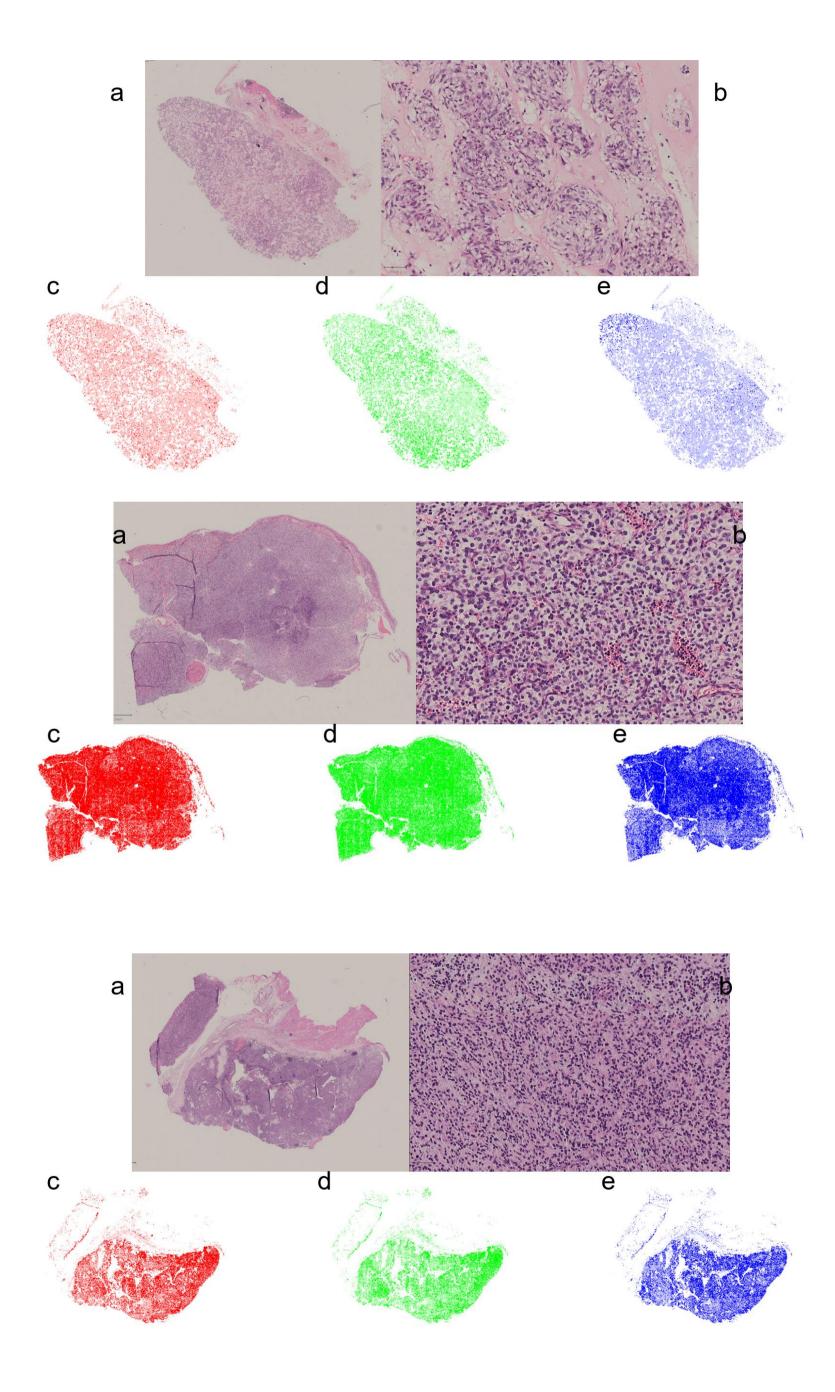
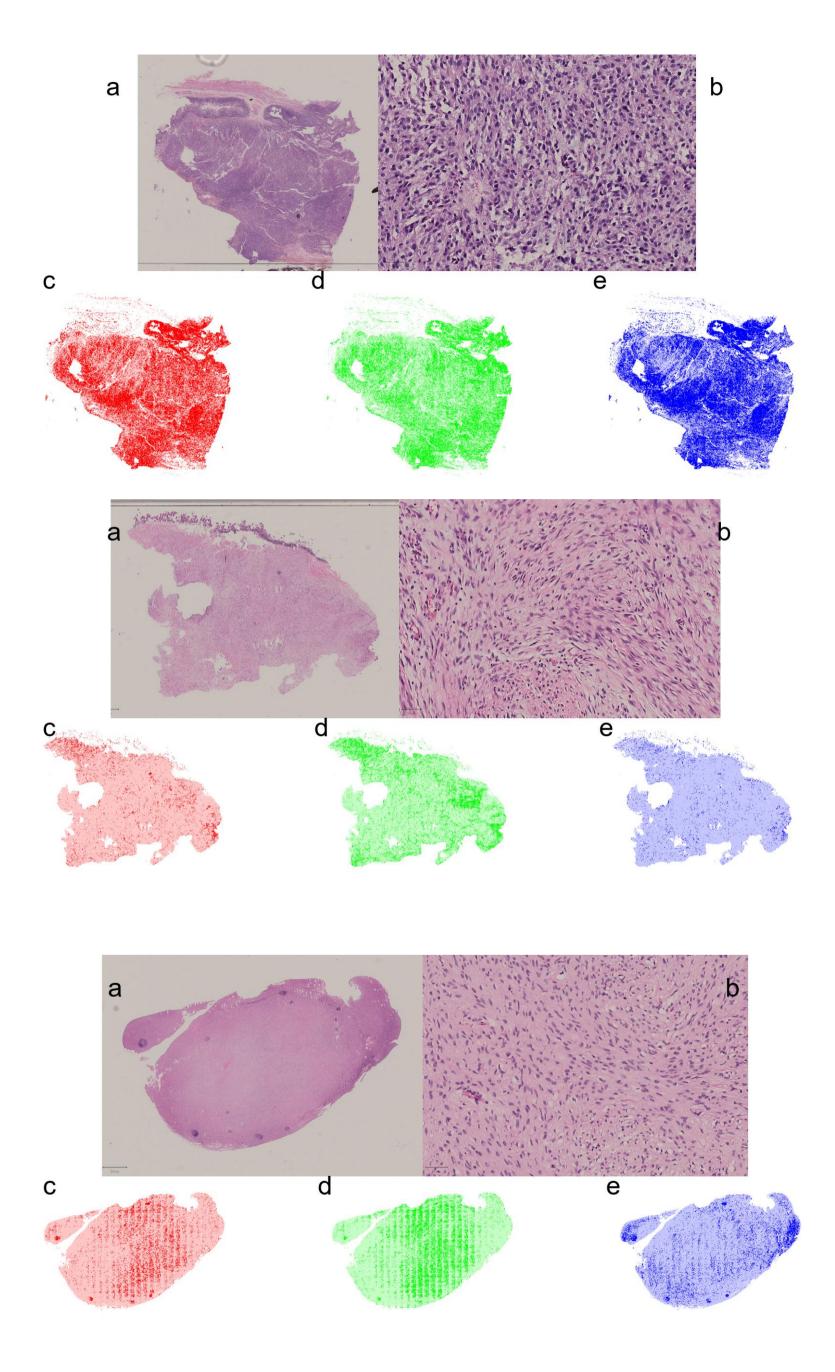
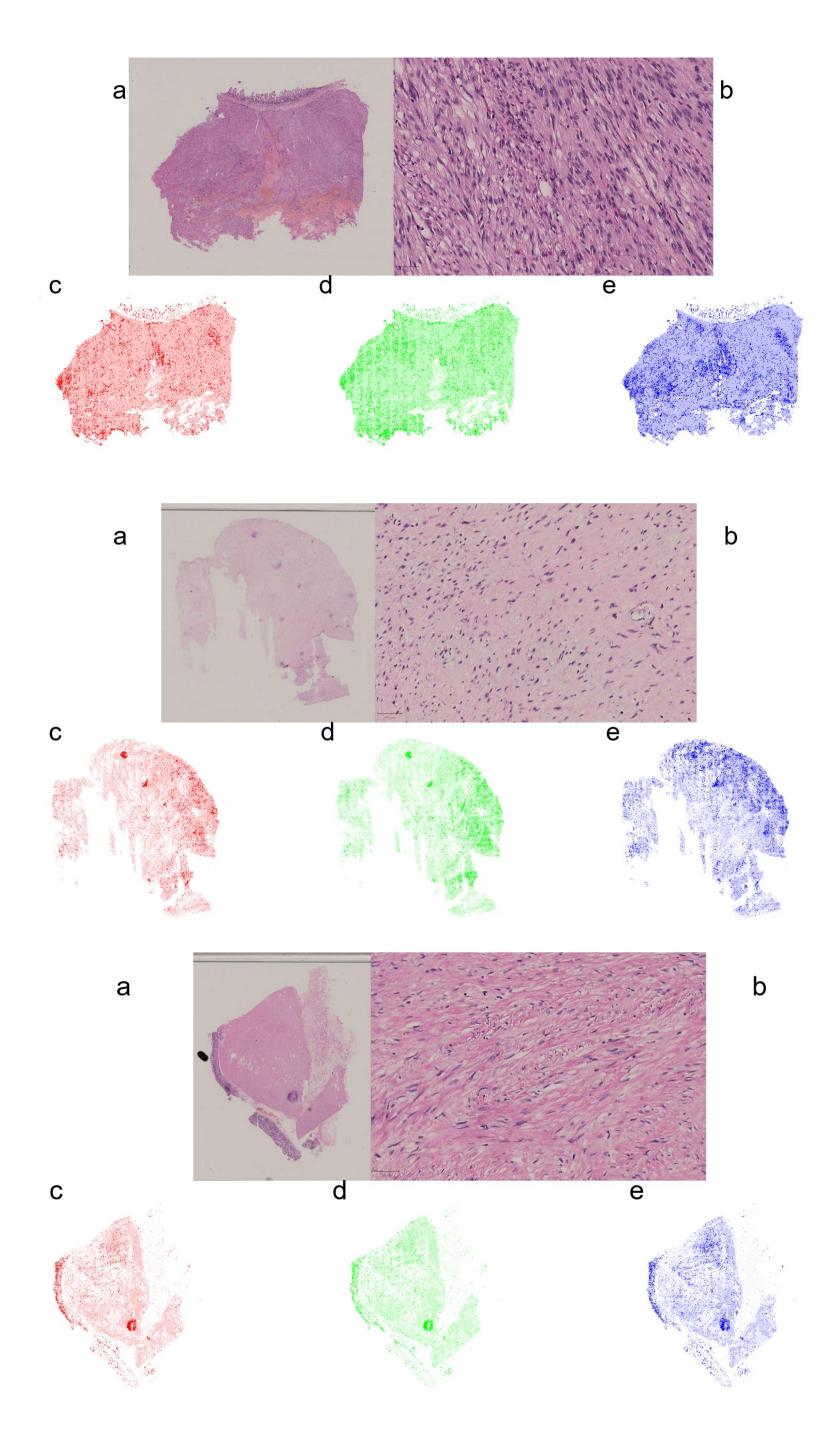
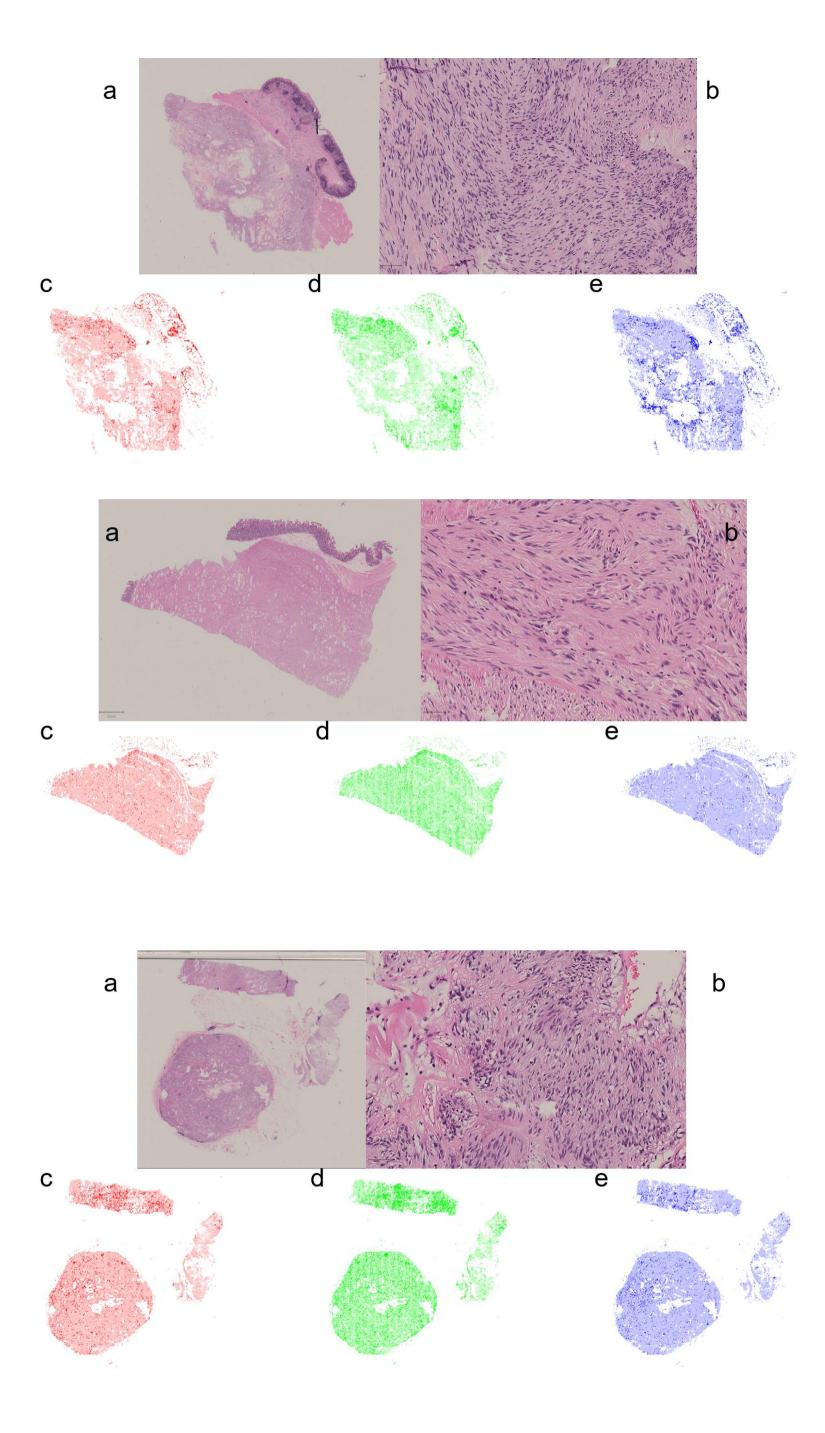


