# Supplementary Materials to Multi-resolution super learner for voxel-wise classification of prostate cancer using multi-parametric MRI

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## Appendix A: Detailed simulation settings

### A.1 Simulation settings for binary PCa classification

As described in Section 4.1 of the main manuscript, the simulated data sets were generated according to model (1):

$$\begin{gathered}\boldsymbol{w}_i \sim \mathcal{MVN}(\mathbf{0}, \boldsymbol{C}(\boldsymbol{S}_i, \boldsymbol{S}_i|\boldsymbol{\theta})),\ c_{ij}^* \sim N(q_{r_{ij},0} + w_{ij}, 1), \\ c_{ij} = I(c_{ij}^* > 0),\ \boldsymbol{e}_{i_k}^k \sim \mathcal{MVN}(\mathbf{0}, \boldsymbol{\Lambda}), \\ \boldsymbol{y}_{ij} \overset{ind}{\sim} \mathcal{MVN}(\boldsymbol{\mu}_{c_{ij},r_{ij}} + \sum_{k=1}^{K} \boldsymbol{e}_{i_{ij}^k}^k + \boldsymbol{\delta}_i, \boldsymbol{\Gamma}_{c_{ij},r_{ij}}). \end{gathered} \tag{1}$$

The model parameters, including the means, $\{\boldsymbol{\mu}_{c,r}, c = 0, 1, r = 0, 1\}$, within-patient covariance, $\{\boldsymbol{\Gamma}_{c_{ij},r_{ij}}, c, r \in \{0, 1\}\}$, of the mpMRI parameters, and probit of the cancer prevalence in the PZ and CG, $q_{r_{ij},0}$, were set based on the estimates from the real data. $\boldsymbol{\mu}_{c,r}$, $c, r \in \{0, 1\}$, was set equal to the estimates from the motivating data set. $\boldsymbol{\Gamma}_{c,r}$, $c, r \in \{0, 1\}$, was set equal to 1/1.5 times the estimates from the motivating data set. We varied the values for $q_{r,0}$, $r = 0, 1$, and $\boldsymbol{\Lambda}$ to simulate regional heterogeneity of different magnitudes. For moderate regional heterogeneity, we set the cancer prevalence in the PZ and CG to 0.4 and 0.2, respectively, and $\boldsymbol{\Lambda}$ equal to a $d \times d$ diagonal matrix ($d = 4$) with diagonal entries 5, 0.18, 0.18, and 0.18. For strong regional heterogeneity, we set the cancer prevalence in the PZ and CG to 0.55 and 0.15, respectively, and $\boldsymbol{\Lambda}$ equal to a $d \times d$ diagonal matrix with diagonal entries 10, 0.36, 0.36, and 0.36. We also varied $\boldsymbol{\theta} = \{\sigma^2, \phi, \nu\}$ to simulate different spatial correlation structures: for moderate spatial correlation, we set $\sigma^2$ (spatial variance) equal to 4, $\phi$ (range parameter, larger $\phi$ indicates larger-scale correlation) equal to 0.2, and $\nu$ (smoothness parameter, smaller $\nu$ indicates larger differentiability) equal to 0.8; for strong spatial correlation, we set $\sigma^2 = 10$, $\phi = 0.5$, and $\nu = 1.5$.

## A.2 Simulation settings for classification of ordinal PCa significance

Regarding the simulation studies for classification of the ordinal clinical significance of PCa, the shapes of the simulated prostate images were still selected with replacement from the images in the motivating data set. Voxel-wise cancer status and mpMRI parameters were simulated according to model (2). We set the between-class boundaries $a_1$ and $a_2$ equal to the median and 70-th percentile, respectively, of the simulated $G^*_{ij}$'s, so as to assign a high prevalence (50%) to the noncancer voxels, a low prevalence (20%) to the clinically significant cancer voxels, and the lowest prevalence (10%) to the clinically insignificant cancer voxels. The generating process for $\boldsymbol{w}_i$, $G^*_{ij}$'s, $q_{r,0}$'s, $\boldsymbol{e}^k_{i_k}$'s, $\boldsymbol{\delta}_i$'s and $\boldsymbol{y}_{ij}$'s was similar to the one in Section 4.1 of the main manuscript, except that $\boldsymbol{y}_{ij}$ was assumed to vary by $G_{ij}$ instead of $c_{ij}$.

$$\begin{aligned} \boldsymbol{w}_i \sim \mathcal{MVN}(\boldsymbol{0}, \boldsymbol{C}(\boldsymbol{S}_i, \boldsymbol{S}_i|\boldsymbol{\theta})),\ G^*_{ij} \sim N(q_{r_{ij},0} + w_{ij}, 1), \\ G_{ij} = I(a_{z-1} \leqslant G^*_{ij} < a_z),\ \boldsymbol{e}^k_{i_k} \sim \mathcal{MVN}(\boldsymbol{0}, \boldsymbol{\Lambda}), \\ \boldsymbol{y}_{ij} \overset{ind}{\sim} \mathcal{MVN}(\boldsymbol{\mu}_{G_{ij},r_{ij}} + \sum_{k=1}^{K} \boldsymbol{e}^k_{i^k_{ij}} + \boldsymbol{\delta}_i, \boldsymbol{\Gamma}_{G_{ij},r_{ij}}). \end{aligned} \tag{2}$$

