Supplementary information for:

# Robust performance of deep learning for distinguishing glioblastoma from single brain metastasis using radiomic features: Model development and validation

Sohi Bae, M.D., Ph.D.<sup>1+</sup>, Chansik An, M.D., Ph.D.<sup>1,2+</sup>, Sung Soo Ahn, M.D., Ph.D.<sup>3\*</sup>, Hwiyoung Kim, Ph.D.<sup>3\*</sup>, Kyunghwa Han, Ph.D.<sup>3</sup>, Sang Wook Kim<sup>4</sup>, Ji Eun Park, M.D., Ph.D.<sup>5</sup>, Ho Sung Kim, M.D., Ph.D.<sup>5</sup>, Seung-Koo Lee, M.D., Ph.D.<sup>3</sup>

## Contents

S1. Detailed diagnostic performance of different combinations of five feature-selection and seven classification methods, using CE mask

S2. Detailed diagnostic performance of different combinations of five feature-selection and seven classification methods, using PT mask

S3. Detailed diagnostic performance of different combinations of five feature-selection and seven classification methods, using combined mask

S4. Importance score of radiomics features used for seven machine learning classifiers

S5. Kappa statistics representing inter-rater agreement between various classifying methods

S6. Comparison of magnetic resonance imaging parameters of patients in the training cohort (from our institution) and those in the external validation cohort (from another tertiary medical center)

S7. Details of feature selection and classification methods

S8. Multi-input DNN implemented for deep learning

**Supplementary Table S1.** Detailed diagnostic performance of different combinations of five featureselection and seven classification methods, using CE mask