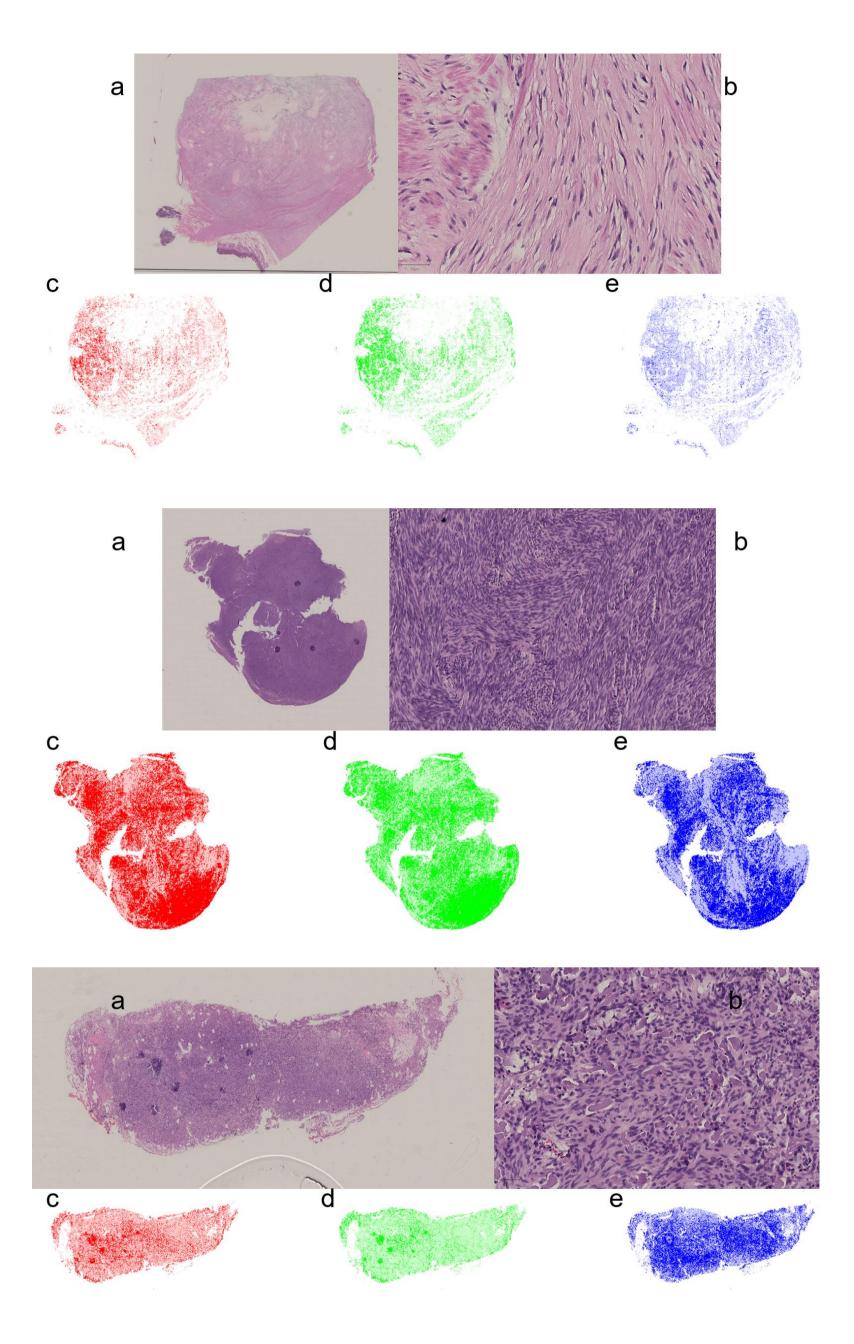
Supplementary Figure 1. Confusion matrix of the prediction generated by the classification model based on deep learning in the best-performing epoch.

