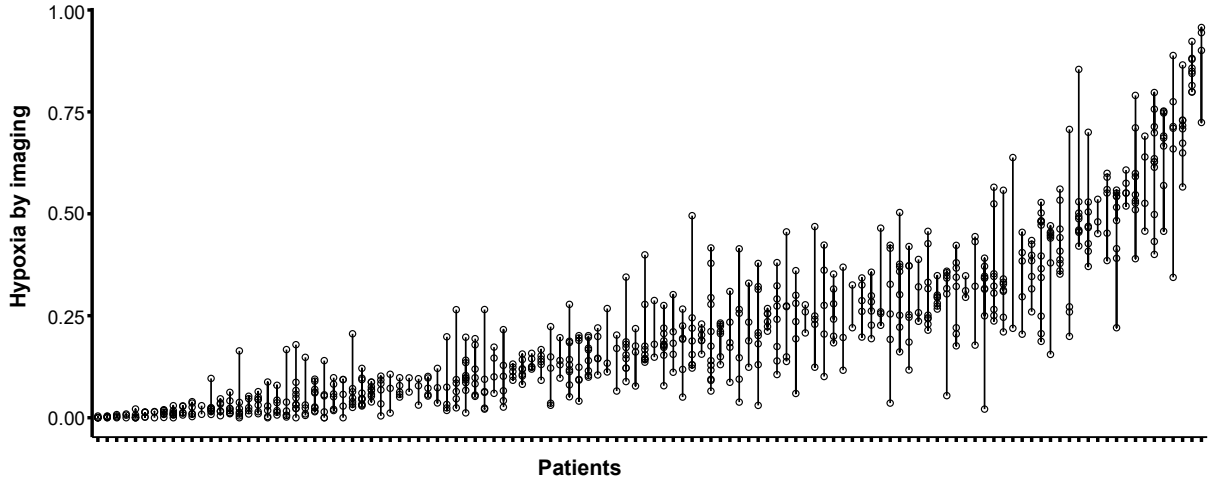
Supplementary material

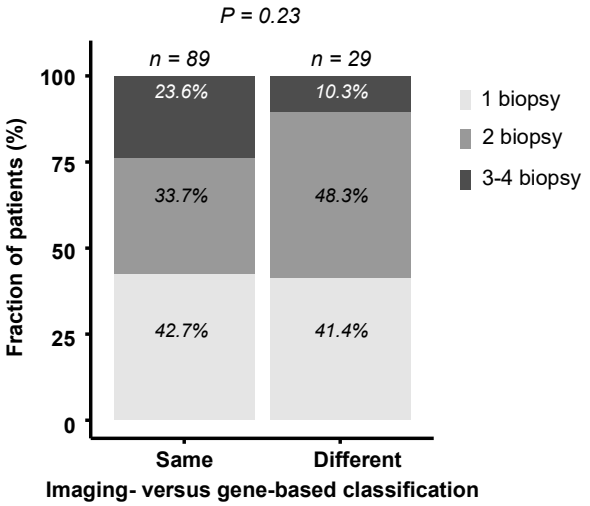
Supplementary Table S1. Patient and tumour characteristics of 118 patients.

Characteristics	No.	%
Diagnostic information		
Histology		
Squamous cell carcinoma	109	92
Adenocarcinoma	3	3
Adenosquamous	6	5
Age (years)		
Median	55.6	
Range	27.7 – 81.6	
Tumour stage (FIGO)		
1B	5	4
2	74	63
3	37	31
4A	2	2
Tumour volume (cm^3)[a]		
Median	31.1	
Range	1.7-186.9	
Pelvic lymph node status[b]		
Positive	52	44
Negative	66	56
Follow up data[c]		
Observation time (months)[d]		
Median	60	
Range	4-60	
Relapse	37	31
Locoregional only	8	7
Distant only	24	20
Locoregional and distant	5	4
Non-disease-specific death[h]	6	5
Disease-specific death	30	25

