Subjective Pathologic Estimates of Viable Tumor in Ablated Hepatocellular Carcinomas (HCC) are Adequate for Routine Practice and for Radiology/Pathology Correlation Studies

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BACKGROUND

The goal of ablating hepatocellular carcinoma (HCC) is to induce complete tumor necrosis. Several studies have reported poor radiology/pathology correlation when evaluating treatment effect, however, no study has compared the viable tumor (VT) percentages to better define the degree of correlation. In addition, the pathologic methods used to assess VT in ablation cavities (AC) in prior studies are poorly described. The aim of this study was to compare subjective and objective estimates of the percentage of viable tumor (PVT) in ablated HCCs to determine if subjective estimates are reliable. In addition, we undertook our own correlation study to determine how well radiologic PVT estimates correlate with pathologic PVT estimates and what factors may influence this correlation.

DESIGN

2 pathologists independently reviewed gross images and slides for 23 ablated HCCs. Each observer subjectively estimated PVT (eyeball estimate), then measured individual microscopic areas of VT foci using formulas based on their shapes and added them to yield a composite viable tumor area (CVTA). The CVTA was converted to a composite viable tumor volume (CVTV) based on the spherical nature of the AC. The CVTV was divided by the volume of the ablation cavity, yielding an objective estimate of PVT. Means and standard deviations were calculated for all estimates and paired sample t-tests examined the inter and intraobserver agreements.

Additionally 2 radiologists performed retrospective blinded evaluations of PVT in 22 ACs. The radiologists evaluated the most recent imaging study before surgery (21 MRI, 1 CT) and determined PVT by consensus. The growth patterns of VT were documented as solid, discontinuous rim (Figure A), or nodular (Figure B). Means and standard deviations were calculated for all estimates. Paired sample t-tests examined the interobserver agreement between radiology and one pathologist's subjective estimate, and between the 2 pathologists. The statistical analysis was repeated after segregating cases by tumor size.

RESULTS

TABLE 1: Objective and Subjective Pathologic Methods of Determining Percent Viable Tumor

Ablation Cavity	Subjective (KM)	Subjective (JH)	Objective (KM)	Objective (JH)	Sampling (sections/cm)
1	2%	5%	1%	1%	1.8
2	0%	0%	0%	0%	0.5
3	20%	5%	2%	1.7%	0.4
4	15%	20%	0.7%	0.9%	0.83
5	8%	5%	4%	4%	3.2
6	0%	0%	0%	0%	1.1
7	30%	50%	43%	40%	1.4
8	25%	10%	3%	1.4%	0.61
9	0%	0%	0%	0%	1.3
10	<1%	<1%	.015%	0.015%	Entire Cavity
11	<1%	<1%	0.3%	0.5%	4.7
12	0%	0%	0%	0%	1.0
13	98%	99%	99%	99.4%	0.7
14	0%	0%	0%	0%	Entire Cavity
15	40%	40%	20%	20%	0.4
16	0%	0%	0%	0%	1.6
17	40%	30%	0.8%	1%	0.4
18	1%	<1%	1%	0.1%	Enitre Cavity
19	30%	30%	25%	30%	1.5
20	95%	95%	100%	100%	1.2
21	85%	95%	96%	96%	4.3
22	0%	0%	0%	0%	Entire Cavity
23	99%	95%	100%	100	1.6

Table 1: The 2 pathologists had strong interobserver agreement of PVT using both the subjective [means: 25.7%(KM), 25.3%(JH); p=0.81] and objective methods [means 21.5%(KM), 21.6%(JH); p=0.75]. The intraobserver agreement between subjective and objective methods was less strong [p=0.09 (KM), p=0.05 (JH)]. Data analysis revealed 5 outliers with poor intraobserver agreement (red highlights). On review, less than 1 section per cm of AC was submitted for each of these 5 cases. The objective estimates were always inappropriately lower than the subjective estimates in these cases because a significant amount of VT was not sampled and thus was not included in the CVTA calculations, which were based on glass slide examination. The paired sample t-tests were recalculated without the poorly sampled ACs and yielded stronger intraobserver agreement between the two methods [p=0.38(KM), p=0.69(JH)].