## A.2 Data distribution across different categories of PCa

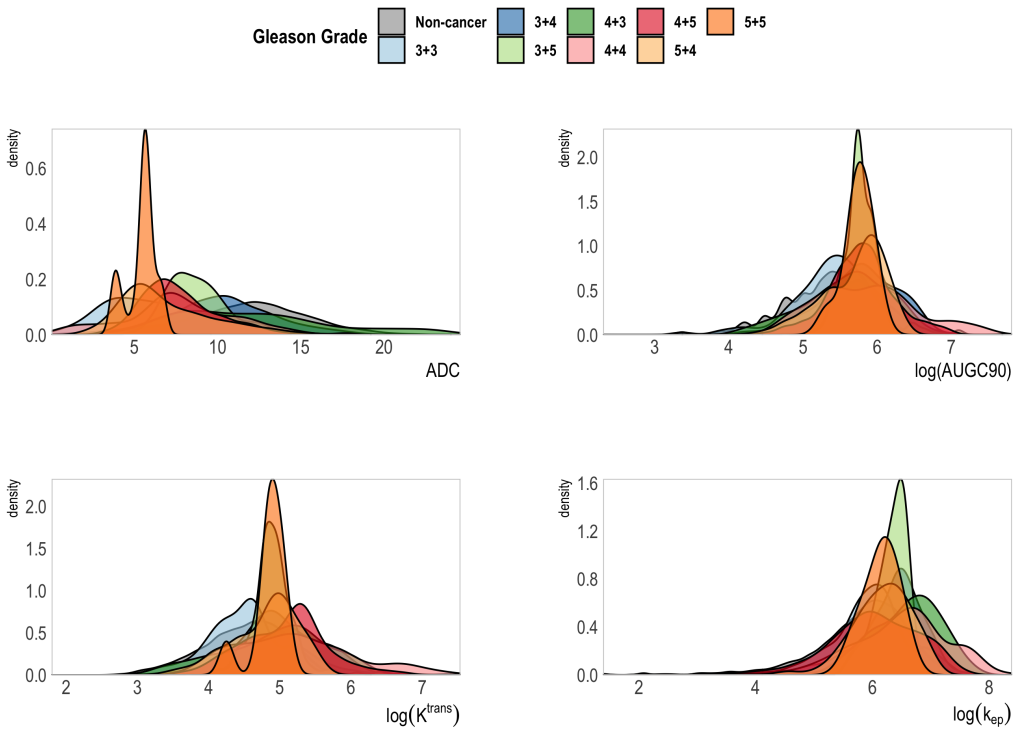


Figure S1. Voxel-wise distribution of the various mpMRI parameters across Gleason grade groups observed from our motivating dataset.

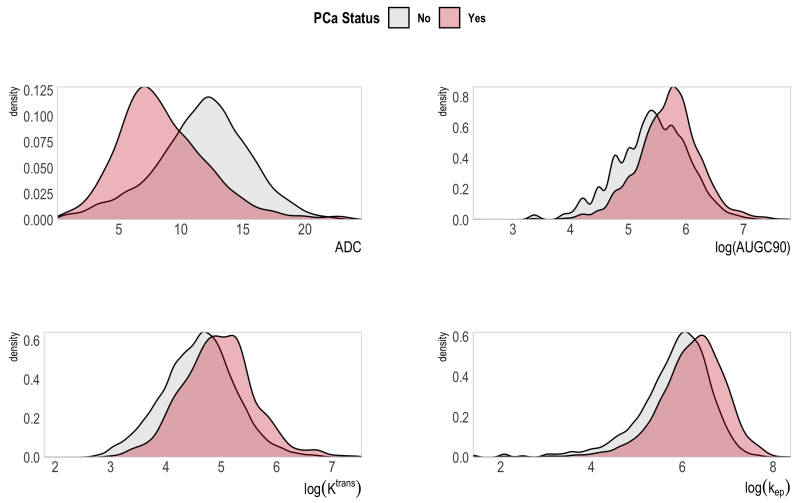


Figure S2. Voxel-wise distribution of the various mpMRI parameters separately for cancer and non-cancer voxels in our motivating dataset.

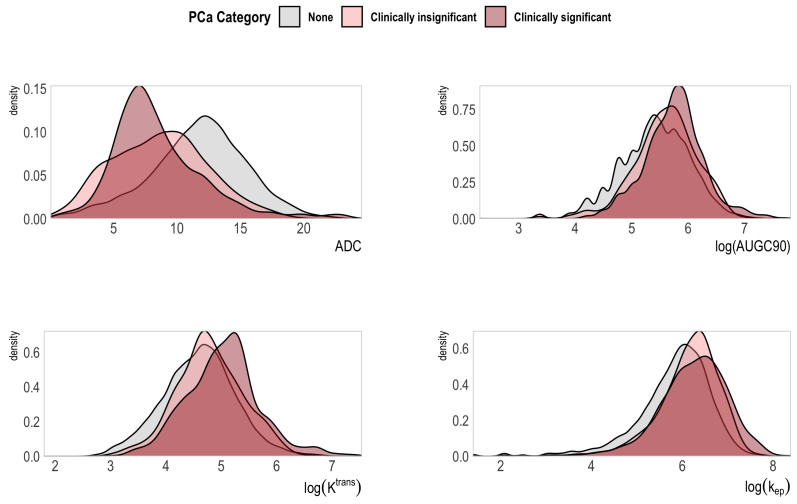


Figure S3. Voxel-wise distribution of the various mpMRI parameters of the voxels under different levels of clinical significance of PCa in our motivating dataset. The sample prevalences of clinically insignificant PCa voxels and clinically significant PCa voxels are 0.167.

### A.3 Examples of synthetic mpMRI and PCa maps

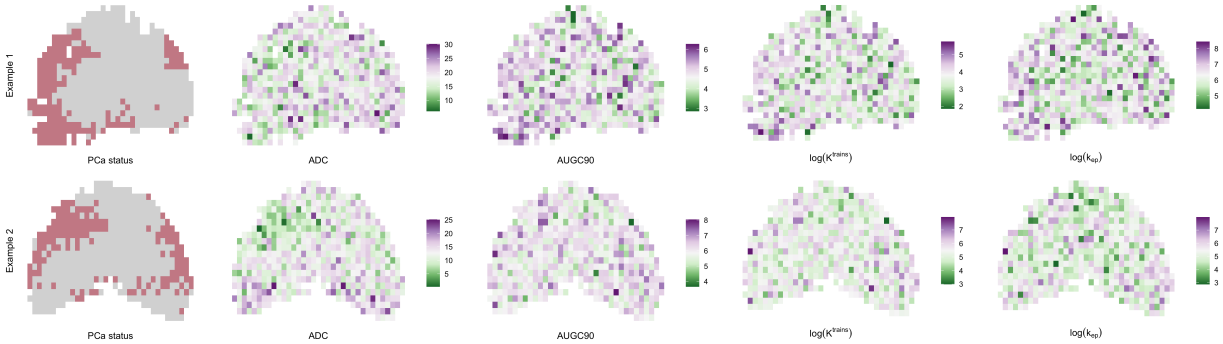


Figure S4. Example maps of voxel-wise PCa status (column 1) and mpMRI parameters (columns 2-5) for two simulated prostate slices under moderate regional heterogeneity and moderate spatial correlation (see Appendix A.1 for details). In the PCa outcome maps, grey and pink indicate non-cancer and cancer, respectively.