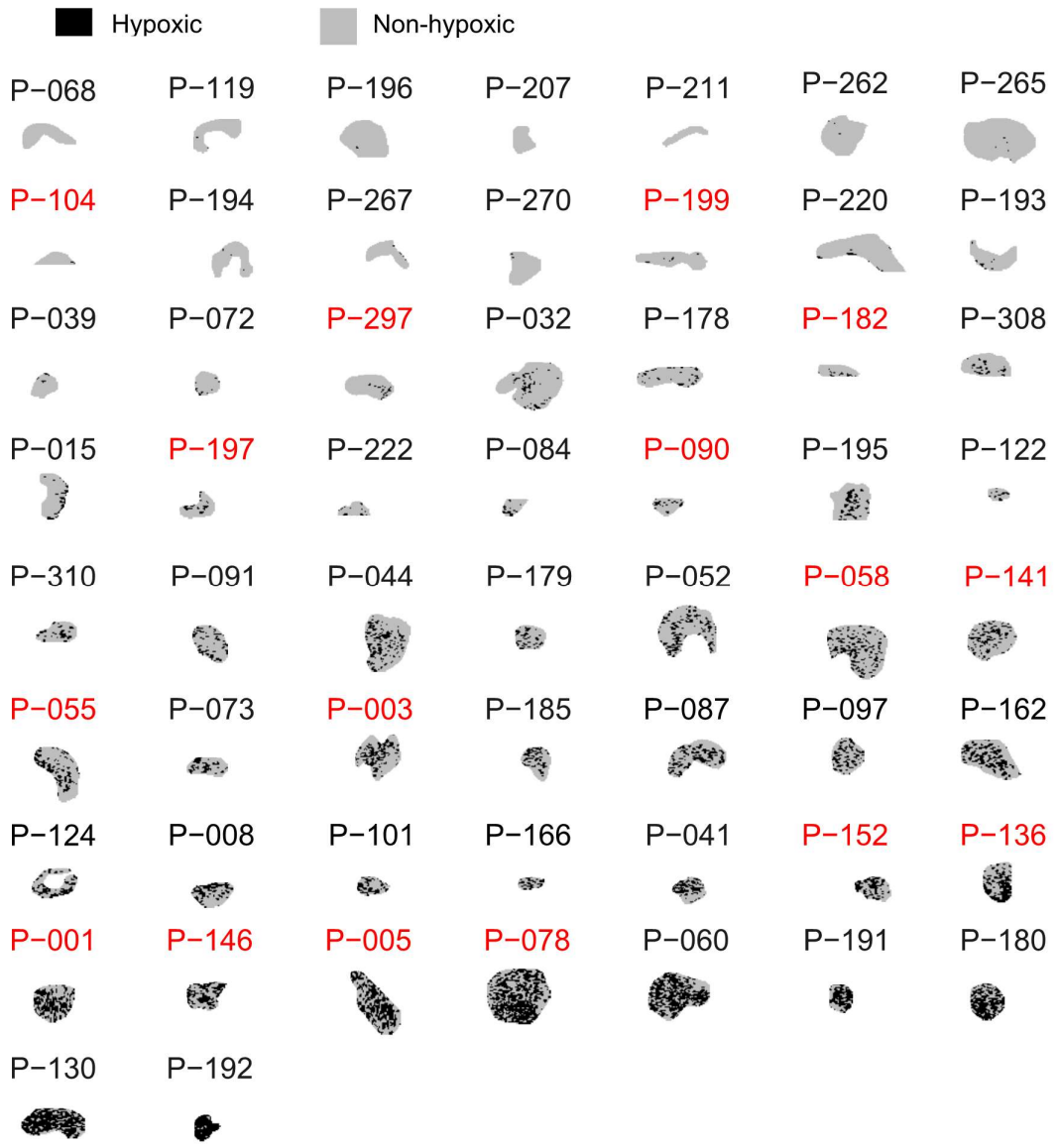
[a]Determined from pre-treatment MR images based on the number of tumour voxels, voxel area in axial plane, and distance between slices, i.e. # of voxels x 0.78 mm x 0.78 mm x 6mm.
[b]Detected at diagnosis by MR imaging.
[c]Follow up data up to 60 months.
[d]Based on patients without relapse (patients dead of other causes are included).
[h]Non-cancer related death before relapse. In addition, two patients died of other causes after experiencing relapse.
% values may not sum to 100 due to rounding.
Abbreviations: FIGO, Federation International de Gynecologie et d'Obstetrique.



