ON-LINE APPENDIX

Details of Texture Analysis

In this work, we measured 42 features from each segmented tissue volume using an in-house-developed Matlab (MathWorks) texture analysis software.[1,2] The 42 features included 13 histogram features, 5 gray-level co-occurrence features, 11 gray-level run-length features, 4 gray-level gradient matrix features, and 9 Laws features. The extraneous math behind each texture feature in detail is described as follows:

Histogram Features

The histogram features included mean, median, SD, entropy, second SD, range, geometric mean, harmonic mean, interquartile range, fourth moment, SD in a 5-pixel neighborhood (SD 5), and SD in a 9-pixel neighborhood (SD 9). SD 5 and SD 9 are SDs calculated on the basis of a pixel and its surrounding 4 and 8 pixels, thus creating 5- and 9-pixel neighborhoods, respectively. Histogram features are spatially invariant and are not affected by relationships with neighboring pixels.[3]

Gray-Level Co-Occurrence Matrix Features

The GLCM features, in contrast to histogram features, are spatially dependent and are influenced by relationships with surrounding pixels. The GLCM is square and symmetric with rows and columns from 0 to N_g, where N_g represents the number of gray tones in the image. This notation allows the GLCM element in row i and column j to represent the number of times a given gray tone of value i is horizontally adjacent to gray tone j in the original quantized image. Herein, GLCMs were calculated using only directly adjacent pixels for simplicity. Horizontal, 45°, vertical, and 135°directions were averaged together to eliminate any directional dependence. The following GLCM features proposed by Haralick et al were tested[4]:

1) $$\text{Contrast} = \sum_{i,j} |i-j|^2 \ p(i,j),$$

2) $$\text{Correlation} = \sum_{i,j} \frac{(i-\mu_i)(j-\mu_j)\,p(i,j)}{\sigma_i\sigma_j},$$

3) $$\text{Angular Second Moment} = \sum_{i,j} p(i,j)^2,$$

4) $$\text{Homogeneity} = \sum_{i,j} \frac{p(i,j)}{1+|i-j|},$$

5) $$\text{Entropy} = \sum_{i,j} \ln[p(i,j)]\,p(i,j),$$

where $p(i, j)$ represents the (i, j) value of the GLCM.

Gray-Level Run-Length Features

The GLRL matrix provides additional insight into a spatial dependence and was created on the basis of the published work of Tang.[5] Similar to GLCM, the GLRL matrix is quantized to N_g gray tones to simplify texture extraction and to yield a more robust technique. The row index i of the GLRL matrix represents the gray tone of value i. In contrast, the column index j is the run-length, which is defined as a number of adjacent and equal value pixels in a given direction. The value of each element in the GLRL matrix represents the number of pixel line segments (run) with run-length j and gray tone i. The same directions considered in GLCM were averaged for the GLRL matrix. The features explored included equations using short-run emphasis (SRE), long-run emphasis (LRE), gray-level nonuniformity (GLN), run-length nonuniformity (RLN), run percentage (RP), low gray-level run emphasis (LGRE), high gray-level run emphasis (HGRE), short-run low gray-level emphasis (SRLGE), short-run high gray-level emphasis (SRHGE), long-run low gray-level emphasis (LRLGE), and long-run high gray-level emphasis (LRHGE), defined as follows:

6) $$\text{SRE} = \frac{1}{n_r}\sum_{i,j} \frac{p(i,j)}{j^2},$$

7) $$\text{LRE} = \frac{1}{n_r}\sum_{i,j} p(i,j)\,j^2,$$

8) $$\text{GLN} = \frac{1}{n_r}\sum_{i}\left[\sum_{j} p(i,j)\right]^2,$$

9) $$\text{RLN} = \frac{1}{n_r}\sum_{j}\left[\sum_{i} p(i,j)\right]^2,$$

10) $$\text{RP} = \frac{n_r}{n_p},$$

11) $$\text{LGRE} = \frac{1}{n_r}\sum_{i,j} \frac{p(i,j)}{i^2},$$

12) $$\text{HGRE} = \frac{1}{n_r}\sum_{i,j} p(i,j)\,i^2,$$

13) $$\text{SRLGE} = \frac{1}{n_r}\sum_{i,j} \frac{p(i,j)}{i^2 j^2},$$

14) $$\text{SRHGE} = \frac{1}{n_r}\sum_{i,j} \frac{p(i,j)\,i^2}{j^2},$$

15) $$\text{LRLGE} = \frac{1}{n_r}\sum_{i,j} \frac{p(i,j)\,j^2}{i^2},$$

16) $$\text{LRHGE} = \sum_{i,j} p(i,j)\,i^2 \ j^2,$$

where $p(i, j)$ represents the (i, j) value of the GLRL matrix, n_r is the total number of runs, and n_p is the total number of pixels. The images were requantized in the texture analysis program using a standard of 30 gray levels. No smoothing filter was applied to the images in the texture analysis program. The images were normalized by the mean and SD to minimize discrimination by the overall gray-level variation, which is unrelated to local image texture.

Gray-Level Gradient Matrix Features

The gray-level gradient matrix was used to provide the histogram of the absolute gradient values in the ROI. As a preprocessing step, the gradient of each pixel within the ROI was computed using a 3 × 3 neighborhood. The gray-level gradient matrix features mathematically summarize the gradient values of the pixels in the ROI and include mean, variance, skewness, and kurtosis.

Laws Features

The Laws features are based on unidimensional vectors described by Kenneth Laws.[6] Vectors described by Laws included level, spot, edge, ripple, wave, undulation, and oscillation. The vectors level, edge, ripple, and spot were used for our analysis. Two 5-pixel vectors were convolved to create 2D filter masks, and certain symmetric pairs were combined to form the final 9 filter masks L1–L9,[7] which were applied across an image.

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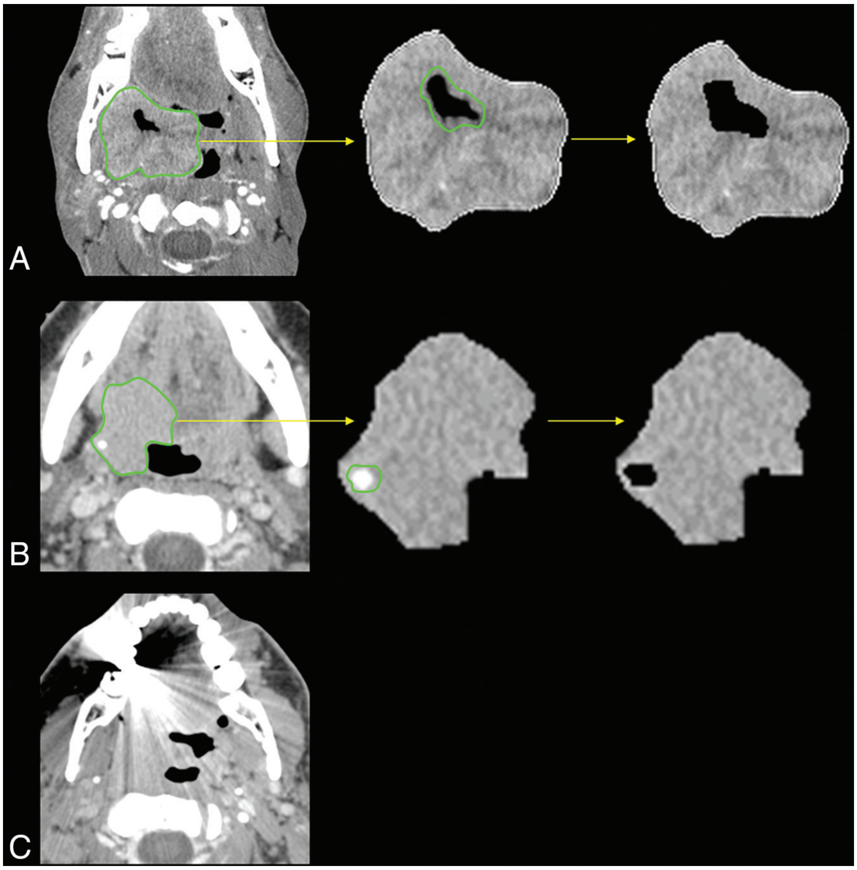

ON-LINE FIGURE. Workflow for image segmentation. We performed whole segmentation of the primary tumor for each section. When the tumor included obvious regions of ulceration (*A*) or obvious calcification (*B*), we manually excluded these regions from the contoured tumor volume. When the presence of severe streak artifacts within the tumor was seen (*C*), we excluded the artifact section and used the only artifact-free section for texture analysis.