# Appendix B: Additional simulation results of binary PCa classification

Table S1. Simulation results of binary PCa classification under moderate regional heterogeneity.

| Spatial Correlation | Base Learner | Method | Classification Results | | |
|---|---|---|---|---|---|
| | | | AUC | S80 | S90 |
| Moderate $\sigma^2 = 4$ $\phi = 0.2$ $\nu = 0.8$ | GLM | Baseline | .777 (.027) | .599 (.051) | .438 (.054) |
| | | SL0 | .833 (.004) | .705 (.008) | .553 (.009) |
| | | SL | .848 (.009) | .743 (.066) | .586 (.022) |
| | QDA | Baseline | .780 (.026) | .603 (.050) | .442 (.053) |
| | | SL0 | .840 (.004) | .717 (.008) | .567 (.009) |
| | | SL | .854 (.009) | .754 (.018) | .598 (.021) |
| | RF | Baseline | .788 (.016) | .616 (.031) | .457 (.033) |
| | | SL0 | .822 (.004) | .688 (.007) | .536 (.007) |
| | | SL | .855 (.007) | .757 (.013) | .601 (.017) |
| | GLM + QDA + RF | SL0 | .841 (.004) | .719 (.007) | .570 (.008) |
| | | SL | .862 (.006) | .772 (.012) | .618 (.015) |
| Strong $\sigma^2 = 10$ $\phi = 0.5$ $\nu = 1.5$ | GLM | Baseline | .778 (.034) | .600 (.063) | .439 (.065) |
| | | SL0 | .832 (.006) | .704 (.011) | .551 (.013) |
| | | SL | .927 (.008) | .893 (.016) | .790 (.026) |
| | QDA | Baseline | .778 (.034) | .600 (.063) | .439 (.064) |
| | | SL0 | .839 (.006) | .715 (.010) | .566 (.012) |
| | | SL | .930 (.008) | .899 (.016) | .799 (.025) |
| | RF | Baseline | .788 (.018) | .616 (.035) | .456 (.037) |
| | | SL0 | .822 (.005) | .688 (.009) | .536 (.010) |
| | | SL | .932 (.007) | .903 (.013) | .805 (.023) |
| | GLM + QDA + RF | SL0 | .840 (.005) | .718 (.009) | .569 (.011) |
| | | SL | .942 (.005) | .921 (.010) | .833 (.017) |

# Appendix C: Additional results on the ordinal PCa outcome

## C.1 Simulation studies

Table S2 reports simulation results of models Baseline, SL0 + $W_1$, SL + $W_1$, SL0 + $W_2$ and SL + $W_2$ assuming more moderate between-voxel correlation than that in Tables 3 using GLM as the base learner. Table S3 reports the simulation results assuming weaker regional heterogeneity than that in Tables 3 using GLM as the base learner. Tables S4 and S5 report simulation results assuming moderate and strong regional heterogeneity, respectively, using QDA as the base learner. Tables S6 and S7 report simulation results assuming that RF is the base learner. Tables S8 and S9 report simulation results when combining the multi-resolution GLM, QDA and RF-based learners.

Table S2. Simulation results for classification of the ordinal clinical significance of PCa assuming moderate between-voxel correlation ($\sigma^2 = 4$, $\phi = 0.2$, $\nu = 0.8$) and strong regional heterogeneity using GLM as the base learner.

| Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|
| Baseline | 1 | 59491 | 0 | 9485 | 0.14 | 0.39 | 0.42 |
| | 2 | 16928 | 0 | 10662 | 1.00 | NA | |
| | 3 | 20578 | 0 | 20808 | 0.50 | 0.49 | |
| SL0 + $W_1$ | 1 | 60466 | 0 | 8511 | 0.12 | 0.34 | 0.38 |
| | 2 | 14879 | 0 | 12711 | 1.00 | NA | |
| | 3 | 15913 | 0 | 25473 | 0.38 | 0.45 | |
| SL + $W_1$ | 1 | 61569 | 0 | 7408 | 0.11 | 0.32 | 0.34 |
| | 2 | 16601 | 0 | 10989 | 1.00 | NA | |
| | 3 | 11735 | 0 | 29651 | 0.28 | 0.38 | |
| SL0 + $W_2$ | 1 | 47771 | 13411 | 7794 | 0.31 | 0.25 | 0.42 |
| | 2 | 7544 | 7940 | 12106 | 0.71 | 0.73 | |
| | 3 | 7994 | 8589 | 24803 | 0.40 | 0.45 | |
| SL + $W_2$ | 1 | 48110 | 15479 | 5388 | 0.30 | 0.21 | 0.39 |
| | 2 | 8677 | 9910 | 9004 | 0.64 | 0.72 | |
| | 3 | 3990 | 10586 | 26810 | 0.35 | 0.35 | |

Table S3. Simulation results for classification of the ordinal clinical significance of PCa assuming moderate regional heterogeneity using GLM as the base learner.