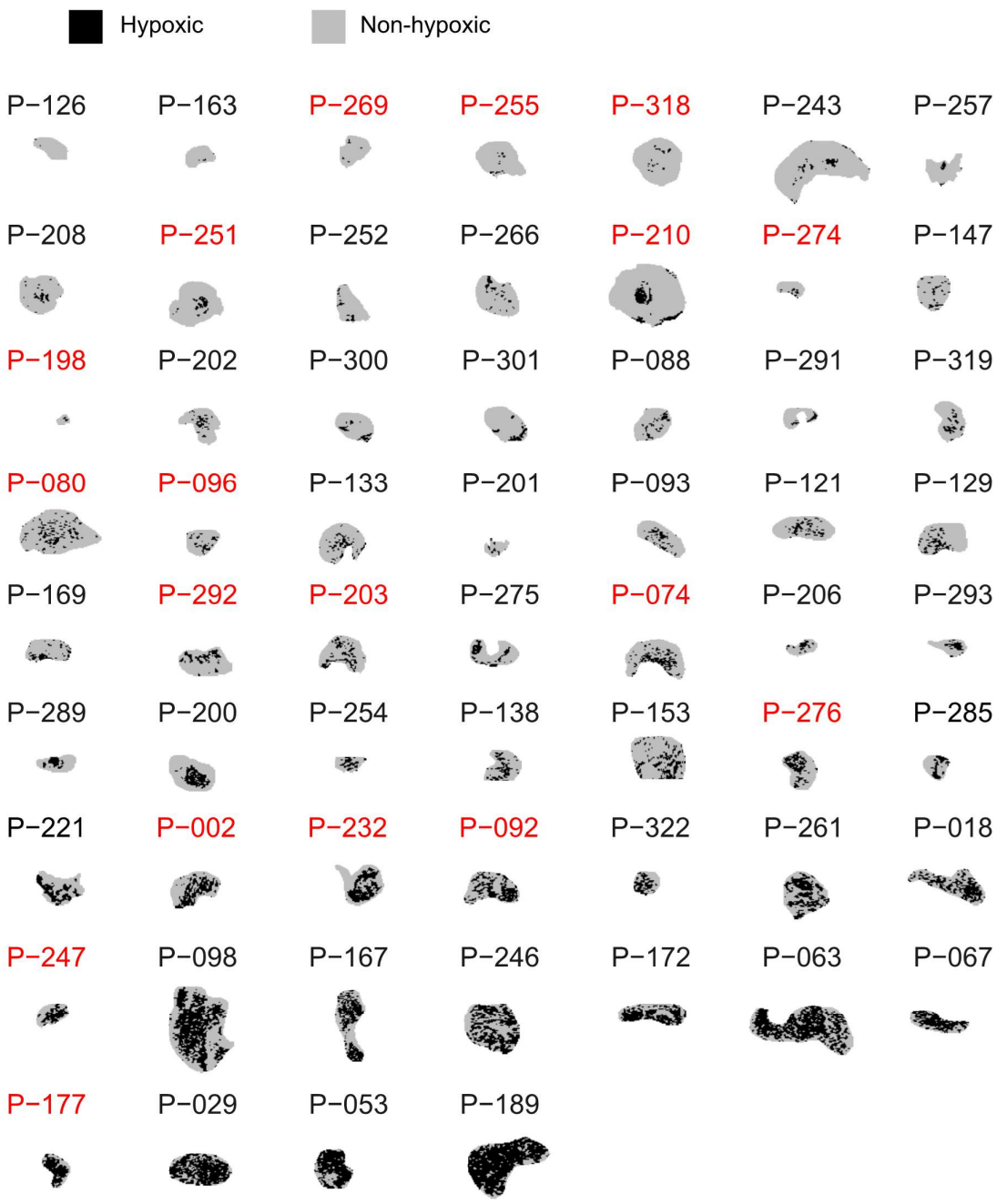
Supplementary Figure S1. Imaging-based biomarker value per image slice. Each dot indicates the value of each image slice and is connected with a line for the individual patients. Patients (n=118) are sorted according to increasing biomarker value using all image slices of the tumour.