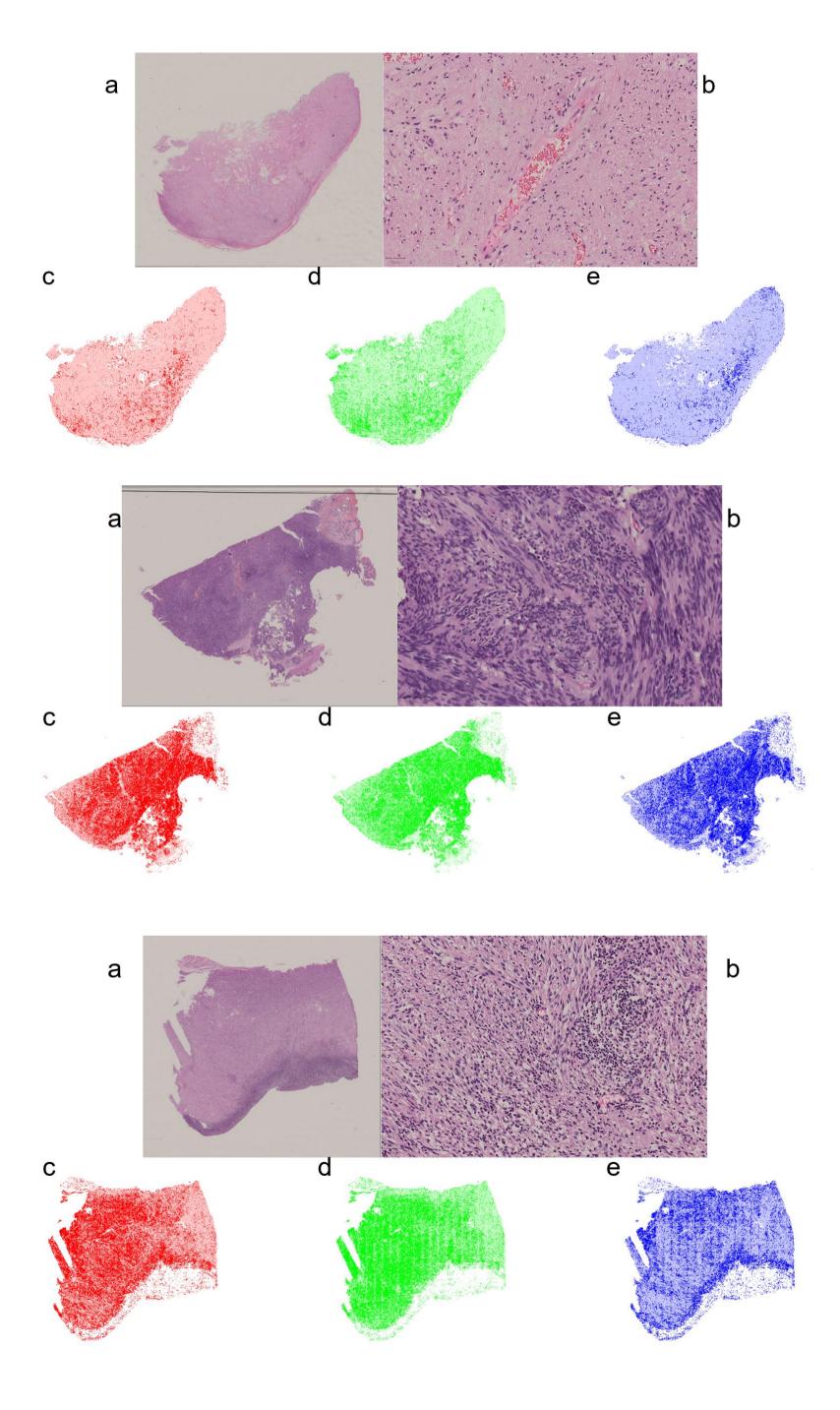


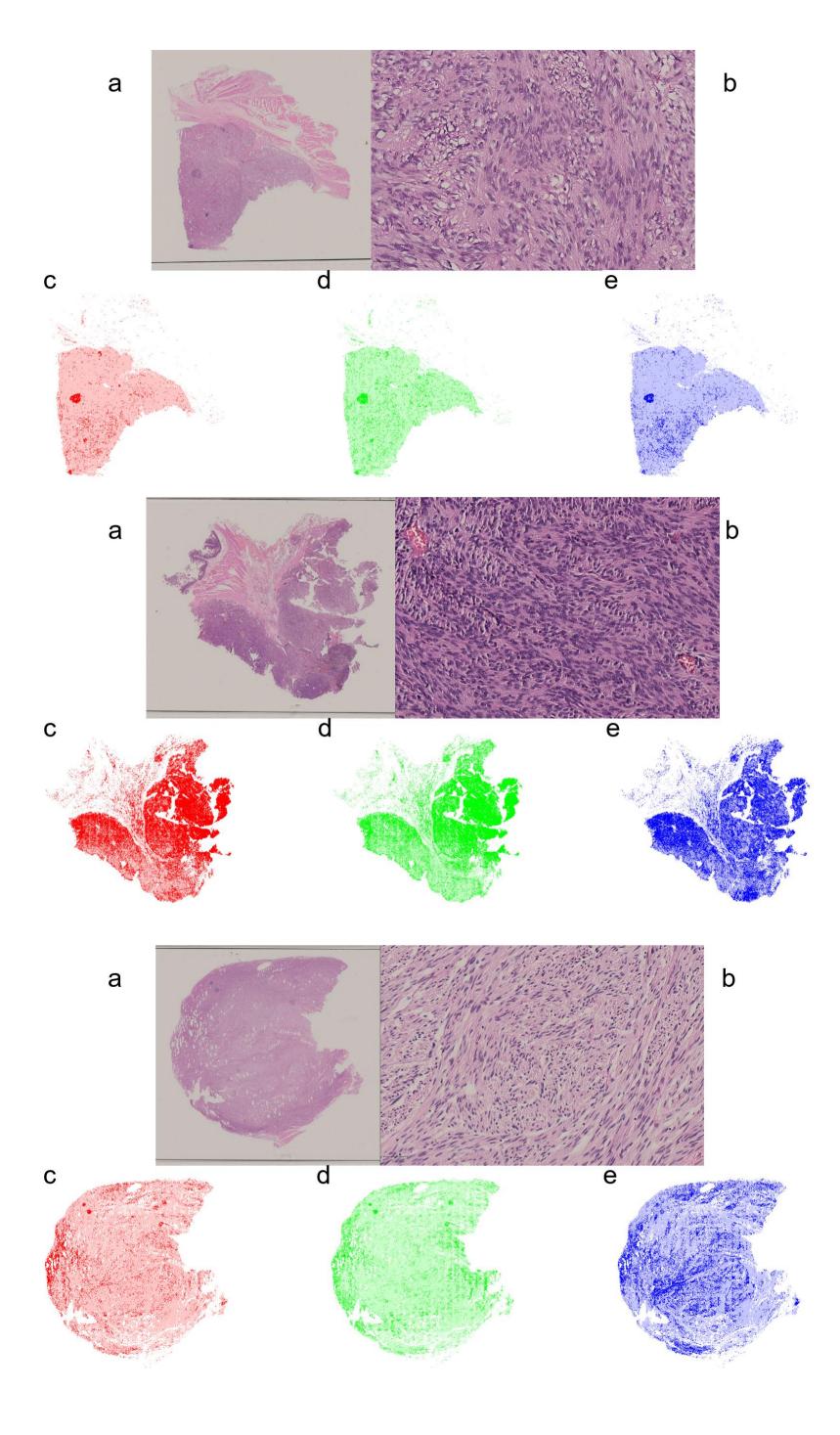


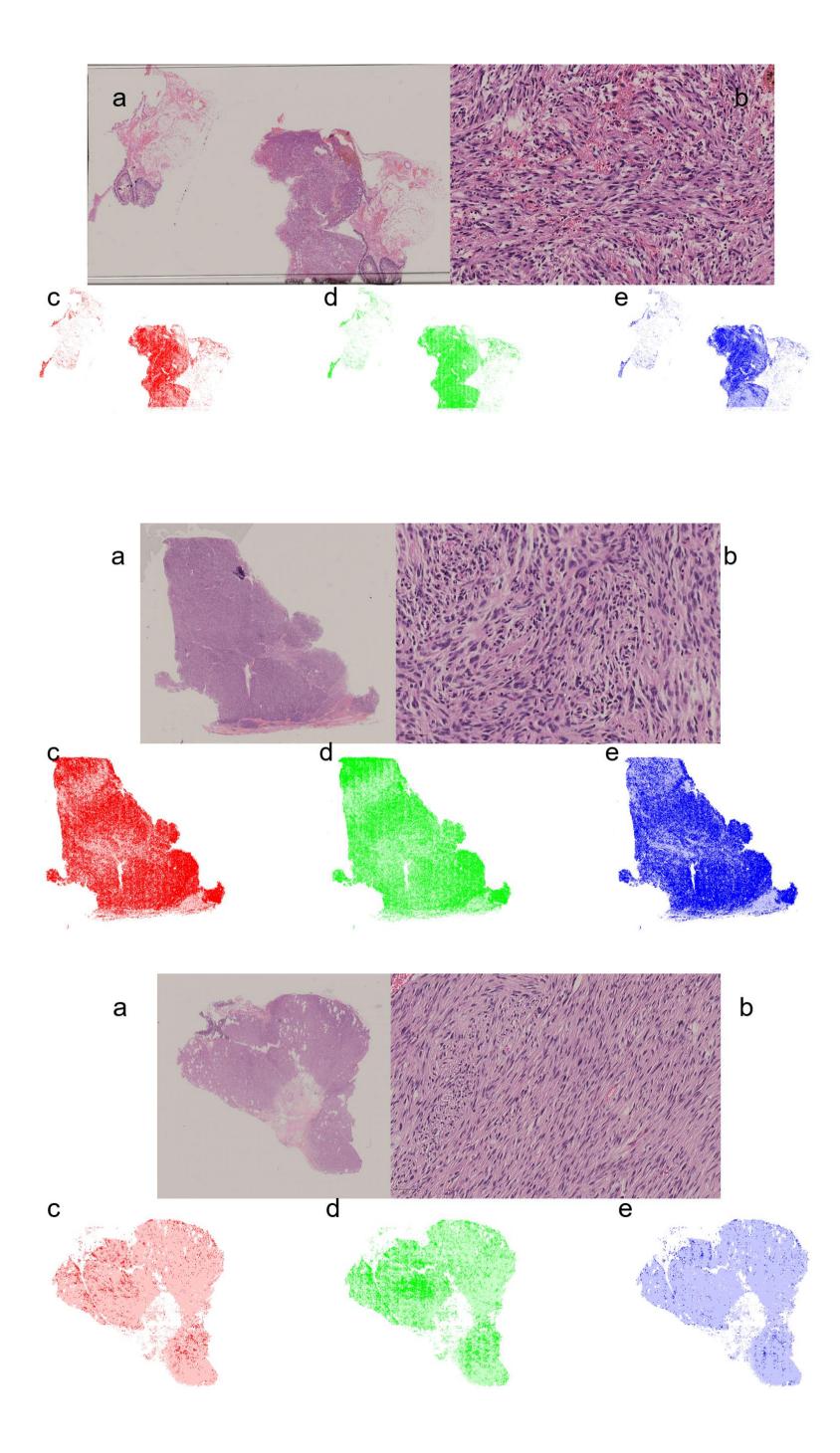


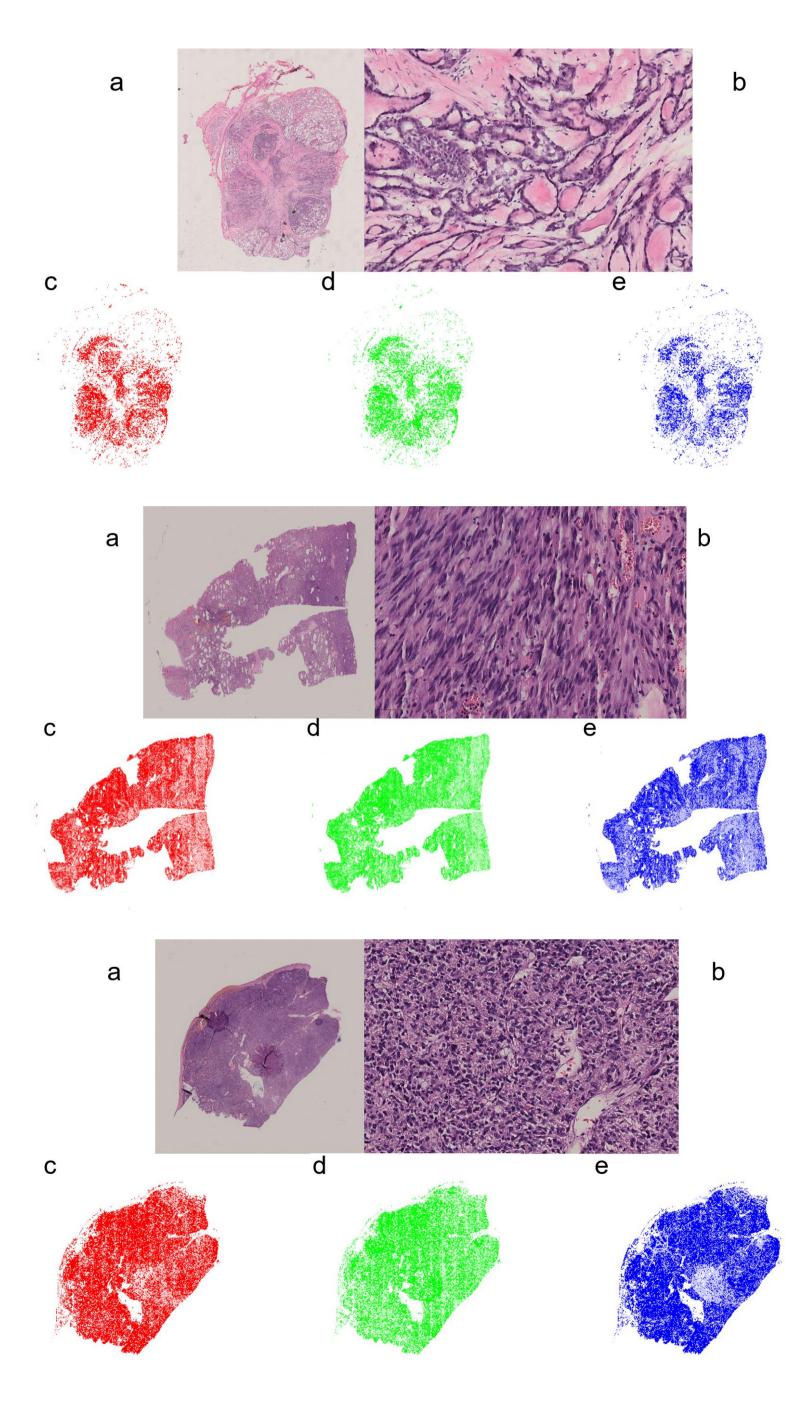


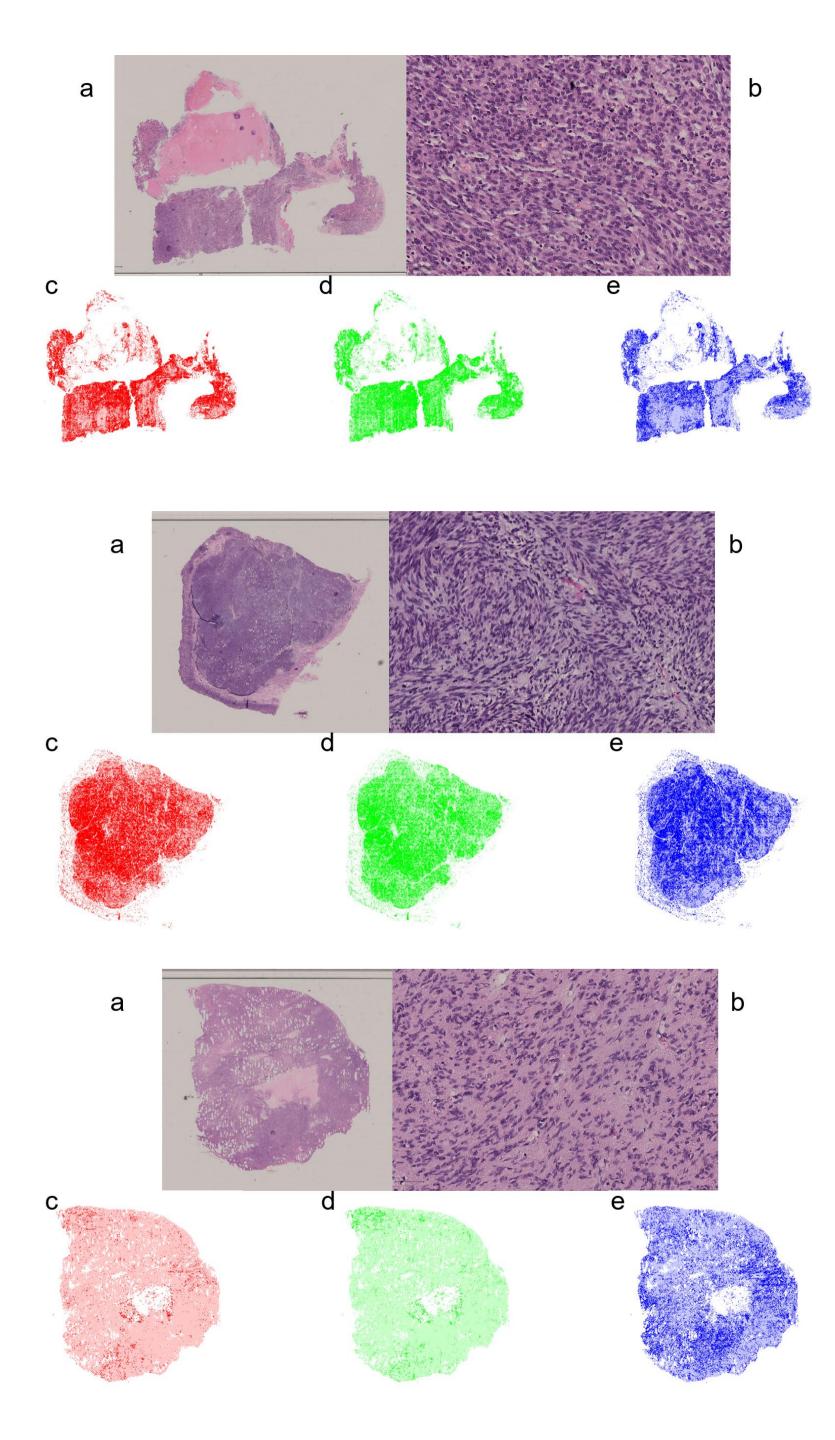


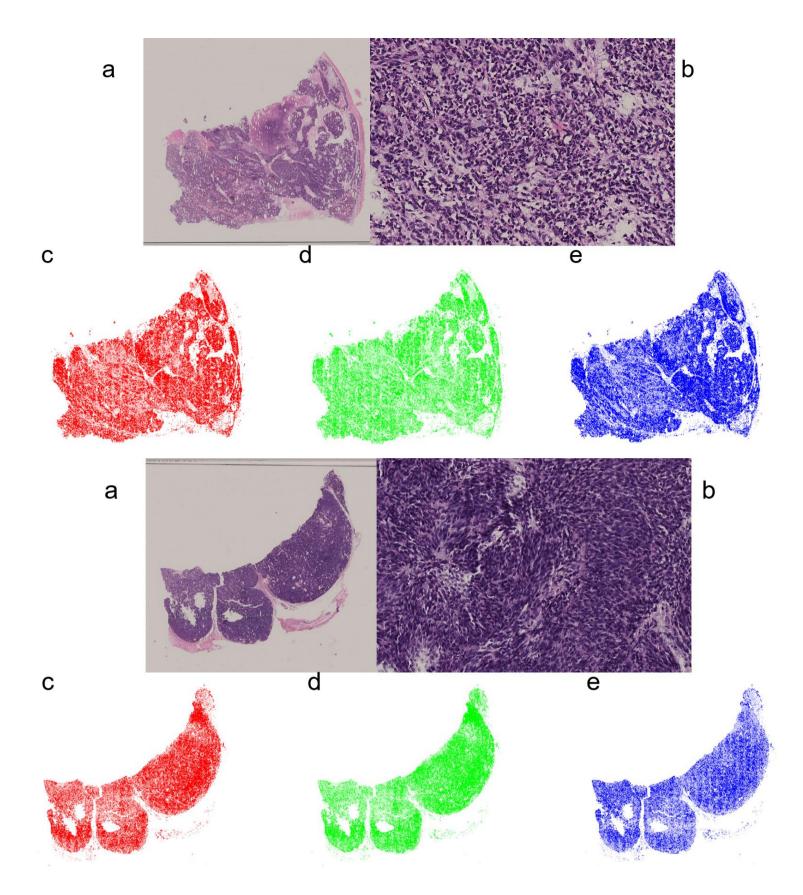




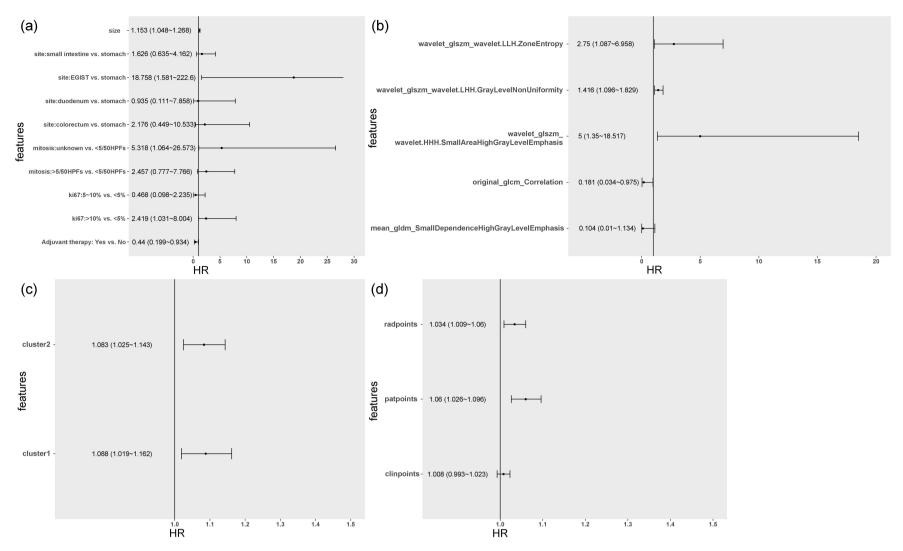




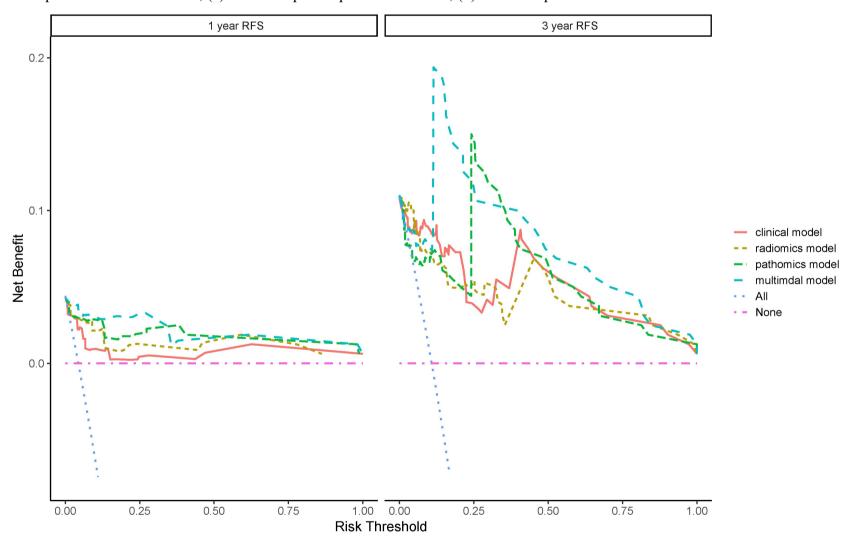




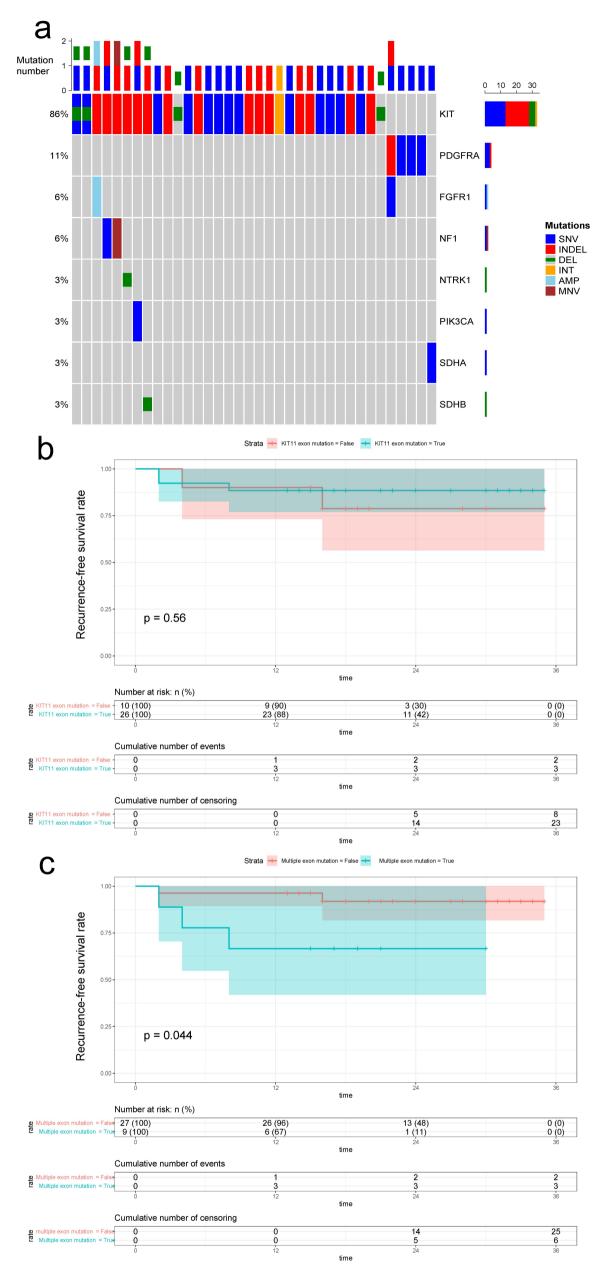
Supplementary Figure 2. Visualized prediction of pathomics deep learning model and texture distribution. (a) The overview of WSI; (b) the detailed view of WSI; (c) the distribution of the pathomics score (the darker the