

Supplementary material :

Supplementary Table 1: Summary of MRI scan acquisition parameters

| Acquisition parameters | Siemens 1.5T (Institution 1) | Philips Achieva 3T (Institution 1) | Siemens 1.5T (Institution 2) | Philips 1.5T (Institution 2) |
|------------------------------------|---------------------------------|---------------------------------------|---------------------------------|---------------------------------|
| Number of patients | 75 | 32 | 37 | 51 |
| Magnetic field strength (Tesla) | 1.5T | 3T | 1.5T | 1.5T |
| T2-Weighted | | | | |
| Matrix (pixels) | 192 × 192 | 268 × 268 | 250 × 250 | 264 × 264 |
| Field of view (mm) | 250 × 250 | 320 × 320 | 256 × 256 | 320 × 320 |
| ET (ms) | 110 | 90 | 125 | 110 |
| RT (ms) | 2500 | 4500 | 2000 | 3500 |
| Slice Thickness (mm) | 1.5 | 1.5 | 2 | 4 |
| ADC map | | | | |
| Matrix (pixels) | 128 × 128 | 144 × 144 | 192 × 144 | 68 × 65 |
| Field of view (mm) | 200 × 200 | 240 × 240 | 192 × 192 | 144 × 144 |
| ET (ms) | 80 | 80 | 95 | 80 |
| RT (ms) | 2300 | 2300 | 2500 | 4000 |
| Slice Thickness (mm) | 3.5 | 3.5 | 3.5 | 4 |
| Diffusion gradient | B50-400-1000 | B100-600-1000 | B50-800 | B80-200-400- 1100 |

Abbreviations: RT: repetition time, ET: echo time

Supplementary Table 2: Patients and tumors characteristics of the initial population (Institution 1 + Institution 2)

| Institution | | Institution 1 | | | Institution 2 | | |
|----------------------------------|-------------|-------------------|--|---------------|-------------------|--|--------------------|
| Patients characteristics | | Selected patients | Excluded patients because of unavailable MRI | p-value | Selected patients | Excluded patients because of unavailable MRI | p-value |
| Number of patients | | 107 | 30 | | 88 | 277 | |
| Age at diagnostic (mean.yo) | | 65.25 | 64.5 | 0.56 | 66.2 | 67.5 | 0.09 |
| PSA (mean. ng/mL) | | 9.10 | 8.18 | 0.50 | 8.47 | 8.84 | 0.61 |
| Post-operative tumour status (%) | pT2 | 35.5 | 46.7 | 0.37 | 44.3 | 37.5 | 0.31 |
| | pT3a-pT3b | 64.5 | 53.3 | | 55.7 | 62.5 | |
| | pT4 | 0 | 0 | | 0 | 0 | |
| Nodal status (%) | pN0 | 87.8 | 73.3 | 0.10 | 96.6 | 96.7 | 0.77 |
| | cN0 | 12.2 | 26.7 | | 3.4 | 3.3 | |
| Surgical margins (%) | R0 | 40.2 | 33.3 | 0.64 | 22.7 | 42.2 | 0.0015 |
| | R1 | 58.9 | 60 | 0.92 | 77.3 | 56.7 | 0.0008 |
| | Rx | 0.9 | 6.7 | 0.22 | 0 | 1.1 | 0.75 |
| Gleason score (%) | Gleason ≤ 7 | 85.5 | 85 | 0.82 | 83.0 | 82.7 | 0.92 |
| | Gleason > 7 | 14.5 | 15 | | 17.0 | 17.3 | |
| Capra-S Score (median) | | 4 | 4 | | 4 | 4 | |
| Number of risk factors | | 1 | 1 | | 1 | 1 | |
| Post-operative PSA (mean. ng/mL) | | 0.012 | 0.017 | 0.07 | 0.016 | 0.017 | 0.36 |
| bRFS (median. months) | | 42.6 | 55.3 | 0.06 | 33.0 | 63.1 | 0.001 |
| Biochemical recurrence (%) | | 15.9 | 16.1 | 0.49 | 38.6 | 28.5 | 0.10 |
| Follow-up (median. months) | | 52.0 | 69.4 | 0.0002 | 41.9 | 77.7 | < 0.0001 |