$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Classifier	Feature selection method	Optimal feature number	Optimal hyperparameters	Mean AUC in the training set	AUC (95% CI) in the test set
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		F score	10	K = 2	0.690	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		MI	15	K =11	0.742	0.744 (0.655, 0.829)
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	1357	RFE	40	$\mathbf{K} = 8$	0.737	(,,
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	kNN	Lasso	37	K = 13	0.707	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Tree- based	150	K = 5	0.721	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		F score	130	NA	0.657	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		MI	20	NA	0.682	0.618 (0.513, 0.717)
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		RFE	20	NA	0.676	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	NB	Lasso	48	NA	0.675	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Tree-				
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		based	63	NA	0.665	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		<b>F</b>	10	$N_{estimators} = 20,$	0.702	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		F score	10	Min_samples leaf = $1$	0.792	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		NG	10	$N_{estimators} = 90,$	0.022	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		MI	10	Min samples leaf $= 5$	0.822	
KF         RFE         40 $Min_samples leaf = 3$ 0.839         0.7/3 (0.684, 0.857)           Lasso         7         N_estimators = 10, Min_samples leaf = 3         0.837           Tree- based         73         N_estimators = 30, Min_samples leaf = 1         0.818           F score         160         N_estimators = 25, Learning_rate = 1         0.826           MI         100         N_estimators = 40, Learning_rate = 0.01         0.821           AdaBoost         RFE         80         N_estimators = 40, Learning_rate = 0.5         0.860           Lasso         51         N_estimators = 40, Learning_rate = 0.5         0.870         0.858 (0.787, 0.926)           Min         160         C = 0.01         0.831         0.870         0.858 (0.787, 0.926)           Lasso         51         N_estimators = 10, Learning_rate = 0.05         0.831         0.831         0.833           L-SVM         RFE         15         C = 0.01         0.837         0.833 (0.755, 0.904)           L-SVM         RFE         15         C = 0.1         0.875         0.833 (0.755, 0.904)           RFE         30         C = 0.02, gamma = 0.0001         0.844         0.0001         0.844           R-SVM         RFE         30	DE	RFE	10	N estimators $= 140$ ,	0.020	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	RF		40	Min samples leaf = $3$	0.839	0.773 (0.684, 0.857)
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		-	_	N estimators = $10$ .		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Lasso	7	Min samples leaf = $3$	0.837	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Tree-		N estimators = $30$ .		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		based	73	Min samples leaf = $1$	0.818	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$				N estimators = $25$ .		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		F score	160	Learning rate $= 1$	0.826	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		NG	100	N estimators = $40$ ,	0.021	
AdaBoost       RFE       80 $N\_estimators = 35, Learning\_rate = 0.5$ 0.860         Lasso       51 $N\_estimators = 40, Learning\_rate = 1.5$ 0.870       0.858 (0.787, 0.926)         Tree- based       68 $N\_estimators = 10, Learning\_rate = 0.05$ 0.831         L-SVM       F score       25       C = 0.01       0.837         L-SVM       RFE       15       C = 0.15       0.873         Lasso       53       C = 1       0.872         Tree- based       72       C = 0.1       0.875       0.833 (0.755, 0.904)         F score       65       C = 0.8, gamma = 0.0001       0.844         MI       30       C = 0.08, gamma = 0.0001       0.844         MI       30       C = 0.1, gamma = 0.0005       0.860         Lasso       51       C = 0.02, gamma = 0.1       0.862         Tree- based       30       C = 2, gamma = 0.05       0.863       0.764 (0.674, 0.848)         LDA       MI       40       NA       0.723         LDA       MI       40       NA       0.832         Lasso       37       NA       0.863       0.818 (0.737, 0.891)		MI	100	Learning rate $= 0.01$	0.821	
AdaBoost       RFE       80       Learning_rate = 0.5       0.860         Lasso       51       N_estimators = 40, Learning_rate = 1.5       0.870       0.858 (0.787, 0.926)         Tree- based       68       N_estimators = 10, Learning_rate = 0.05       0.831         F score       25       C = 0.01       0.837         MI       160       C = 0.05       0.837         L-SVM       RFE       15       C = 0.15       0.872         Tree- based       72       C = 0.1       0.875       0.833 (0.755, 0.904)         F score       65       C = 0.8, gamma = 0.0001       0.844         MI       30       C = 0.08, gamma = 0.0005       0.860         K-SVM       RFE       30       C = 0.1, gamma = 0.0005       0.860         Lasso       51       C = 0.02, gamma = 0.1       0.862         Tree- based       30       C = 2, gamma = 0.05       0.863       0.764 (0.674, 0.848)         LDA       MI       40       NA       0.723         LDA       MI       40       NA       0.832         LBA       MI       40       NA       0.832         LDA       MI       40       NA       0.832			0.0	N estimators = $35$ .	0.070	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	AdaBoost	RFE	80	Learning rate $= 0.5$	0.860	
Lasso 51 Learning_rate = 1.5 Tree- based 68 N_estimators = 10, Learning_rate = 0.05 0.831 F score 25 C = 0.01 0.837 MI 160 C = 0.05 0.837 Lasso 53 C = 1 0.872 Tree- based 72 C = 0.1 0.875 0.833 (0.755, 0.904) F score 65 C = 0.8, gamma = 0.844 MI 30 C = 0.08, gamma = 0.844 MI 30 C = 0.08, gamma = 0.838 R-SVM RFE 30 C = 0.1, gamma = 0.838 R-SVM RFE 30 C = 0.1, gamma = 0.860 Lasso 51 C = 0.02, gamma = 0.1 0.862 Tree- based 30 C = 2, gamma = 0.1 0.863 LDA MI 40 NA 0.723 H 40 NA 0.832 LDA AMI 40 NA 0.832 LDA NA 0.863 0.818 (0.737, 0.801)		Ŧ	<b>-</b> 1	N estimators = $40$ ,	0.070	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		Lasso	51	Learning rate $= 1.5$	0.870	0.858 (0.787, 0.926)
$\frac{based}{Learning_rate = 0.05} = \frac{0.831}{0.831}$ $L-SVM = \begin{bmatrix} F \ score & 25 & C = 0.01 & 0.837 \\ MI & 160 & C = 0.05 & 0.837 \\ MI & 160 & C = 0.05 & 0.837 \\ C = 0.15 & 0.873 \\ C = 1 & 0.872 \\ Tree- & 72 & C = 0.1 & 0.875 & 0.833 (0.755, 0.904) \\ \hline F \ score & 65 & C = 0.8, gamma = \\ 0.0001 & 0.844 \\ MI & 30 & C = 0.08, gamma = \\ 0.0001 & 0.838 \\ R-SVM & RFE & 30 & C = 0.1, gamma = \\ 0.0005 & 0.860 \\ Lasso & 51 & C = 0.02, gamma = 0.1 & 0.862 \\ Tree- & 30 & C = 2, gamma = 0.05 & 0.863 & 0.764 (0.674, 0.848) \\ \hline F \ score & 50 & NA & 0.723 \\ LDA & MI & 40 & NA & 0.723 \\ RFE & 40 & NA & 0.832 \\ LBA & RFE & 40 & NA & 0.862 \\ \hline RFE & 40 & NA & 0.832 \\ LBA & 0.863 & 0.818 (0.737, 0.801) \\ \hline \end{bmatrix}$		Tree-		N estimators = 10.	0.001	
$ \begin{array}{c ccccc} & & & & & & & & & & & & & & & & &$		based	68	Learning rate $= 0.05$	0.831	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		F score	25	C = 0.01	0.837	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		MI	160	C = 0.05	0.837	
L-SVM       IABL       IS       IC = 0.15       0.873         Lasso       53       C = 1       0.872         Tree-       72       C = 0.1       0.875       0.833 (0.755, 0.904)         F score       65       C = 0.8, gamma = 0.0001       0.844         MI       30       C = 0.08, gamma = 0.838       0.8001         R-SVM       RFE       30       C = 0.1, gamma = 0.860       0.860         Lasso       51       C = 0.02, gamma = 0.1       0.862         Tree-       30       C = 2, gamma = 0.1       0.862         Tree-       30       C = 2, gamma = 0.05       0.863       0.764 (0.674, 0.848)         LDA       MI       40       NA       0.723         LDA       MI       40       NA       0.832         LDA       MI       40       NA       0.863       0.818 (0.737, 0.891)		RFE	15	C = 0.15	0.873	
Integration       Image: Section       Image:	L-SVM	Lasso	53	C = 1	0.872	
Interm72 $C = 0.1$ $0.875$ $0.833 (0.755, 0.904)$ F score65 $C = 0.8, gamma = 0.0001$ $0.844$ MI30 $C = 0.08, gamma = 0.0001$ $0.838$ R-SVMRFE30 $C = 0.1, gamma = 0.860$ $0.860$ Lasso51 $C = 0.02, gamma = 0.1$ $0.862$ Tree- based30 $C = 2, gamma = 0.05$ $0.863$ $0.764 (0.674, 0.848)$ LDAMI40NA $0.723$ LDAMI40NA $0.832$ Lasso37NA $0.863$ $0.818 (0.737, 0.891)$		Tree-	00		0.072	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		based	72	C = 0.1	0.875	0.833 (0.755, 0.904)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		F score	65	C = 0.8, gamma = 0.0001	0.844	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		MI	30	C = 0.08, gamma =	0.838	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	R-SVM	RFE	30	C = 0.1, gamma =	0.860	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Lasso	51	C = 0.02 gamma = 0.1	0.862	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Tree-	51	c = 0.02, 5umma = 0.1	0.002	
$LDA \begin{array}{ccccccccc} F score & 50 & NA & 0.723 \\ MI & 40 & NA & 0.792 \\ RFE & 40 & NA & 0.832 \\ Lasso & 37 & NA & 0.863 & 0.818 (0.737, 0.891) \end{array}$		based	30	C = 2, gamma = 0.05	0.863	0.764 (0.674, 0.848)
LDA MI 40 NA 0.792 RFE 40 NA 0.832 Lasso 37 NA 0.863 0.818 (0.737.0.891)		F score	50	NA	0.723	
LDA RFE 40 NA 0.832 Lasso 37 NA 0.863 0.818 (0.737.0.891)		MI	40	NA	0.792	
Lasso 37 NA 0.863 0.818 (0.737 0.891)	LDA	RFE	40	NA	0.832	
$\mathbf{L}_{1,0,0,0,0,0,0,0,0$		Lasso	37	NA	0.863	0.818 (0.737, 0.891)

