better-perfused tumors; however, no significant association was observed ($R^2 = 0.07$).

Conclusion

- This exploratory study demonstrates the feasibility of DVH-based voxel dosimetry to quantify intratumoral dose heterogeneity following ^{90}Y glass microsphere radioembolization in HCC patients.
- Higher pretreatment Tc-99m MAA SPECT/CT-derived TNR showed a trend toward more homogeneous dose distribution, suggesting that tumor perfusion may influence microsphere deposition and dose coverage.
- However, the weak association between TNR and post-treatment dose heterogeneity indicates that TNR alone may not fully capture voxel-level absorbed dose patterns within heterogeneous tumors.
- This study is limited by a small cohort size. Additionally, voxel-wise dosimetry is affected by registration uncertainty due to differences in spatial resolution between SPECT/CT and MRI-derived tumor contours.

References

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