Supplementary Table 3: Inter-reader variability assessment - segmentation

| PatientID | Hausdorff E1-E2 (mm) | Dice E1 - E2 | Hausdorff E1 - E3 (mm) | Dice E1 - E3 | Hausdorff E2 - E3 (mm) | Dice E2 - E3 |
|-------------|----------------------|--------------|------------------------|--------------|------------------------|--------------|
| Patient#001 | 1.17 | 0.75 | 0.77 | 0.8 | 0.68 | 0.84 |
| Patient#002 | 0.58 | 0.83 | 0.66 | 0.8 | 0.3 | 0.88 |
| Patient#003 | 0.45 | 0.81 | 0.78 | 0.77 | 0.45 | 0.81 |
| Patient#007 | 0.74 | 0.84 | 0.34 | 0.92 | 0.88 | 0.81 |
| Patient#009 | 0.84 | 0.78 | 1.43 | 0.68 | 0.77 | 0.81 |
| Patient#010 | 0.97 | 0.79 | 0.82 | 0.81 | 0.53 | 0.89 |
| Patient#013 | 1.24 | 0.67 | 1.68 | 0.56 | 0.73 | 0.71 |
| Patient#014 | 2.70 | 0.64 | 2.27 | 0.66 | 0.55 | 0.84 |
| Patient#017 | 0.97 | 0.73 | 0.77 | 0.76 | 0.37 | 0.87 |
| Patient#018 | 0.74 | 0.82 | 1.14 | 0.76 | 0.75 | 0.84 |
| Patient#021 | 1.34 | 0.62 | 0.94 | 0.70 | 0.35 | 0.83 |
| Patient#022 | 0.59 | 0.82 | 0.44 | 0.81 | 0.63 | 0.79 |
| Patient#024 | 1.31 | 0.60 | 0.53 | 0.69 | 0.89 | 0.76 |
| Patient#025 | 0.82 | 0.79 | 0.51 | 0.84 | 0.47 | 0.86 |
| Patient#026 | 0.95 | 0.77 | 0.82 | 0.80 | 0.54 | 0.85 |

Abbreviations: E1-3: Expert 1-3, ADC : ADC SZE_{GLSZM} value depending on the selected ROI

Supplementary Table 4: Inter-reader variability assessment – BCR predictions

| PatientID | Age (y) | PSA preop | Gleason | PSA postop | TR | Margins | Capra | Nb risk Factors | ADC E1 | ADC E2 | ADC E3 | BCR | BCR ADC E1 | BCR ADC E2 | BCR ADC E3 |
|-------------|---------|-----------|---------|------------|-----|---------|-------|-----------------|--------|--------|--------|-----|------------|------------|------------|
| Patient#001 | 68 | 7.35 | 4 + 3 | 0.02 | T3a | R0 | 4 | 1 | 0.78 | 0.76 | 0.77 | 0 | 0 | 0 | 0 |
| Patient#002 | 723 | 14.06 | 3 + 4 | 0.01 | T3a | R1 | 6 | 2 | 0.70 | 0.72 | 0.72 | 0 | 0 | 0 | 0 |
| Patient#003 | 65 | 4.90 | 4 + 3 | 0.01 | T3b | R1 | 7 | 2 | 0.75 | 0.74 | 0.72 | 1 | 0 | 0 | 0 |
| Patient#007 | 701 | 7.65 | 5 + 5 | 0.01 | T2c | R0 | 4 | 1 | 0.51 | 0.51 | 0.51 | 1 | 1 | 1 | 1 |
| Patient#009 | 67 | 7.50 | 4 + 3 | 0.03 | T3a | R1 | 6 | 2 | 0.65 | 0.63 | 0.54 | 1 | 0 | 0 | 0 |
| Patient#010 | 61 | 6.60 | 3 + 4 | 0.01 | T2c | R1 | 4 | 1 | 0.64 | 0.67 | 0.69 | 0 | 0 | 0 | 0 |
| Patient#013 | 73 | 10.00 | 4 + 4 | 0.01 | T2c | R1 | 6 | 2 | 0.47 | 0.44 | 0.43 | 1 | 1 | 1 | 1 |
| Patient#014 | 71 | 6.09 | 3 + 4 | 0.01 | T3a | R0 | 3 | 1 | 0.76 | 0.74 | 0.76 | 0 | 0 | 0 | 0 |
| Patient#017 | 54 | 4.20 | 3 + 4 | 0.03 | T2c | R1 | 3 | 1 | 0.41 | 0.39 | 0.41 | 1 | 1 | 1 | 1 |
| Patient#018 | 65 | 14.00 | 3 + 3 | 0.01 | T2c | R1 | 4 | 1 | 0.68 | 0.67 | 0.70 | 0 | 0 | 0 | 0 |
| Patient#021 | 63 | 7.99 | 3 + 4 | 0.01 | T3a | R0 | 3 | 1 | 0.43 | 0.40 | 0.40 | 1 | 1 | 1 | 1 |
| Patient#022 | 71 | 7.50 | 4 + 4 | 0.02 | T3a | R0 | 5 | 2 | 0.74 | 0.71 | 0.72 | 0 | 0 | 0 | 0 |
| Patient#024 | 63 | 9.40 | 4 + 3 | 0.02 | T3a | R1 | 6 | 2 | 0.81 | 0.82 | 0.81 | 0 | 0 | 0 | 0 |
| Patient#025 | 59 | 7.95 | 4 + 3 | 0.02 | T3a | R0 | 4 | 1 | 0.77 | 0.76 | 0.76 | 0 | 0 | 0 | 0 |
| Patient#026 | 62 | 8.30 | 5 + 5 | 0.01 | T3b | R1 | 9 | 3 | 0.73 | 0.73 | 0.73 | 0 | 0 | 0 | 0 |

