Supplement Material-2

Section 1: SpaTIL Feature Extraction

The whole-slide tissue scans for corresponding patients from D_1 (N=70) were obtained for extracting spatial tissue infiltrating lymphocytes features (SpaTIL) relating to (i) the spatial architecture of tissue infiltrating lymphocytes (TIL) clusters, (ii) co-localization of clusters of both TILs and cancer nuclei, and (iii) variation in density of TIL clusters across the tissue slide image.

Identification of lymphocytes. The first step in the process was to identify the spatial location of the TILs on digitized H&E stained images. The watershed algorithm was used to automatically detect nuclei. Once the nuclei were detected, a support vector machine using 7 image-derived features related to texture, shape, and color attributes of the segmented nuclei was used to classify the individual nuclei as corresponding either to TILs or to non-TILs.

Quantitative evaluation of spatial arrangement of TILs.

Spatial TIL graph construction. For extraction of SpaTIL features, sets of clusters of proximal TILs and non-TILs were identified. For this purpose, we represented the centroids of each of the individual TILs and non-TILs as nodes of a graph. Each node was connected to others based on a weighted Euclidean norm in which a weighting function favors the connectivity between proximal nodes. Using this process, we generated multiple subgraphs of TILs and non-TILs.

SpaTIL features. The first set of SpaTIL features comprised 20 features related to spatial arrangement of TILs, extracted from the TIL cluster graphs. These features included descriptors such as number of lymphocytes, ratio between area of TIL clusters and area of whole-slide images, and ratio between the number of TILs within the cluster and the cluster area. The second set included the ratio between the non-lymphocyte clusters to the closest lymphocyte clusters, intersection area of lymphocyte and non-lymphocyte, and a value indicating if the nearest cluster neighbor of a specific lymphocyte cluster is either lymphocyte or non-lymphocyte.

These features are listed in Table S4. We calculated Pearson's correlation coefficient between developed QuRiS and SpaTIL features.

Section 2: Correlation coefficient for SpaTIL features and QuRiS

Table S.4: Pearson correlation coefficient of QuRiS with individual SpaTIL features using D1 cohort with N=70 patients.