| Spatial Correlation | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Moderate $\sigma^2 = 4$ $\phi = 0.2$ $\nu = 0.8$ | Baseline | 1 | 60524 | 0 | 9120 | 0.13 | 0.36 | 0.40 |
| | | 2 | 16293 | 0 | 11564 | 1.00 | NA | |
| | | 3 | 18495 | 0 | 23292 | 0.44 | 0.47 | |
| | SL0 + $W_1$ | 1 | 61149 | 0 | 8495 | 0.12 | 0.33 | 0.37 |
| | | 2 | 15064 | 0 | 12793 | 1.00 | NA | |
| | | 3 | 15673 | 0 | 26114 | 0.38 | 0.45 | |
| | SL + $W_1$ | 1 | 62275 | 0 | 7370 | 0.11 | 0.31 | 0.33 |
| | | 2 | 16593 | 0 | 11265 | 1.00 | NA | |
| | | 3 | 10920 | 0 | 30867 | 0.26 | 0.38 | |
| | SL0 + $W_2$ | 1 | 48481 | 13529 | 7635 | 0.30 | 0.24 | 0.41 |
| | | 2 | 7616 | 8199 | 12042 | 0.71 | 0.73 | |
| | | 3 | 7914 | 8589 | 25284 | 0.39 | 0.44 | |
| | SL + $W_2$ | 1 | 49119 | 15442 | 5083 | 0.29 | 0.20 | 0.37 |
| | | 2 | 8465 | 10511 | 8882 | 0.62 | 0.71 | |
| | | 3 | 3528 | 10717 | 27542 | 0.34 | 0.34 | |
| Strong $\sigma^2 = 10$ $\phi = 0.5$ $\nu = 1.5$ | Baseline | 1 | 60165 | 0 | 9323 | 0.13 | 0.37 | 0.40 |
| | | 2 | 16341 | 0 | 11454 | 1.00 | NA | |
| | | 3 | 18520 | 0 | 23174 | 0.44 | 0.47 | |
| | SL0 + $W_1$ | 1 | 60923 | 0 | 8561 | 0.12 | 0.34 | 0.38 |
| | | 2 | 15149 | 0 | 12646 | 1.00 | NA | |
| | | 3 | 15760 | 0 | 25933 | 0.38 | 0.45 | |
| | SL + $W_1$ | 1 | 63432 | 3336 | 2720 | 0.09 | 0.20 | 0.25 |
| | | 2 | 12317 | 5206 | 10272 | 0.81 | 0.57 | |
| | | 3 | 3160 | 3572 | 34962 | 0.16 | 0.27 | |
| | SL0 + $W_2$ | 1 | 48395 | 13376 | 7718 | 0.30 | 0.24 | 0.41 |
| | | 2 | 7695 | 8090 | 12010 | 0.71 | 0.73 | |
| | | 3 | 7901 | 8472 | 25321 | 0.39 | 0.44 | |
| | SL + $W_2$ | 1 | 54941 | 12961 | 1587 | 0.21 | 0.11 | 0.27 |
| | | 2 | 6216 | 14062 | 7516 | 0.49 | 0.61 | |
| | | 3 | 916 | 8999 | 31778 | 0.24 | 0.22 | |

Table S4. Simulation results for classification of the ordinal clinical significance of PCa assuming moderate regional heterogeneity using QDA as the base learner.

| Spatial Correlation | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Moderate $\sigma^2 = 4$ $\phi = 0.2$ $\nu = 0.8$ | Baseline | 1 | 59145 | 1870 | 8630 | 0.15 | 0.35 | 0.39 |
| | | 2 | 14948 | 3272 | 9637 | 0.88 | 0.52 | |
| | | 3 | 17053 | 1691 | 23043 | 0.45 | 0.44 | |
| | SL0 + $W_1$ | 1 | 61215 | 0 | 8429 | 0.12 | 0.33 | 0.36 |
| | | 2 | 16169 | 0 | 11688 | 1.00 | NA | |
| | | 3 | 14361 | 0 | 27425 | 0.34 | 0.42 | |
| | SL + $W_1$ | 1 | 62875 | 0 | 6770 | 0.10 | 0.30 | 0.32 |
| | | 2 | 16572 | 0 | 11285 | 1.00 | NA | |
| | | 3 | 9894 | 0 | 31893 | 0.24 | 0.36 | |
| | SL0 + $W_2$ | 1 | 49249 | 13657 | 6738 | 0.29 | 0.24 | 0.39 |
| | | 2 | 8474 | 10047 | 9337 | 0.64 | 0.69 | |
| | | 3 | 7075 | 9091 | 25620 | 0.39 | 0.39 | |
| | SL + $W_2$ | 1 | 49691 | 15652 | 4301 | 0.29 | 0.19 | 0.36 |
| | | 2 | 8331 | 11013 | 8513 | 0.60 | 0.70 | |
| | | 3 | 3180 | 10332 | 28274 | 0.32 | 0.31 | |
| Strong $\sigma^2 = 10$ $\phi = 0.5$ $\nu = 1.5$ | Baseline | 1 | 58734 | 1898 | 8856 | 0.15 | 0.35 | 0.39 |
| | | 2 | 14991 | 3259 | 9545 | 0.88 | 0.53 | |
| | | 3 | 17068 | 1762 | 22862 | 0.45 | 0.45 | |
| | SL0 + $W_1$ | 1 | 60964 | 0 | 8525 | 0.12 | 0.33 | 0.37 |
| | | 2 | 16127 | 0 | 11668 | 1.00 | NA | |
| | | 3 | 14424 | 0 | 27270 | 0.35 | 0.43 | |
| | SL + $W_1$ | 1 | 63617 | 3810 | 2062 | 0.08 | 0.19 | 0.24 |
| | | 2 | 11909 | 6480 | 9406 | 0.77 | 0.55 | |
| | | 3 | 2590 | 4047 | 35056 | 0.16 | 0.25 | |
| | SL0 + $W_2$ | 1 | 49161 | 13433 | 6895 | 0.29 | 0.24 | 0.39 |
| | | 2 | 8453 | 9915 | 9427 | 0.64 | 0.69 | |
| | | 3 | 7104 | 8867 | 25723 | 0.38 | 0.39 | |
| | SL + $W_2$ | 1 | 55798 | 12432 | 1259 | 0.20 | 0.11 | 0.26 |
| | | 2 | 6166 | 14560 | 7069 | 0.48 | 0.59 | |
| | | 3 | 802 | 8541 | 32350 | 0.22 | 0.20 | |

Table S5. Simulation results for classification of the ordinal clinical significance of PCa assuming strong regional heterogeneity using QDA as the base learner.