Abbreviations: BCR: Biochemical Recurrence ground-truth. PSA: Prostate Specific Antigen. Preop: pre-operative. Postop: post-operative. E1-3: Expert 1-3. ADC : ADC SZE_{GLSZM} value depending on the selected delineated volume of interest.

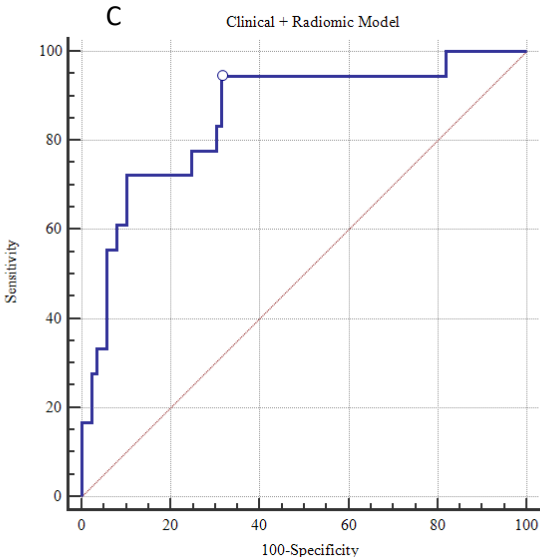
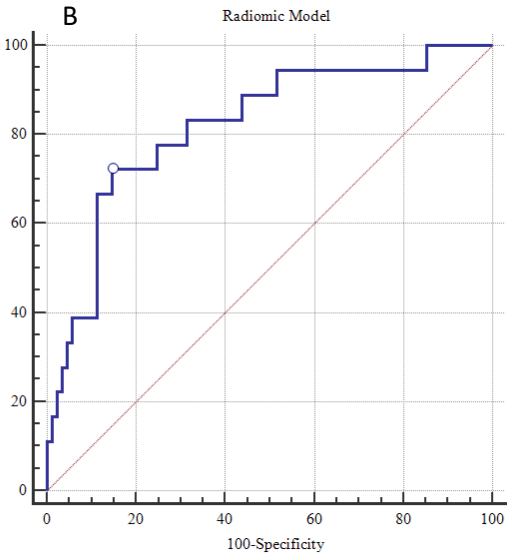
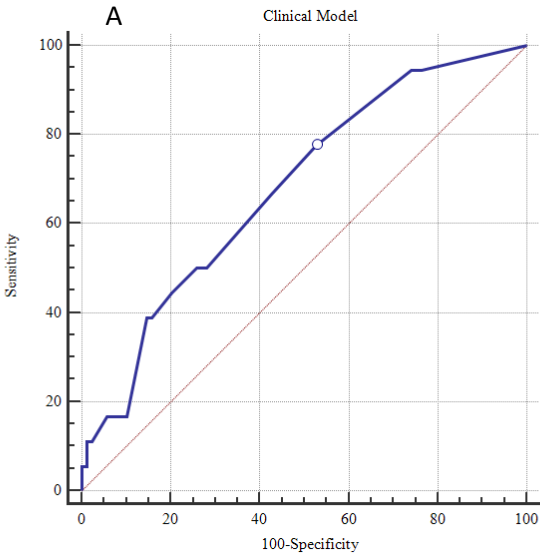
Supplementary Table 5 : Radiomics Quality Score