color, the larger the value); (d) the distribution of the cluster1 score (the darker the color, the larger the value); (e) the distribution of the cluster2 score (the darker the color, the larger the value).



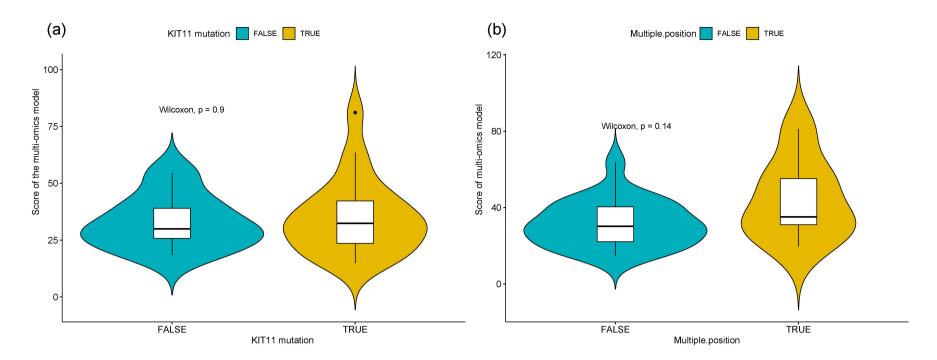
Supplementary Figure 3. Forest plots of unimodal models and the multimodal model. (a) The forest plot of clinical model; (b) the forest plot of radiomics model; (c) the forest plot of pathomics model; (d) the forest plots of the multimodal model.



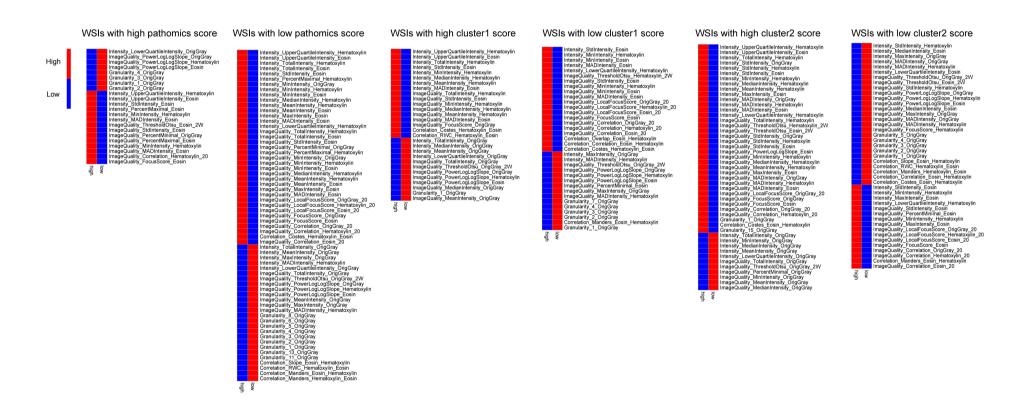
Supplementary Figure 4. DCA curves of uni-modal and multi-modal model