Idx	SpaTIL Feature	Correlation Coefficient	Idx	SpaTIL Feature	Correlation Coefficient
1	avg of ratio of the nuceli cluster density to its closest lym cluster cluster'	-0.068548217	48	'ratio of number of unique lym nodes to all lym nodes'	-0.116244702
2	'avg of ratio of the nuceli cluster density to its second closest lym cluster density'	-0.150885109	49	'average distance of nuclei to nearest lym'	-0.175162033
3	'avg of ratio of the nuceli cluster density to its third closest lym cluster density'	-0.082589705	50	'lympTotArea'	-0.194999154
4	'avg of ratio of the nuceli cluster density to its first three closest lym cluster mean density'	0.160823937	51	'lymAvgArea'	-0.137579828
5	'std of ratio of the nuceli cluster density to its closest lym cluster cluster'	-0.028989277	52	'lymMedianArea'	-0.008865348
6	'std of ratio of the nuceli cluster density to its second closest lym cluster density'	-0.20681203	53	'lymStdArea'	-0.089769515
7	'std of ratio of the nuceli cluster density to its third closest lym cluster density'	-0.024038741	54	'lymModeArea'	0.058361397
8	'std of ratio of the nuceli cluster density to its first three closest lym cluster mean density'	0.135962339	55	'nonLympTotArea'	0.079192836
9	'var of ratio of the nuceli cluster density to its closest lym cluster cluster'	-0.008784743	56	'nonLymAvgArea'	0.001491959
10	'var of ratio of the nuceli cluster density to its second closest lym cluster density'	-0.197582571	57	'nonLymMedianArea'	0.044094657
11	'var of ratio of the nuceli cluster density to its third closest lym cluster density'	-0.024123586	58	'nonLymStdArea'	-0.078023118
12	'var of ratio of the nuceli cluster density to its first three closest lym cluster mean density'	0.132752781	59	'nonLymModeArea'	-0.08835839
13	'min of ratio of the nuceli cluster density to its closest lym cluster cluster'	-0.04774157	60	'lympTotDensity'	-0.067530353
14	'min of ratio of the nuceli cluster density to its second closest lym cluster density'	-0.194530973	61	'lymAvgDensity'	-0.086611609
15	'min of ratio of the nuceli cluster density to its third closest lym cluster density'	-0.196108574	62	'lymMedianDensity'	-0.064898542
16	'min of ratio of the nuceli cluster density to its first three closest lym cluster mean density'	0.034175957	63	'lymStdDensity'	0.071426038
17	'max of ratio of the nuceli cluster density to its closest lym cluster cluster'	-0.024092555	64	'lymModeDensity'	-0.034241092
18	'max of ratio of the nuceli cluster density to its second closest lym cluster density'	-0.141794394	65	'nonLympTotDensity'	0.107552768
19	'max of ratio of the nuceli cluster density to its third closest lym cluster density'	-0.156591248	66	'nonLymAvgDensity'	-0.007827012
20	'max of ratio of the nuceli cluster density to its first three closest lym cluster mean density'	0.031379749	67	'nonLymMedianDensity'	0.220731128
21	'range of ratio of the nuceli cluster density to its closest lym cluster cluster'	-0.210614368	68	'nonLymStdDensity'	0.237694262
22	'range of ratio of the nuceli cluster density to its second closest lym cluster density'	-0.141450778	69	'nonLymModeDensity'	0.032356646
23	'range of ratio of the nuceli cluster density to its third closest lym cluster density'	0.004059192	70	'intersectedArea'	0.023812444
24	'range of ratio of the nuceli cluster density to its first three closest lym cluster mean density'	-0.014271201	71	'avg1Nearest'	-0.13938205
25	'avg of reciprocal of number of least lym cluster to encompass nuclei cluster'	0.195204313	72	'median1Nearest'	-0.021537739
26	'std of reciprocal of number of least lym cluster to encompass nuclei cluster'	0.223889325	73	'mode1Nearest'	-0.079029197
27	'var of reciprocal of number of least lym cluster to encompass nuclei cluster'	0.16548175	74	'avg2Nearest'	0.108534514
28	'min of reciprocal of number of least lym cluster to encompass nuclei cluster'	-0.212727524	75	'median2Nearest'	0.029155776
29	'max of reciprocal of number of least lym cluster to encompass nuclei cluster'	-0.212670795	76	'mode2Nearest'	0.077753569
30	'range of reciprocal of number of least lym cluster to encompass nuclei cluster'	-0.209706821	77	'avg3Nearest'	0.19617502
31	'avg of area ratio of nuclei cluster to encompassed lym clusters'	-0.115741545	78	'median3Nearest'	0.138335766
32	'std of area ratio of nuclei cluster to encompassed lym clusters'	-0.097028858	79	'mode3Nearest'	0.164061198
33	'var of area ratio of nuclei cluster to encompassed lym clusters'	-0.083277923	80	'avg4Nearest'	0.144128255
34	'min of area ratio of nuclei cluster to encompassed lym clusters'	0.028592185	81	'median4Nearest'	-0.024208296
35	'max of area ratio of nuclei cluster to encompassed lym clusters'	0.055189072	82	'mode4Nearest'	0.153365785
36	'range of area ratio of nuclei cluster to encompassed lym clusters'	0.070868536	83	'avg5Nearest'	-0.061147535
37	'avg of density ratio of nuclei cluster to encompassed lym clusters'	0.05082384	84	'median5Nearest'	-0.082526071
38	'std of density ratio of nuclei cluster to encompassed lym clusters'	0.14941434	85	'mode5Nearest'	-0.06654644
39	'var of density ratio of nuclei cluster to encompassed lym clusters'	0.21056833			
40	'min of density ratio of nuclei cluster to encompassed lym clusters'	0.239931268			
41	'max of density ratio of nuclei cluster to encompassed lym clusters'	0.247720455			
42	'range of density ratio of nuclei cluster to encompassed lym clusters'	0.0896348			
43	'1-norm of the vector by ratio of nucleiDegree to LymDegree'	0.141759087			
44	'1-norm of the vector by ratio of nucleiCloseness to LymCloseness'	0.220381499			
45	'1-norm of the vector by ratio of nucleiBetweenness minus LymBetweenness'	0.237424695			
46	'1-norm of the vector by ratio of nucleiEigenvector to LymEigenvector'	0.235044918			
47	'1-norm of the vector by ratio of nucleiSumIndex to LymSumIndex'	0.10614462			

Section 3: Heat map for individual Radiomic features from QuRiS and SpaTIL features.

Figure S.7- Pearson correlation coefficient for individual Radiomic features from QuRiS against SpaTIL features. QuRiS and specifically, intratumoral Haralick features were observed to be correlated with features explaining ratio between cancerous clusters to closest lymphocyte clusters. They were also observed to be correlated with the density of cancerous clusters.