| Item | Points | Current Study |
|--|--|---------------|
| Image protocol quality – well-documented image protocols (e.g., contrast, slice thickness, energy, etc.) and/or usage of public image protocols allow reproducibility/replicability | +1 (if protocols are well-documented)+1 (if public protocol is used) | 2 |
| Multiple segmentations – possible actions are: segmentation by different physicians/algorithms/software, perturbing segmentations by (random) noise, segmentation at different breathing cycles. Analyze feature robustness to segmentation variabilities | +1 | 1 |
| Phantom study on all scanners – detect inter-scanner differences and vendor-dependent features. Analyze feature robustness to these sources of variability | +1 | 0 |
| Imaging at multiple time points – collect individuals’ images at additional time points. Analyze feature robustness to temporal variabilities (e.g., organ movement, organ expansion/shrinkage). | +1 | 0 |
| Feature reduction or adjustment for multiple testing – decreases the risk of overfitting. Overfitting is inevitable if the number of features exceeds the number of samples. Consider feature robustness when selecting features | –3 (if neither measure is implemented)+3 (if either measure is implemented) | 3 |
| Multivariable analysis with non radiomic features (e.g., EGFR mutation) – is expected to provide a more holistic model. Permits correlating/inferencing between radiomics and non radiomics features | +1 | 1 |
| Detect and discuss biological correlates – demonstration of phenotypic differences (possibly associated with underlying gene–protein expression patterns) deepens understanding of radiomics and biology | +1 | 0 |
| Cut-off analyses – determine risk groups by either the median, a previously published cut-off or report a continuous risk variable. Reduces the risk of reporting overly optimistic results | +1 | 1 |
| Discrimination statistics – report discrimination statistics (e.g., C-statistic, ROC curve, AUC) and their statistical significance (e.g., p-values, confidence intervals). One can also apply resampling method (e.g., bootstrapping, cross-validation) | +1 (if a discrimination statistic and its statistical significance are reported)+1 (if also an resampling method technique is applied) | 1 |
| Calibration statistics – report calibration statistics (e.g., Calibration-in-the-large/slope, calibration plots) and their statistical significance (e.g., p-values, confidence intervals). One can also apply resampling method (e.g., bootstrapping, cross-validation) | +1 (if a calibration statistic and its statistical significance are reported)+1 (if also an resampling method technique is applied) | 1 |

| | | |
|--|--|----|
| Prospective study registered in a trial database – provides the highest level of evidence supporting the clinical validity and usefulness of the radiomics biomarker | +7 (for prospective validation of a radiomics signature in an appropriate trial) | 0 |
| Comparison to ‘gold standard’ – assess the extent to which the model agrees with/is superior to the current ‘gold standard’ method (e.g.. TNM-staging for survival prediction). This comparison shows the added value of radiomics | –5 (if validation is missing)+2 (if validation is based on a dataset from the same institute)+3 (if validation is based on a dataset from another institute)+4 (if validation is based on two datasets from two distinct institutes)+4 (if the study validates a previously published signature)+5 (if validation is based on three or more datasets from distinct institutes)*Datasets should be of comparable size and should have at least 10 events per model feature. | 4 |
| Potential clinical utility – report on the current and potential application of the model in a clinical setting (e.g.. decision curve analysis) | +2 | 2 |
| Cost-effectiveness analysis – report on the cost-effectiveness of the clinical application (e.g.. quality adjusted life years generated) | +2 | 2 |
| Open science and data – make code and data publicly available. Open science facilitates knowledge transfer and reproducibility of the study | +1 | 0 |
| Comparison to ‘gold standard’ – assess the extent to which the model agrees with/is superior to the current ‘gold standard’ method (e.g.. TNM-staging for survival prediction). This comparison shows the added value of radiomics | +1 (if scans are open source)+1 (if region of interest segmentations are open source)+1 (if code is open source)+1 (if radiomics features are calculated on a set of representative ROIs and the calculated features + representative ROIs are open source) | 0 |
| Total | 36 | 18 |