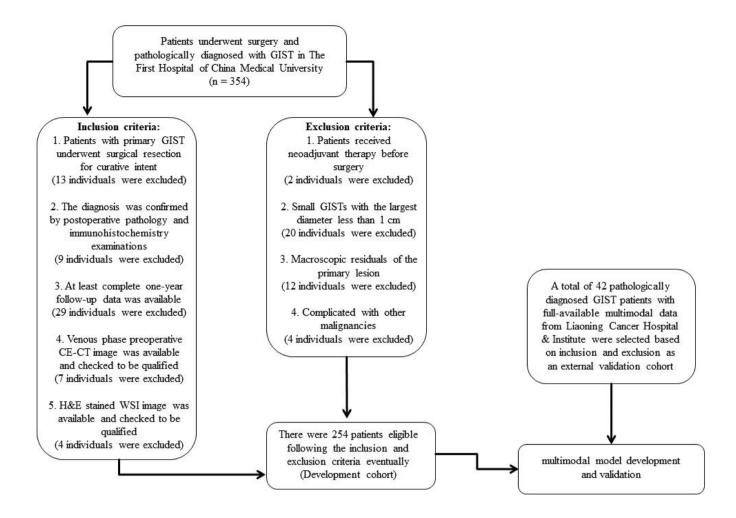
Supplementary Figure 5. Analysis of the results of targeted gene mutation detection. (a) gene mutation landscape of 36 patients who underwent targeted gene mutation detection; (b) Kaplan-Meier analysis on RFS stratified by KIT-11 mutation status (n = 36 patients); (c) Kaplan-Meier analysis on RFS stratified by multiple mutation status (n = 36 patients). P-values were calculated using the log-rank test. SNV: single nucleotide variation; INDEL: insertion/deletion mutation; DEL: deletion mutation; INT: interposition mutation; AMP: copy number amplification; MNV: multiple nucleotide variation.



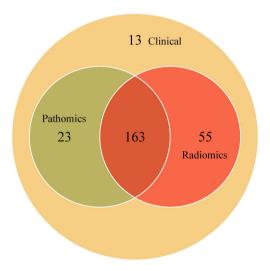
Supplementary Figure 6. The relationship between the phenotype of gene mutation and predictions of multi-omics model. (a) comparison of multimodal model's predictive scores in KIT11 mutation group and non-KIT11 mutation group; (b) comparison of multimodal model's predictive scores in multiple mutation position group and non-multiple mutation position group (n = 36 patients).



Supplementary Figure 7. The distribution of texture features categorized by different level of pathomics score, cluster1 score and cluster2 score.