| Spatial Correlation | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Moderate $\sigma^2 = 4$ $\phi = 0.2$ $\nu = 0.8$ | Baseline | 1 | 58424 | 1265 | 9287 | 0.15 | 0.38 | 0.41 |
| | | 2 | 15978 | 1952 | 9660 | 0.93 | 0.55 | |
| | | 3 | 19307 | 1115 | 20964 | 0.49 | 0.48 | |
| | SL0 + $W_1$ | 1 | 60502 | 0 | 8075 | 0.12 | 0.34 | 0.37 |
| | | 2 | 15865 | 0 | 11725 | 1.00 | NA | |
| | | 3 | 14704 | 0 | 26682 | 0.36 | 0.43 | |
| | SL0 + $W_2$ | 2 | 16347 | 0 | 11243 | 1.00 | NA | 0.40 |
| | | 3 | 10320 | 0 | 31066 | 0.25 | 0.37 | |
| | | 1 | 48577 | 13453 | 6947 | 0.30 | 0.24 | |
| | | 2 | 8433 | 9595 | 9562 | 0.65 | 0.70 | |
| | | 3 | 7236 | 9099 | 25051 | 0.39 | 0.40 | |
| | SL + $W_2$ | 1 | 48046 | 16241 | 4690 | 0.30 | 0.20 | 0.37 |
| | | 2 | 8343 | 10462 | 8785 | 0.62 | 0.72 | |
| | | 3 | 3449 | 10129 | 27808 | 0.33 | 0.33 | |
| Strong $\sigma^2 = 10$ $\phi = 0.5$ $\nu = 1.5$ | Baseline | 1 | 58969 | 1544 | 9525 | 0.16 | 0.37 | 0.41 |
| | | 2 | 16008 | 2342 | 9665 | 0.92 | 0.56 | |
| | | 3 | 19251 | 1374 | 21398 | 0.49 | 0.47 | |
| | SL0 + $W_1$ | 1 | 61263 | 0 | 8775 | 0.13 | 0.34 | 0.37 |
| | | 2 | 16173 | 0 | 11842 | 1.00 | NA | |
| | | 3 | 15106 | 0 | 26917 | 0.36 | 0.43 | |
| | SL + $W_1$ | 1 | 64151 | 3480 | 2407 | 0.08 | 0.20 | 0.25 |
| | | 2 | 12569 | 5579 | 9868 | 0.80 | 0.57 | |
| | | 3 | 3150 | 3789 | 35085 | 0.16 | 0.26 | |
| | SL0 + $W_2$ | 1 | 49228 | 13479 | 7331 | 0.30 | 0.25 | 0.40 |
| | | 2 | 8584 | 9621 | 9809 | 0.66 | 0.70 | |
| | | 3 | 7515 | 8947 | 25561 | 0.39 | 0.40 | |
| | SL + $W_2$ | 1 | 55376 | 13242 | 1420 | 0.21 | 0.12 | 0.27 |
| | | 2 | 6405 | 14309 | 7301 | 0.49 | 0.61 | |
| | | 3 | 953 | 8972 | 32097 | 0.24 | 0.21 | |

Table S6. Simulation results for classification of the ordinal clinical significance of PCa assuming moderate regional heterogeneity using RF as the base learner.

| Spatial Correlation | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Moderate $\sigma^2 = 4$ $\phi = 0.2$ $\nu = 0.8$ | Baseline | 1 | 56143 | 4822 | 8679 | 0.19 | 0.33 | 0.39 |
| | | 2 | 13031 | 6568 | 8258 | 0.76 | 0.58 | |
| | | 3 | 15148 | 4406 | 22234 | 0.47 | 0.43 | |
| | SL0 + $W_1$ | 1 | 60782 | 0 | 8862 | 0.13 | 0.34 | 0.37 |
| | | 2 | 16504 | 0 | 11354 | 1.00 | NA | |
| | | 3 | 15303 | 0 | 26484 | 0.37 | 0.43 | |
| | SL + $W_1$ | 1 | 62777 | 0 | 6867 | 0.10 | 0.30 | 0.32 |
| | | 2 | 16573 | 0 | 11284 | 1.00 | NA | |
| | | 3 | 9982 | 0 | 31805 | 0.24 | 0.36 | |
| | SL0 + $W_2$ | 1 | 48698 | 13242 | 7705 | 0.30 | 0.26 | 0.40 |
| | | 2 | 8884 | 9325 | 9649 | 0.67 | 0.70 | |
| | | 3 | 7962 | 8508 | 25317 | 0.39 | 0.41 | |
| | SL + $W_2$ | 1 | 49647 | 15591 | 4406 | 0.29 | 0.19 | 0.36 |
| | | 2 | 8367 | 10916 | 8574 | 0.61 | 0.70 | |
| | | 3 | 3225 | 10036 | 28226 | 0.32 | 0.32 | |
| Strong $\sigma^2 = 10$ $\phi = 0.5$ $\nu = 1.5$ | Baseline | 1 | 55754 | 4903 | 8831 | 0.20 | 0.34 | 0.39 |
| | | 2 | 12999 | 6626 | 8170 | 0.76 | 0.59 | |
| | | 3 | 15118 | 4443 | 22131 | 0.47 | 0.43 | |
| | SL0 + $W_1$ | 1 | 60582 | 0 | 8907 | 0.13 | 0.34 | 0.37 |
| | | 2 | 16499 | 0 | 11296 | 1.00 | NA | |
| | | 3 | 15317 | 0 | 26376 | 0.37 | 0.43 | |
| | SL + $W_1$ | 1 | 63664 | 3787 | 2038 | 0.08 | 0.18 | 0.24 |
| | | 2 | 11869 | 6482 | 9444 | 0.77 | 0.55 | |
| | | 3 | 2550 | 4032 | 35111 | 0.16 | 0.25 | |
| | SL0 + $W_2$ | 1 | 48635 | 13094 | 7760 | 0.30 | 0.26 | 0.40 |
| | | 2 | 8883 | 9230 | 9682 | 0.67 | 0.70 | |
| | | 3 | 7940 | 8335 | 25418 | 0.39 | 0.41 | |
| | SL + $W_2$ | 1 | 56034 | 12213 | 1241 | 0.19 | 0.11 | 0.26 |
| | | 2 | 6198 | 14511 | 7085 | 0.48 | 0.59 | |
| | | 3 | 798 | 8492 | 32403 | 0.22 | 0.20 | |