Supplementary Figure 1: Receiver operating characteristic (ROC) curves without Combat Harmonization Method

- A: clinical model - training**
- B: radiomic model - training**
- C: clinical – radiomic model - training**



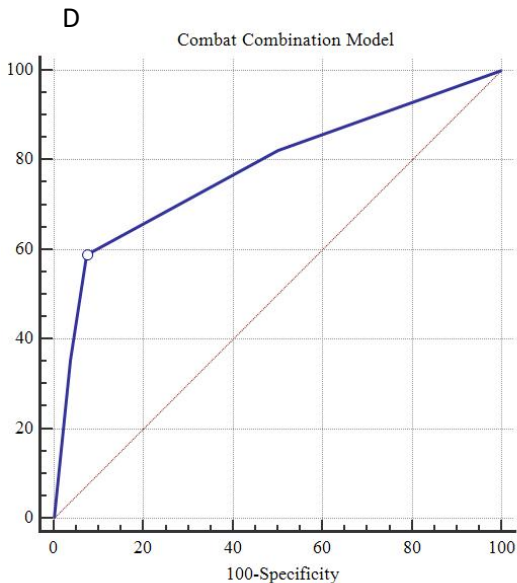
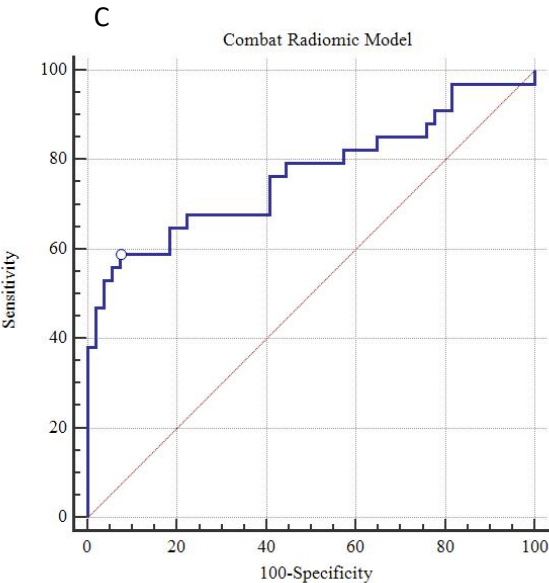
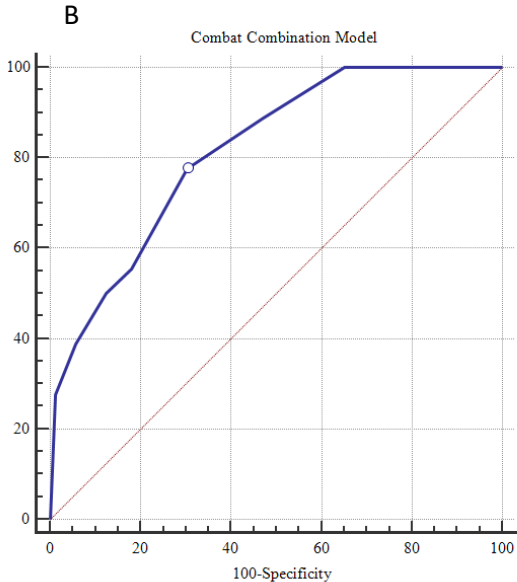
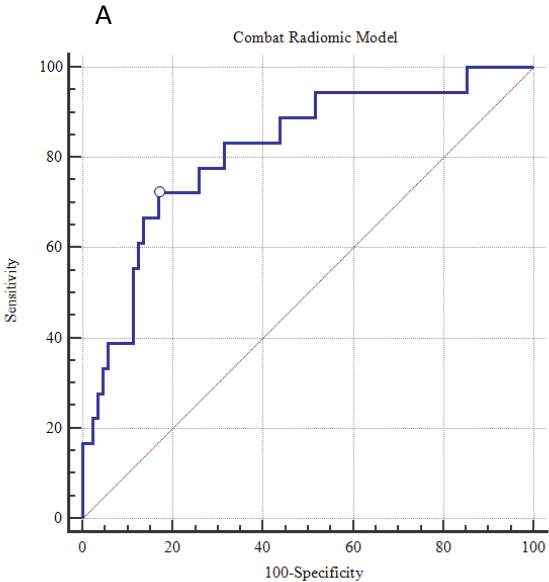
Supplementary Figure 2: Receiver operating characteristic (ROC) curves after Combat Harmonization Method