Supplementary Figure 8. Flow chart



Supplementary Figure 9. Venn diagram of patients in our study with available clinical information, CE-CT images, and H&E stained images

#### Supplementary Table 1. Functions of prediction scores given by sub-pathomics models

```
Cluster1 score = (45.455*pfeature_40) + (14.113-8.821*pfeature_675) + (45.971*pfeature_1121) + (60.237*pfeature_1249-12.047) + (94.683-72.833*pfeature_1638) + (24.183-18.602*pfeature_258) + (3.018*pfeature_1782-0.603) + (12.969-6.485*pfeature_1824) + (10.402-7.43*pfeature_2041)

Cluster2 score = (34.026-34.026*pfeature_509) + (26.748-33.435*pfeature_741) + (37.418*pfeature_934-3.742) + (31.074*pfeature_1019) + (3.718*pfeature_1153-0.186) + (24.177*pfeature_1298) + (55.556-55.556*pfeature_1313) + (20.219*pfeature_1576-2.022) + (31.328*pfeature_1919-3.133) + (53.247-66.559*pfeature_285) + (11.936-18.363*pfeature_395) + (154.621*pfeature_1512-9.277)
```

# **Supplementary Table 2. The explanation of the radiomics features**

Feature	Structure	Explanation
original_glcm_Correlation	original	Radiomics features extracted directly from the
	glcm	original images. Glcm: Gray Level Co-occurrence Matrix. A Gray
	8.0	Level Co-occurrence Matrix (GLCM) of
		size Ng×Ng describes the second-order joint
		probability function of an image region
		constrained by the mask and is defined as $P(i,j \delta,\theta)$ . The $(i,j)$ th element of this matrix
		represents the number of times the combination
		of levels i and j occur in two pixels in the image,
		that are separated by a distance of $\delta$ pixels along angle $\theta$ . The distance $\delta$ from the center voxel is
		defined as the distance according to the infinity
		norm. For $\delta=1$ , this results in 2 neighbors for
		each of 13 angles in 3D (26-connectivity) and for $\delta$ =2 a 98-connectivity (49 unique angles).
	Correlation	Correlation: Correlation is a value between 0
		(uncorrelated) and 1 (perfectly correlated)
		showing the linear dependency of gray level values to their respective voxels in the GLCM.
mean gldm SmallDependenceHighGrayLevelEmp	mean	The average gray level intensity within the ROI.
hasis		
	gldm	Gldm: Gray Level Dependence Matrix. A GLDM
		quantifies gray level dependencies in an image. A
		gray level dependency is defined as a the number
		of connected voxels within distance $\delta$ that are dependent on the center voxel. A neighbouring
		voxel with gray level j is considered dependent
		on center voxel with gray level i if $ i-j  \le \alpha$ . In a gray level dependence
		gray level dependence matrix $P(i,j)$ the $(i,j)$ th element describes the
		number of times a voxel with gray
		level i with j dependent voxels in its neighbourhood appears in image.
	SmallDependenceHighGrayLevelEmp	Measures the joint distribution of small
11	hasis	dependence with higher gray-level values.
wavelet_glszm_wavelet.LLH.ZoneEntropy	wavelet	Original images were processed by wavelet filter which concluded three filters in three dimensions.
	glszm	Glszm: Gray-level size zone matrix. When glszm
		is wider and non-zero elements gathered in the
		right side, there is a rougher origin image. This is because the width of GLSZM is determined by
		the size of the largest connected domain, and the
		elements on the right side of GLSZM correspond
		to the number of connected domains with larger
		areas. The wider the GLSZM, it means that there are larger connected domains in the original
		image; the more non-zero elements on the right
		side of the GLSZM, it means that the areas of the
		connected domains in the original image are larger, and to the naked eye, there will be several
		larger areas in the image. sub-region.
	wavelet.LLH.ZoneEntropy	Zone Entropy measures the
		uncertainty/randomness in the distribution of zone sizes and gray levels. A higher value
		indicates more heterogeneneity in the texture
wavalat alagus wavalat IIIII G	wovelet IIIII Constit A II'-1 Const	patterns.
wavelet_glszm_wavelet.HHH.SmallAreaHighGray LevelEmphasis	wavelet.HHH.SmallAreaHighGrayLev elEmphasis	SmallAreaHighGrayLevelEmphasis (SAHGLE) measures the proportion in the image of the joint
1	1	distribution of smaller size zones with higher
wavelet alama1-tIIII C I BI II 'C	wavelet LIHLC INI TI 'C '	gray-level values.
wavelet_glszm_wavelet.LHH.GrayLevelNonUnifo	wavelet.LHH.GrayLevelNonUniformit	GrayLevelNonUniformity (GLN) measures the

rmity	у	variability of gray-level intensity values in the
		image, with a lower value indicating more
		homogeneity in intensity values.

All the explanations were gathered from Welcome to pyradiomics documentation! — pyradiomics v3.1.0rc2.post5+g6a761c4 documentation.

# **Supplementary Table 3. Acquisition Parameters of CT Images**

Discovery CT750 HD (GE)
Revolution CT (GE)
Aquilion (TOSHIBA)
iCT 256 (PHILIPS)
Optima CT680 Series (GE)
SOMATOM Definition Flash (SIEMENS)
120kV
1-2mm
512*512

## **Supplementary Table 4. The explanation of the pathomics features**

Feature	Module	Explanation
Correlation_Correlation_Eosin_Hematoxylin	MeasureColocalization	The correlation between a pair of images Eosin and Hematoxylin, calculated
		as Pearson's correlation coefficient. The formula is covariance(Eosin,
		$Hematoxylin)/[std(Eosin) \times std(Hematoxylin)].$
Correlation_Costes_Eosin_Hematoxylin		Costes' automated threshold estimates maximum threshold of intensity for
		each image based on correlation. Manders coefficient is applied on
		thresholded images as Eosini_coloc = Eosini when Hematoxylini >
		Hematoxylinthr and Hematoxylini_coloc = Hematoxylini when Eosini >
		Eosinthr where Hematoxylinthr and Eosinthr are thresholds calculated using
		Costes' automated threshold method. (i = intensity, thr = threshold)
Correlation_Costes_Hematoxylin_Eosin		Costes' automated threshold estimates maximum threshold of intensity for
		each image based on correlation. Manders coefficient is applied on
		thresholded images as Hematoxylini_coloc = Hematoxylini when Eosini >
		Eosinthr and Eosini_coloc = Eosini when Hematoxylini > Hematoxylinthr
		where Eosinthr and Hematoxylinthr are thresholds calculated using Costes'
		automated threshold method.
Correlation_K_Eosin_Hematoxylin		
Correlation_K_Hematoxylin_Eosin		
Correlation_Manders_Eosin_Hematoxylin		The Manders coefficient for a pair of images Eosin and Hematoxylin is
		measured as M1 = sum(Eosini_coloc)/sum(Eosini) and M2 =
		sum(Hematoxylini_coloc)/sum(Hematoxylini), where Eosini_coloc = Eosini
		when Hematoxylini > 0, 0 otherwise and Hematoxylini_coloc =
		Hematoxylini when Eosini >0, 0 otherwise.
Correlation_Manders_Hematoxylin_Eosin		The Manders coefficient for a pair of images Hmatoxylin and Eosin is
		measured as M1 = sum(Hematoxylini_coloc)/sum(Hematoxylini) and M2 =
		sum(Eosini_coloc)/sum(Eosini), where Hematoxylini_coloc = Hematoxylini
		when Eosini > 0, 0 otherwise and Eosini_coloc = Eosini when
		Hematoxylini >0, 0 otherwise.
Correlation_Overlap_Eosin_Hematoxylin		The overlap coefficient is a modification of Pearson's correlation where
		average intensity values of the pixels are not subtracted from the original
		intensity values. For a pair of images Eosin and Hematoxylin, the overlap
		coefficient is measured as r = sum(Eosini * Hematoxylini) / sqrt
Correlation PWC Facin Hamatayyılin		(sum(Eosini*Eosini)*sum(Hematoxylini*Hematoxylini)).
Correlation_RWC_Eosin_Hematoxylin		The RWC coefficient for a pair of images Eosin and Hematoxylin is measured as RWC1 = sum(Eosini coloc*Wi)/sum(Eosini) and RWC2 =
		sum(Hematoxylini coloc*Wi)/sum(Hematoxylini), where Wi is Weight
		sum(11cmatoxymin_coloc wij/sum(11cmatoxymin), where wi is weight

Correlation RWC Hematoxylin Eosin Correlation Slope Eosin Hematoxylin Granularity\_10\_OrigGray MeasureGranularity Granularity 11 OrigGray Granularity 12 OrigGray Granularity 13 OrigGray Granularity\_14\_OrigGray Granularity 1 OrigGray Granularity 2 OrigGray Granularity 3 OrigGray Granularity 4 OrigGray Granularity 5 OrigGray Granularity\_6\_OrigGray Granularity 7 OrigGray Granularity 8 OrigGray Granularity\_9\_OrigGray ImageQuality\_Correlation\_Eosin\_20 MeasureImageQuality ImageQuality\_Correlation\_OrigGray\_20 ImageQuality FocusScore Eosin ImageQuality FocusScore Hematoxylin ImageQuality FocusScore OrigGray ImageQuality\_LocalFocusScore\_Eosin\_20 ImageQuality LocalFocusScore Hematoxylin 20 ImageQuality LocalFocusScore OrigGray 20 ImageQuality MADIntensity Eosin

ImageQuality MADIntensity Hematoxylin

defined as Wi = (Eosinmax - Di)/Eosinmax where Eosinmax is the maximum of Ranks among Eosin and Hematoxylin based on the max intensity, and Di = abs(Rank(Eosini) - Rank(Hematoxylini)) (absolute difference in ranks between Eosin and Hematoxylini) and Eosini\_coloc = Eosini when Hematoxylini > 0, 0 otherwise and Hematoxylini\_coloc = Hematoxylini when Eosini > 0, 0 otherwise.