Table S7. Simulation results for classification of the ordinal clinical significance of PCa assuming strong regional heterogeneity using RF as the base learner.

| Spatial Correlation | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Moderate $\sigma^2 = 4$ $\phi = 0.2$ $\nu = 0.8$ | Baseline | 1 | 55253 | 4842 | 8882 | 0.20 | 0.34 | 0.39 |
| | | 2 | 12821 | 6795 | 7973 | 0.75 | 0.58 | |
| | | 3 | 15366 | 4384 | 21635 | 0.48 | 0.44 | |
| | SL0 + $W_1$ | 1 | 60012 | 0 | 8965 | 0.13 | 0.35 | 0.38 |
| | | 2 | 16254 | 0 | 11336 | 1.00 | NA | |
| | | 3 | 15401 | 0 | 25985 | 0.37 | 0.44 | |
| | SL + $W_1$ | 1 | 61693 | 0 | 7284 | 0.11 | 0.30 | 0.33 |
| | | 2 | 16267 | 0 | 11323 | 1.00 | NA | |
| | | 3 | 10211 | 0 | 31175 | 0.25 | 0.37 | |
| | SL0 + $W_2$ | 1 | 48080 | 12942 | 7955 | 0.30 | 0.26 | 0.41 |
| | | 2 | 8862 | 8941 | 9787 | 0.68 | 0.70 | |
| | | 3 | 8009 | 8413 | 24964 | 0.40 | 0.42 | |
| | SL + $W_2$ | 1 | 47961 | 16150 | 4866 | 0.30 | 0.20 | 0.37 |
| | | 2 | 8354 | 10350 | 8885 | 0.62 | 0.72 | |
| | | 3 | 3419 | 10004 | 27964 | 0.32 | 0.33 | |
| Strong $\sigma^2 = 10$ $\phi = 0.5$ $\nu = 1.5$ | Baseline | 1 | 55815 | 5060 | 9164 | 0.20 | 0.34 | 0.40 |
| | | 2 | 13061 | 6857 | 8097 | 0.76 | 0.58 | |
| | | 3 | 15544 | 4493 | 21986 | 0.48 | 0.44 | |
| | SL0 + $W_1$ | 1 | 60899 | 0 | 9139 | 0.13 | 0.35 | 0.38 |
| | | 2 | 16645 | 0 | 11370 | 1.00 | NA | |
| | | 3 | 15767 | 0 | 26256 | 0.38 | 0.44 | |
| | SL + $W_1$ | 1 | 64120 | 3433 | 2485 | 0.08 | 0.19 | 0.25 |
| | | 2 | 12469 | 5468 | 10078 | 0.80 | 0.57 | |
| | | 3 | 3028 | 3570 | 35425 | 0.16 | 0.26 | |
| | SL0 + $W_2$ | 1 | 48754 | 13095 | 8189 | 0.30 | 0.26 | 0.41 |
| | | 2 | 9045 | 9046 | 9923 | 0.68 | 0.70 | |
| | | 3 | 8214 | 8339 | 25470 | 0.39 | 0.42 | |
| | SL + $W_2$ | 1 | 55396 | 13190 | 1452 | 0.21 | 0.12 | 0.27 |
| | | 2 | 6388 | 14191 | 7435 | 0.49 | 0.61 | |
| | | 3 | 933 | 8656 | 32435 | 0.23 | 0.21 | |

Table S8. Simulation results of GLM + QDA + RF for classifying the ordinal clinical significance of PCa assuming moderate regional heterogeneity.

| Spatial Correlation | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Moderate $\sigma^2 = 4$ $\phi = 0.2$ $\nu = 0.8$ | SL0 + $W_1$ | 1 | 61024 | 0 | 8621 | 0.12 | 0.33 | 0.36 |
| | | 2 | 16180 | 0 | 11677 | 1.00 | NA | |
| | | 3 | 14085 | 0 | 27702 | 0.34 | 0.42 | |
| | SL + $W_1$ | 1 | 63155 | 0 | 6489 | 0.09 | 0.29 | 0.31 |
| | | 2 | 16440 | 0 | 11417 | 1.00 | NA | |
| | | 3 | 9206 | 0 | 32581 | 0.22 | 0.35 | |
| | SL0 + $W_2$ | 1 | 48114 | 14220 | 7311 | 0.31 | 0.23 | 0.39 |
| | | 2 | 8102 | 10361 | 9395 | 0.63 | 0.69 | |
| | | 3 | 6584 | 8927 | 26276 | 0.37 | 0.39 | |
| | SL + $W_2$ | 1 | 50473 | 15254 | 3918 | 0.28 | 0.18 | 0.35 |
| | | 2 | 8164 | 11347 | 8347 | 0.59 | 0.69 | |
| | | 3 | 2890 | 10245 | 28651 | 0.31 | 0.30 | |
| Strong $\sigma^2 = 10$ $\phi = 0.5$ $\nu = 1.5$ | SL0 + $W_1$ | 1 | 60814 | 0 | 8675 | 0.12 | 0.33 | 0.36 |
| | | 2 | 16169 | 0 | 11626 | 1.00 | NA | |
| | | 3 | 14171 | 0 | 27522 | 0.34 | 0.42 | |
| | SL + $W_1$ | 1 | 63582 | 4570 | 1337 | 0.09 | 0.16 | 0.22 |
| | | 2 | 10582 | 8792 | 8421 | 0.68 | 0.51 | |
| | | 3 | 1605 | 4696 | 35392 | 0.15 | 0.22 | |
| | SL0 + $W_2$ | 1 | 48102 | 14000 | 7387 | 0.31 | 0.23 | 0.39 |
| | | 2 | 8122 | 10252 | 9421 | 0.63 | 0.69 | |
| | | 3 | 6620 | 8765 | 26308 | 0.37 | 0.39 | |
| | SL + $W_2$ | 1 | 57296 | 11324 | 869 | 0.18 | 0.10 | 0.24 |
| | | 2 | 5793 | 15441 | 6561 | 0.44 | 0.55 | |
| | | 3 | 552 | 7890 | 33251 | 0.20 | 0.18 | |