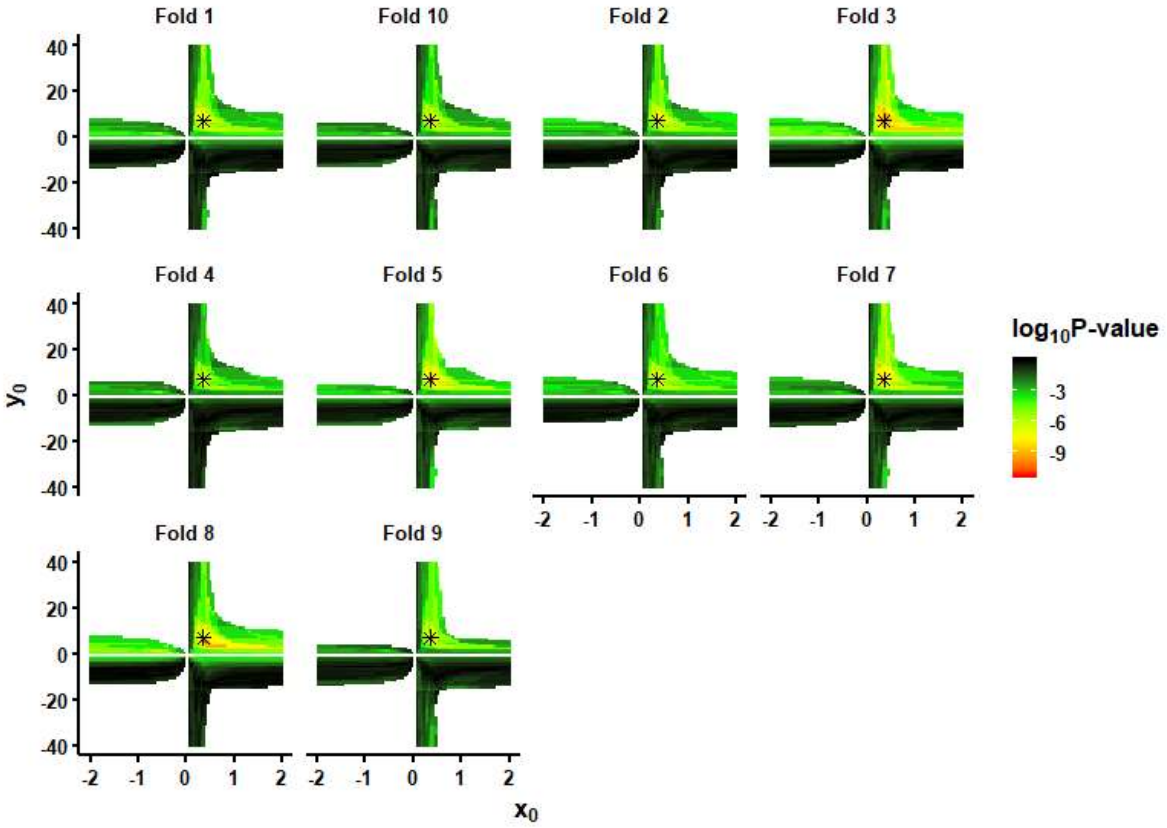
Supplementary Figure S2. Similarity in classification by imaging and genes in relation to number of biopsies used for gene-based classification. Fraction of patients with 1, 2 or 3-4 biopsies used to generate the gene-based biomarker for patients classified with the same or different hypoxia status by imaging (whole tumour) and genes. Number of patients (*n*) and *P*-value from Fisher's exact test are indicated. Grouping patients with 1-2 *versus* 3-4 biopsies, or 1 *versus* 2-4 biopsies, gave no significant association to the consistency in classification by imaging and genes (Fisher's exact test).



Supplementary Figure S3. Binary images of tumours with less clustering of hypoxic regions. Voxels in hypoxic and non-hypoxic regions are shown for the image slice covering the biopsy region (slice 1). Red colour indicates tumours that were differently classified by imaging of the biopsy region (the slice shown) and genes.



Supplementary Figure S4. Binary images of tumours with more clustering of hypoxic regions. Voxels in hypoxic and non-hypoxic regions are shown for the image slice covering the biopsy region (slice 1). Red colour indicates tumours that were differently classified by imaging of the biopsy region (the slice shown) and genes.



Supplementary Figure S5. Determination of optimal line for separation of more and less hypoxic tumours when combining the imaging- and gene-based biomarker. Numerous lines, having intersection point with the gene-based (y_0) and imaging-based (x_0) biomarker axes ranging from -40 to 40 in steps of 1, and from -2 to 2 in steps of 0.05, respectively, were tested. The line was identified by 10-fold cross-validation, including the 77 patients not used to construct the gene-based biomarker. The lines giving at least 10 percent of the tumours in each group were evaluated, and the results for each of the 10 analyses are shown. The colour code indicates *P*-values from log-rank test of patients with more or less hypoxic tumour, defined by the different lines. PFS was used as endpoint. The line defined by x_0 = 0.35 and y_0 = 7, indicated with black stars were found to yield the strongest association to PFS in all 10 analyses. Parabola shaped lines for separating the more and less hypoxic tumours were also tested, but did not improve the prognostic value compared to the linear lines (data not shown).