On-line Table: Texture parameters differentiating local control and local failure

Texture Parameter	Local Control (*n* = 40) Median (IQR)	Local Failure (*n* = 22) Median (IQR)	*P* Value
Histogram			
Mean	1069.3 (71.1)	1101.9 (37.4)	.029[a]
Median	1116.5 (34.3)	1111.7 (35.5)	.314
SD	315.9 (81.8)	288.0 (72.9)	.011[a]
Entropy	5.22 (0.82)	4.94 (0.85)	.303
Second SD	27.1 (33.8)	20.8 (22.7)	.051
Range	78.7 (91.8)	59.9 (67.4)	.054
Geometric mean	809.4 (134.4)	864.0 (100.8)	.007[a]
Harmonic mean	154.7 (89.6)	189.3 (89.2)	.006[a]
IQR	40.6 (133.5)	32.5 (31.0)	.317
Fourth moment	6.23e +10 (1.97e +10)	5.66e +10 (2.18e +10)	.012[a]
Test	0.514 (0.153)	0.477 (0.191)	.617
SD 5	24.7 (34.9)	20.3 (19.3)	.054
SD 9	25.1 (34.7)	20.9 (17.7)	.118
GLCM			
Entropy	0.361 (0.208)	0.322 (0.266)	.385
Contrast	47.8 (25.6)	44.1 (28.3)	.471
Correlation	0.639 (0.015)	0.634 (0.020)	.311
Energy	0.166 (0.109)	0.187 (0.112)	.965
Homogeneity	0.724 (0.103)	0.743 (0.109)	.190
GLGM			
MGR	2.57 (1.34)	2.56 (2.19)	.233
VGR	6466.8 (3140.1)	7533.3 (5619.6)	.083
Skewness	40.0 (10.1)	40.9 (12.9)	.527
Kurtosis	1688.4 (893.0)	1761.7 (1063.0)	.508

Texture Parameter	Local Control (*n* = 40) Median (IQR)	Local Failure (*n* = 22) Median (IQR)	*P* Value
GLRL			
SRE	0.043 (0.011)	0.036 (0.011)	<.001[a]
LRE	0.037 (0.010)	0.031 (0.008)	<.001[a]
GLN	0.047 (0.012)	0.039 (0.006)	<.001[a]
RLN	0.037 (0.012)	0.030 (0.008)	<.001[a]
RP	428.5 (26.8)	442.2 (44.7)	.008[a]
LGRE	437.2 (32.6)	453.3 (37.6)	.003[a]
HGRE	423.6 (24.5)	434.0 (25.6)	.002[a]
SRLGE	437.4 (27.7)	450.8 (41.0)	.004[a]
SRHGE	577.9 (263.4)	553.4 (318.5)	.848
LRLGE	661.1 (379.7)	635.2 (351.7)	.691
LRHGE	537.4 (334.7)	591.4 (299.0)	.767
Laws features			
L1	404036.3 (307886.8)	386481.0 (330488)	.216
L2	49366.7 (45454.0)	50608.1 (37670.9)	.317
L3	16009.1 (13311.8)	15298.0 (14900.5)	.264
L4	99353.3 (75231.7)	98633.8 (76368.2)	.251
L5	10516.7 (9847.6)	10883.7 (10867.3)	.303
L6	5203.9 (5943.8)	4515.4 (6145.8)	.251
L7	6677.8 (7118.5)	6532.3 (7548.5)	.296
L8	6672.8 (4928.2)	6044.6 (4712.3)	.324
L9	48033.3 (41158.8)	43796.0 (38121.1)	.211

Note:—IQR indicates interquartile range; GLGM, gray-level gradient matrix; MGR, mean gradients; VGR, variance of gradients; SRHGE, short-run high gray-level emphasis; LRE, long-run emphasis; GLN, gray-level nonuniformity; RP, run percentage; LGRE, low gray-level run emphasis; HGRE, high gray-level run emphasis; SRHGE, short-run high gray-level emphasis; LRLGE, long-run low gray-level emphasis; LRHGE, long-run high gray-level emphasis.

[a] Indicates a significant difference by the Mann-Whitney *U* test ($P < .05$).