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Characterization of tumor dose heterogeneity for 90Y microsphere therapies using voxel- based dosimetry

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Abstract

Purpose: Dosimetry for 90Y microsphere therapies (YMT) with Standard (SM) and Partition (PM) models provide only uniform dose estimates to tumor and liver. Our objective is to calculate tumor dose heterogeneity, known to effect response, using voxel-based dosimetry and investigate the limitations of SM and PM.

Methods: Voxel-based dosimetry was performed on 17 YMT patients using Monte Carlo DOSXYZnrc. 90Y activity and tissue/density distributions were based on quantitative 90Y bremsstrahlung SPECT/CT. Tumors (n=31), liver, and treatment lobe/segments were segmented on diagnostic CT or MR. Dose volume histograms (DVH) were created for tumors and normal liver. Bland-Altman analysis compared voxel-based mean absorbed doses to tumor and liver with SM and PM. Tumor and normal liver absorbed dose heterogeneity were investigated through metrics: integral uniformity (IU), D10/D90, COV. Correlations of heterogeneity with voxel-based mean doses and volumes were evaluated.

Results: Heterogeneity metrics (mean ± 1σ) for tumor dose were COV = 0.48 ± 0.28, D10/D90 = 4.7 ± 3.9, and IU = 0.8 ± 0.18. Heterogeneity metrics correlated with tumor volume ($r > 0.58$) but not tumor mean doses ($r < 0.20$). Voxel-based tumor mean doses correlated with PM ($r = 0.84$) but not SM ($r = 0.08$). Both yielded poor limits of agreement with of 83 ± 174 and -28 ± 181 Gy, respectively. Normal liver heterogeneity metrics (mean ± 1σ) were COV = 0.83 ± 0.29, D10/D90 = 12 ± 15, and IU = 0.97 ± 0.03. Only D10/D90 ($r = 0.49$) correlated with mean normal liver absorbed dose. Voxel-based normal liver/lobe mean doses correlated with PM ($r = 0.96$), but had poor limits of agreement (26 ± 29 Gy).

Conclusion: Tumor doses have high levels of heterogeneity that increase with volume but are independent of dose. Voxel-based DVH and dose heterogeneity metrics will promote accurate characterization of tumor response following YMT.

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Key Results:

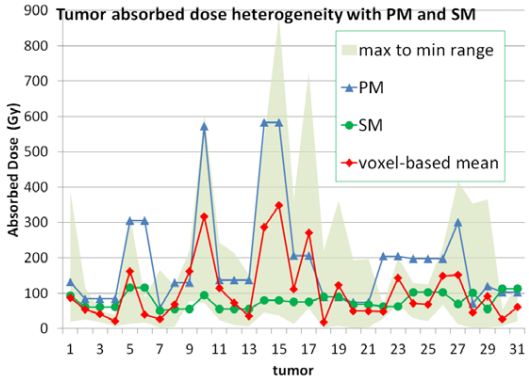

FIG. 1: This figure shows the tumor dose heterogeneity (max to min range of individual absorbed dose tumor estimates in beige shadow), together with the mean voxel-based tumor absorbed dose (red) and those for the PM (blue) and SM (green).
High levels of heterogeneity are observed. The PM and SM are unable to encompass the heterogeneity which is represented as the shaded area for each tumor. The PM tracks the mean voxel-based dose better than the SM. Unfortunately, the PM overestimates for 28/31 with a large mean difference of 83 ± 174 Gy.

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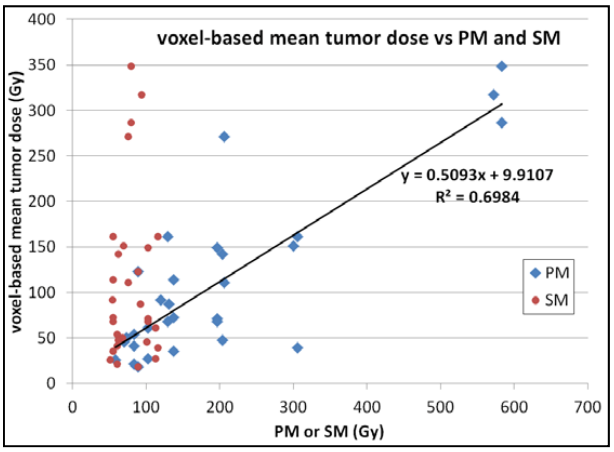

FIG. 2: A plot of mean tumor voxel-based dose versus those from PM and SM showing that the PM is a better surrogate for true mean doses than the SM. No correlation between voxel-based and SM was found. Voxel-based and PM were correlated, but notice that the PM overestimates the true mean dose by a factor of ~2.

TABLE 1: Correlations of heterogeneity metrics with voxel-based mean absorbed doses. Checkered cells indicate that no correlation was found. D10 and D90 are derived from cumulative dose volume histograms. D90 is the minimum dose in the hottest 90% of tumor volume. Similarly, D10 is the minimum dose in the hottest 10% of the tumor volume. COV is the coefficient of variation (= standard deviation/mean).

non-uniformity metric	Linear fits of heterogeneity metrics (correlation coefficient)			
	versus voxel-based mean dose (Gy)		versus volume (cc)	
	tumor (N=31) y = mx + b (corr coef)	normal liver (N=17) y = mx + b (corr coef)	tumor (N=31) y = mx + b (corr coef)	normal liver (N=17) y = mx + b (corr coef)
COV			7.0E-4x + 0.34 (0.68)	
max/min			2.0E-1x + 15 (0.32)	
D10/D90		4.1E-1x – 3.6 (0.49)	9.4E-3x + 2.7 (0.64)	-9.6E-3x + 25 (0.44)
IU			4.0E-4x + 0.71 (0.59)	

TABLE 2: Bland Altman analyses of dosimetry models with voxel-based mean absorbed dose as truth. Biases calculated as PM or SM minus voxel-based mean absorbed dose. Both SM and PM overestimate the normal liver dose compared to voxel-based means.

	Bland Altman analysis with voxel-based mean dose as truth	
	tumor (N=31) bias ± 2σ (Gy)	normal liver (N=17) bias ± 2σ (Gy)
Standard Model	-28.1 ± 180.7	40.1 ± 26.8
Partition Model	83.4 ± 174.4	25.7 ± 29.3

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