TABLE 2: Radiology/Pathology Correlation of Percent Viable Tumor in Ablation Cavities, Arranged by Cavity Size

Ablation Cavity	Path Subjective	Path Objective	Radiology	Cavity Size (cm)	VT Growth Pattern
1	2%	1%	5.4%	5.6	Nodular
2	0%	0%	0%	5.5	
3	20%	2%	0%	5.1	Nodular
4	15%	0.7%	0%	4.8	Nodular
5	8%	4%	0%	4.7	Discontinuous Rim
6	0%	0%	0%	3.7	
7	30%	43%	4.3%	3.5	Nodular
8	25%	3%	0%	3.3	Nodular
9	0%	0%	0%	3	
10	<1%	.015%	0%	3	Discontinuous Rim
11	<1%	.03%	0%	3	Discontinuous Rim
12	0%	0%	0%	3	
13	98%	99%	4.7%	2.7	Solid
14	0%	0%	0%	2.7	
15	40%	20%	22.2%	2.6	Nodular
16	0%	0%	0%	2.5	
17	40%	0.8%	0%	2.5	Discontinuous Rim
18	1%	1%	0%	2.5	Nodular
19	30%	25%	0%	2	Discontinuous Rim
20	95%	100%	4.4%	1.7	Solid
21	85%	96%	16.7%	1.4	Solid
22	0%	0%	0%	1	

Table 2: 15 ACs had VT on pathology (68%) and 6 had VT on imaging (22%). Radiology's sensitivity for detecting VT was 40% and the specificity was 100%. Pathology detected significantly more VT than radiology (pathology mean = 22.3% vs. radiology mean = 2.6%; p=0.005). Five cavities had tumor growth in a discontinuous rim pattern (Figure A), 7 in a nodular pattern (Figure B), and 3 in a sold pattern (Table 3). Radiology did not detect VT in cavities with a discontinuous rim pattern (sensitivity = 0%). VT was detected in 3 cavities with a nodular growth pattern (sensitivity = 43%) and in all cavities with a solid growth pattern (sensitivity = 100%). There was no significant difference in PVT estimates in cavities ≥ 3.5 cm (p=0.07), but there was a significant difference in cavities < 3.5 cm (p=0.01).

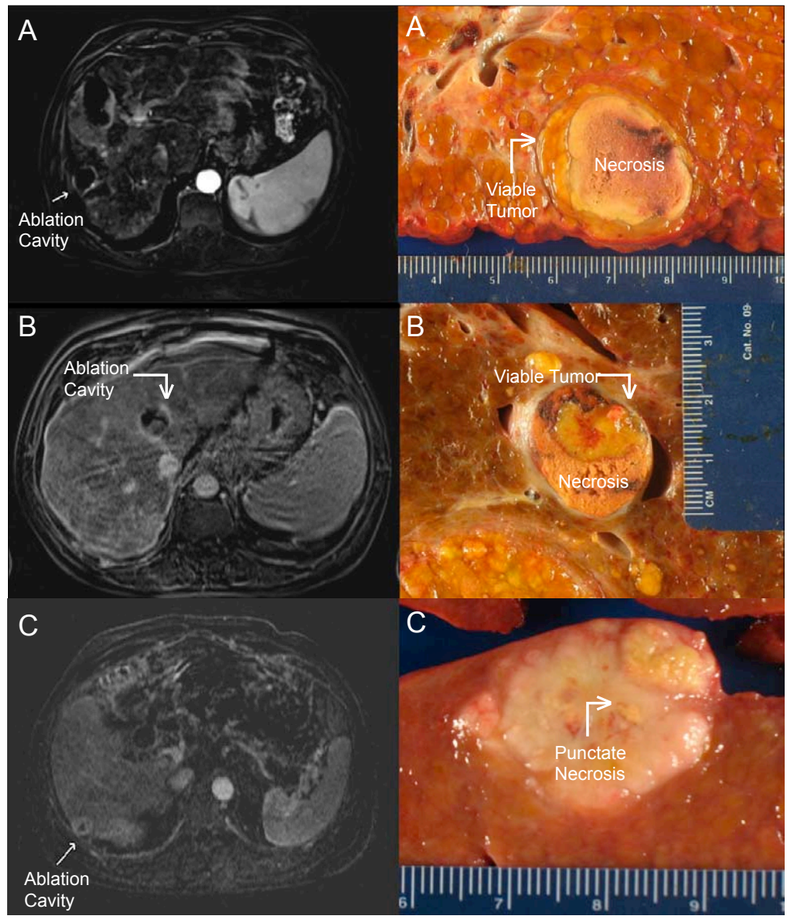

Figure 1: Discontinuous Rim (Cavity 19, A), Nodular (Cavity 15, B), and Solid (Cavity 13, C) Patterns of Viable Tumor Growth in HCC Ablation Cavities

CONCLUSIONS:

A subjective assessment of PVT in HCC ACs correlates well with measured PVT in well sampled cases, validating subjective pathologic assessment of PVT for routine practice and for radiology/pathology correlation studies. This study clarifies that the risk of under estimation by radiology is greatest in small lesions (<3.5 cm) and suggests that the sensitivity of detection is heavily influenced by the tumor growth pattern within the cavity.