Table S9. Simulation results of GLM + QDA + RF for classifying the ordinal clinical significance of PCa assuming strong regional heterogeneity.

| Spatial Correlation | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Moderate $\sigma^2 = 4$ $\phi = 0.2$ $\nu = 0.8$ | SL0 + $W_1$ | 1 | 60292 | 0 | 8685 | 0.13 | 0.33 | 0.37 |
| | | 2 | 15868 | 0 | 11722 | 1.00 | NA | |
| | | 3 | 14320 | 0 | 27065 | 0.35 | 0.43 | |
| | SL + $W_1$ | 1 | 62548 | 0 | 6429 | 0.09 | 0.29 | 0.31 |
| | | 2 | 16196 | 1 | 11393 | 1.00 | NA | |
| | | 3 | 9104 | 0 | 32281 | 0.22 | 0.36 | |
| | SL0 + $W_2$ | 1 | 47441 | 14005 | 7531 | 0.31 | 0.24 | 0.40 |
| | | 2 | 8083 | 9894 | 9613 | 0.64 | 0.70 | |
| | | 3 | 6673 | 8904 | 25809 | 0.38 | 0.40 | |
| | SL + $W_2$ | 1 | 49966 | 15108 | 3903 | 0.28 | 0.18 | 0.35 |
| | | 2 | 8093 | 11104 | 8393 | 0.60 | 0.69 | |
| | | 3 | 2888 | 10060 | 28438 | 0.31 | 0.30 | |
| Strong $\sigma^2 = 10$ $\phi = 0.5$ $\nu = 1.5$ | SL0 + $W_1$ | 1 | 61141 | 0 | 8897 | 0.13 | 0.34 | 0.37 |
| | | 2 | 16245 | 0 | 11770 | 1.00 | NA | |
| | | 3 | 14734 | 0 | 27289 | 0.35 | 0.43 | |
| | SL + $W_1$ | 1 | 64154 | 4545 | 1340 | 0.08 | 0.16 | 0.23 |
| | | 2 | 10801 | 8734 | 8480 | 0.69 | 0.51 | |
| | | 3 | 1686 | 4679 | 35658 | 0.15 | 0.22 | |
| | SL0 + $W_2$ | 1 | 48144 | 14103 | 7791 | 0.31 | 0.24 | 0.40 |
| | | 2 | 8256 | 10020 | 9738 | 0.64 | 0.70 | |
| | | 3 | 6937 | 8839 | 26247 | 0.38 | 0.40 | |
| | SL + $W_2$ | 1 | 57678 | 11490 | 870 | 0.18 | 0.10 | 0.24 |
| | | 2 | 5943 | 15471 | 6601 | 0.45 | 0.56 | |
| | | 3 | 586 | 7911 | 33525 | 0.20 | 0.18 | |

## C.2 Application to Patient Data

Tables S10 and S11 report the ordinal classification results on patient data using QDA and RF, respectively, as the base learner. Table S12 reports the ordinal classification results on patient data when combining the multi-resolution GLM, QDA and RF together. Each Table reports the results using either the predicted probabilities for the first two categories or the classified cancer categories from the stage-one multi-resolution base learners as the covariates for the stage-two model in the proposed super learner.

Table S10. Ordinal classification results on patient data using QDA as the base learner.

| Stage-one Output | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | | | |
| | | 1 | 87136 | 297 | 1554 | 0.021 | 0.152 | |
| | Baseline | 2 | 5891 | 10 | 342 | 0.998 | 0.975 | 0.168 |
| | | 3 | 9782 | 90 | 1835 | 0.843 | 0.508 | |
| | | 1 | 87515 | 0 | 1472 | 0.017 | 0.155 | |
| | SL0 + $W_1$ | 2 | 5937 | 0 | 306 | 1.000 | NA | 0.167 |
| | | 3 | 10136 | 0 | 1571 | 0.866 | 0.531 | |
| Probabilities | | 1 | 87952 | 0 | 1035 | 0.012 | 0.146 | |
| for the First | SL + $W_1$ | 2 | 5984 | 0 | 259 | 1.000 | NA | 0.152 |
| Two Categories | | 3 | 9011 | 0 | 2696 | 0.770 | 0.324 | |
| | | 1 | 65662 | 13795 | 9530 | 0.262 | 0.086 | |
| | SL0 + $W_2$ | 2 | 2484 | 1312 | 2447 | 0.790 | 0.925 | 0.321 |
| | | 3 | 3702 | 2344 | 5661 | 0.516 | 0.679 | |
| | | 1 | 64615 | 17302 | 7070 | 0.274 | 0.080 | |
| | SL + $W_2$ | 2 | 2590 | 1733 | 1920 | 0.722 | 0.921 | 0.324 |
| | | 3 | 3000 | 2768 | 5939 | 0.493 | 0.602 | |
| | | 1 | 87136 | 297 | 1554 | 0.021 | 0.152 | |
| | Baseline | 2 | 5891 | 10 | 342 | 0.998 | 0.975 | 0.168 |
| | | 3 | 9782 | 90 | 1835 | 0.843 | 0.508 | |
| | | 1 | 87431 | 0 | 1556 | 0.017 | 0.150 | |
| | SL0 + $W_1$ | 2 | 5846 | 0 | 397 | 1.000 | NA | 0.163 |
| | | 3 | 9582 | 0 | 2125 | 0.818 | 0.479 | |
| | | 1 | 87684 | 0 | 1303 | 0.015 | 0.146 | |
| | SL + $W_1$ | 2 | 6111 | 0 | 132 | 1.000 | NA | 0.153 |
| Categories | | 3 | 8842 | 0 | 2865 | 0.755 | 0.334 | |
| | | 1 | 82439 | 1400 | 5148 | 0.074 | 0.118 | |
| | SL0 + $W_2$ | 2 | 4345 | 527 | 1371 | 0.916 | 0.779 | 0.182 |
| | | 3 | 6696 | 460 | 4551 | 0.611 | 0.589 | |
| | | 1 | 76014 | 8874 | 4099 | 0.146 | 0.088 | |
| | SL + $W_2$ | 2 | 3397 | 1764 | 1082 | 0.717 | 0.870 | 0.227 |
| | | 3 | 3915 | 2946 | 4846 | 0.586 | 0.517 | |