A: radiomic model – training

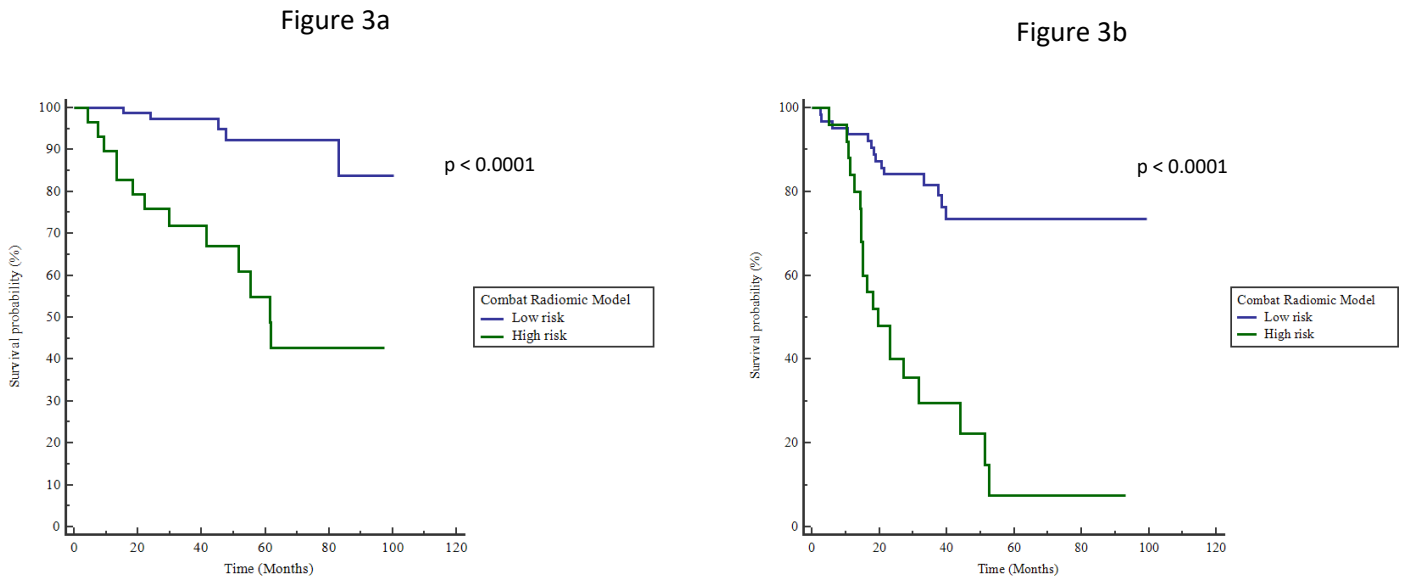
C: radiomic model – testing

B: clinical – radiomic model – training

D: clinical – radiomic model - testing



Supplementary Figure 3: Kaplan-Meier estimates of biochemical relapse free survival using the “Combat” radiomic model in the training (a) and testing (b) cohorts.



Supplementary Figure 4: Kaplan-Meier estimates of biochemical relapse free survival using the “Combat” clinical-radiomic model in the training (a) and testing (b) cohorts.