The RWC coefficient for a pair of images Hematoxylin and Eosin is measured as RWC1 = sum(Hematoxylini\_coloc\*Wi)/sum(Hematoxylini) and RWC2 = sum(Eosini\_coloc\*Wi)/sum(Eosini), where Wi is Weight defined as Wi = (Hematoxylinmax - Di)/Hematoxylinmax where Hematoxylinmax is the maximum of Ranks among Hematoxylin and Eosin based on the max intensity, and Di = abs(Rank(Hematoxylini) - Rank(Eosini)) (absolute difference in ranks between Hematoxylini and Eosin) and Hematoxylini\_coloc = Hematoxylini when Eosini > 0, 0 otherwise and Eosini coloc = Eosini when Hematoxylini > 0, 0 otherwise.

The slope of the least-squares regression between a pair of images Eosin and Hematoxylin. Calculated using the model  $A \times \text{Eosin} + B = \text{Hematoxylin}$ , where A is the slope.

MeasureGranularity outputs spectra of size measurements of the textures in the image. Image granularity is a texture measurement that tries to fit a series of structure elements of increasing size into the texture of the image and outputs a spectrum of measures based on how well they fit. Granularity is measured as described by Ilya Ravkin [1]. Basically, MeasureGranularity: 1 -Downsamples the image (if you tell it to). This is set in Subsampling factor for granularity measurements or Subsampling factor for background reduction. 2 - Background subtracts anything larger than the radius in pixels set in Radius of structuring element. 3 - For as many times as you set in Range of the granular spectrum, it gets rid of bright areas that are only 1 pixel across, reports how much signal was lost by doing that, then repeats. i.e. The first time it removes one pixel from all bright areas in the image, (effectively deleting those that are only 1 pixel in size) and then reports what % of the signal was lost. It then takes the first-iteration image and repeats the removal and reporting (effectively reporting the amount of signal that is two pixels in size). etc

A measure of the correlation of the image for a given spatial scale. This is a measure of the image spatial intensity distribution computed across sub-regions of an image for a given spatial scale [2]. If an image is blurred, the correlation between neighboring pixels becomes high, producing a high correlation value. Some care is required in selecting an appropriate spatial scale because differences in the spatial scale capture various features: moderate scales capture the blurring of intracellular features better than small scales and larger scales are more likely to reflect cell confluence than focal blur. You should select a spatial scale no bigger than the objects of interest, although you can select as many scales as desired and check empirically which is best.

A measure of the intensity variance across the image. This score is calculated using a normalized variance. Higher focus scores correspond to lower blurriness. More specifically, the focus score computes the intensity variance of the entire image divided by mean image intensity. Since it is tailored for auto-focusing applications, it assumes that the overall intensity and the number of objects in the image is constant, making it less useful for comparison images of different fields of view. For distinguishing extremely blurry images, however, it performs well.

A measure of the intensity variance between image sub-regions. A local version of the Focus Score, it subdivides the image into non-overlapping tiles, computes the normalized variance for each, and takes the mean of these values as the final metric. It is potentially more useful for comparing focus between images of different fields of view, but is subject to the same caveats as the Focus Score. It can be useful in differentiating good versus badly segmented images in the cases when badly segmented images usually contain no cell objects with high background noise.

Median absolute deviation (MAD) of pixel intensity values.

ImageQuality MADIntensity OrigGray ImageQuality\_MaxIntensity\_Eosin Maximum of pixel intensity values. ImageQuality\_MaxIntensity\_Hematoxylin ImageQuality MaxIntensity OrigGray ImageQuality MeanIntensity Eosin Mean of pixel intensity values. ImageQuality\_MeanIntensity\_Hematoxylin ImageQuality\_MeanIntensity\_OrigGray ImageQuality\_MedianIntensity\_Eosin Median of pixel intensity values. ImageQuality MedianIntensity Hematoxylin ImageQuality MedianIntensity OrigGray Minimum of pixel intensity values. ImageQuality\_MinIntensity\_Eosin ImageQuality\_MinIntensity\_Hematoxylin ImageQuality MinIntensity OrigGray ImageQuality PercentMaximal Eosin Percent of pixels at the maximum intensity value of the image. ImageQuality PercentMaximal Hematoxylin ImageQuality\_PercentMaximal\_OrigGray ImageQuality\_PercentMinimal\_Eosin Percent of pixels at the minimum intensity value of the image. ImageQuality\_PercentMinimal\_Hematoxylin ImageQuality PercentMinimal OrigGray ImageQuality PowerLogLogSlope Eosin The slope of the image log-log power spectrum. The power spectrum contains the frequency information of the image, and the slope gives a ImageQuality\_PowerLogLogSlope\_Hematoxylin measure of image blur. A higher slope indicates more lower frequency components, and hence more blur [3]. ImageQuality PowerLogLogSlope OrigGray ImageQuality\_StdIntensity\_Eosin Standard deviation of pixel intensity values. ImageQuality\_StdIntensity\_Hematoxylin ImageQuality\_StdIntensity\_OrigGray ImageQuality ThresholdOtsu Eosin 2W The automatically calculated threshold for each image for the thresholding method of choice. ImageQuality ThresholdOtsu Hematoxylin 2W ImageQuality\_ThresholdOtsu\_OrigGray\_2W ImageQuality\_TotalIntensity\_Eosin Sum of all pixel intensity values. ImageQuality\_TotalIntensity\_Hematoxylin ImageQuality TotalIntensity OrigGray Intensity LowerQuartileIntensity Eosin The intensity value of the pixel for which 25% of the pixels in the object MeasureImageIntensity Intensity\_LowerQuartileIntensity\_Hematoxylin have lower values. Intensity\_LowerQuartileIntensity\_OrigGray Intensity\_MADIntensity\_Eosin Median absolute deviation (MAD) of pixel intensity values. Intensity MADIntensity Hematoxylin Intensity MADIntensity OrigGray Intensity\_MaxIntensity\_Eosin Maximum of pixel intensity values. Intensity\_MaxIntensity\_Hematoxylin Intensity\_MaxIntensity\_OrigGray Intensity MeanIntensity Eosin Mean of pixel intensity values. Intensity MeanIntensity Hematoxylin Intensity\_MeanIntensity\_OrigGray Intensity MedianIntensity Eosin Median of pixel intensity values. Intensity\_MedianIntensity\_Hematoxylin Intensity MedianIntensity OrigGray Intensity MinIntensity Eosin Minimum of pixel intensity values. Intensity\_MinIntensity\_Hematoxylin Intensity\_MinIntensity\_OrigGray Percent of pixels at the maximum intensity value of the image. Intensity PercentMaximal Eosin Intensity PercentMaximal Hematoxylin Intensity\_PercentMaximal\_OrigGray Intensity\_StdIntensity\_Eosin Standard deviation of pixel intensity values. Intensity StdIntensity Hematoxylin Intensity\_StdIntensity\_OrigGray Sum of all pixel intensity values. Intensity TotalIntensity Eosin Intensity TotalIntensity\_Hematoxylin Intensity TotalIntensity OrigGray Intensity UpperQuartileIntensity Eosin The intensity value of the pixel for which 75% of the pixels in the object Intensity\_UpperQuartileIntensity\_Hematoxylin have lower values. Intensity\_UpperQuartileIntensity\_OrigGray

All the explanations were gathered from <u>Measurement — CellProfiler 4.2.6 documentation</u> (cellprofiler-manual.s3.amazonaws.com)

## **Supplementary Table 5. Results of PH assumption test**

Model	Global p value
Radiomics	0.44
Pathomics	0.13
Clinical	0.152
Radiomics&Pathomics pre-fusion	0.17
Radiomics&Pathomics post-fusion	0.43
Clinical&Radiomics pre-fusion	0.57
Clinical&Radiomics post-fusion	0.95
Clinical&Pathomics pre-fusion	0.53
Clinical&Pathomics post-fusion	0.89
Radiomics&Pathomics&Clinical pre-fusion	0.529
Radiomics&Pathomics&Clinical post-fusion	0.93

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