Table S11. Ordinal classification results on patient data using RF as the base learner.

| Stage-one Output | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Probabilities for the First Two Categories | Baseline | 1 | 84951 | 1021 | 3015 | 0.045 | 0.143 | 0.180 |
| | | 2 | 5511 | 169 | 563 | 0.973 | 0.898 | |
| | | 3 | 8719 | 470 | 2518 | 0.785 | 0.587 | |
| | SL0 + $W_1$ | 1 | 87393 | 0 | 1594 | 0.018 | 0.146 | 0.158 |
| | | 2 | 5833 | 0 | 410 | 1.000 | NA | |
| | | 3 | 9113 | 0 | 2594 | 0.778 | 0.436 | |
| | SL + $W_1$ | 1 | 87309 | 0 | 1678 | 0.019 | 0.125 | 0.134 |
| | | 2 | 5970 | 0 | 273 | 1.000 | NA | |
| | | 3 | 6456 | 0 | 5251 | 0.551 | 0.271 | |
| | SL0 + $W_2$ | 1 | 65908 | 13174 | 9905 | 0.259 | 0.086 | 0.311 |
| | | 2 | 3206 | 1291 | 1746 | 0.793 | 0.923 | |
| | | 3 | 2977 | 2385 | 6345 | 0.458 | 0.647 | |
| | SL + $W_2$ | 1 | 64888 | 17586 | 6513 | 0.271 | 0.050 | 0.295 |
| | | 2 | 2304 | 2545 | 1394 | 0.592 | 0.888 | |
| | | 3 | 1100 | 2626 | 7981 | 0.318 | 0.498 | |
| Categories | Baseline | 1 | 84927 | 1037 | 3023 | 0.046 | 0.143 | 0.180 |
| | | 2 | 5475 | 172 | 596 | 0.972 | 0.898 | |
| | | 3 | 8671 | 481 | 2555 | 0.782 | 0.586 | |
| | SL0 + $W_1$ | 1 | 87495 | 0 | 1492 | 0.017 | 0.149 | 0.160 |
| | | 2 | 5964 | 0 | 279 | 1.000 | NA | |
| | | 3 | 9363 | 0 | 2344 | 0.800 | 0.430 | |
| | SL + $W_1$ | 1 | 87515 | 0 | 1472 | 0.017 | 0.132 | 0.139 |
| | | 2 | 6115 | 0 | 128 | 1.000 | NA | |
| | | 3 | 7197 | 0 | 4510 | 0.615 | 0.262 | |
| | SL0 + $W_2$ | 1 | 78988 | 2218 | 7781 | 0.112 | 0.115 | 0.209 |
| | | 2 | 4558 | 305 | 1380 | 0.951 | 0.903 | |
| | | 3 | 5683 | 687 | 5337 | 0.544 | 0.633 | |
| | SL + $W_2$ | 1 | 70088 | 13920 | 4979 | 0.212 | 0.064 | 0.263 |
| | | 2 | 3199 | 1770 | 1274 | 0.716 | 0.906 | |
| | | 3 | 1610 | 3141 | 6956 | 0.406 | 0.473 | |

Table S12. Ordinal classification results for GLM + QDA + RF on patient data.

| Stage-one Output | Method | True PCa Category | Classified Category 1 | 2 | 3 | FPR | FDR | Overall Error Rate |
|---|---|---|---|---|---|---|---|---|
| Probabilities for the First Two Categories | SL0 + $W_1$ | 1 | 86704 | 0 | 2283 | 0.026 | 0.141 | 0.158 |
| | | 2 | 5865 | 0 | 378 | 1.000 | NA | |
| | | 3 | 8381 | 0 | 3326 | 0.716 | 0.444 | |
| | SL + $W_1$ | 1 | 86358 | 0 | 2629 | 0.030 | 0.125 | 0.143 |
| | | 2 | 6023 | 0 | 220 | 1.000 | NA | |
| | | 3 | 6369 | 0 | 5338 | 0.544 | 0.348 | |
| | SL0 + $W_2$ | 1 | 66003 | 15079 | 7905 | 0.258 | 0.076 | 0.304 |
| | | 2 | 2487 | 2004 | 1752 | 0.679 | 0.897 | |
| | | 3 | 2931 | 2318 | 6458 | 0.448 | 0.599 | |
| | SL + $W_2$ | 1 | 66130 | 16911 | 5946 | 0.257 | 0.058 | 0.290 |
| | | 2 | 2600 | 2826 | 817 | 0.547 | 0.877 | |
| | | 3 | 1456 | 3266 | 6985 | 0.403 | 0.492 | |
| Categories | SL0 + $W_1$ | 1 | 87613 | 0 | 1374 | 0.015 | 0.146 | 0.156 |
| | | 2 | 5944 | 0 | 299 | 1.000 | NA | |
| | | 3 | 9016 | 0 | 2691 | 0.770 | 0.383 | |
| | SL + $W_1$ | 1 | 86699 | 0 | 2288 | 0.026 | 0.131 | 0.145 |
| | | 2 | 6090 | 0 | 153 | 1.000 | NA | |
| | | 3 | 6989 | 0 | 4718 | 0.597 | 0.341 | |
| | SL0 + $W_2$ | 1 | 78898 | 4093 | 5996 | 0.113 | 0.109 | 0.206 |
| | | 2 | 4395 | 770 | 1078 | 0.877 | 0.873 | |
| | | 3 | 5263 | 1192 | 5252 | 0.551 | 0.574 | |
| | SL + $W_2$ | 1 | 71464 | 13560 | 3963 | 0.219 | 0.077 | 0.266 |
| | | 2 | 3573 | 1909 | 761 | 0.662 | 0.893 | |
| | | 3 | 2664 | 2589 | 6454 | 0.411 | 0.418 | |