Tree-	(5	NT A	0.912	
based	00	INA	0.815	

 $\overline{\text{CE}}$  = contrast-enhancing, AUC = area under the receiver operating characteristic curve, CI = confidence interval, , kNN = k-nearest neighbor, NB = naïve Bayes, RF = random forest, Ada = adaptive boosting, L-SVM = linear support vector machine, R-SVM = radial basis function support vector machine, LDA = linear discriminant analysis, MI = mutual information, RFE = recursive feature elimination, Lasso = least absolute shrinkage and selection operator

**Supplementary Table S2.** Detailed diagnostic performance of different combinations of five featureselection and seven classification methods, using PT mask

Classifier	Feature selection method	Optimal feature number	Optimal hyperparameters	Mean AUC in the training set	AUC (95% CI) in the test set
	F score	15	K = 2	0.701	
	MI	5	K = 8	0.699	
kNN	RFE	50	K = 13	0.640	
	Lasso	6	<b>K</b> = 17	0.750	0.694 (0.589, 0.794)
	Tree- based	35	K = 3	0.660	
	F score	5	NA	0.673	0.753 (0.656, 0.838)
	MI	15	NA	0.645	
NB	RFE	25	NA	0.638	
	Lasso	6	NA	0.660	
	Tree- based	33	NA	0.658	
	F score	5	N_estimators = 10, Min_samples leaf = 4	0.639	
	MI	5	N_estimators = 20, Min_samples leaf = 4	0.739	0.700 (0.599, 0.798)
RF	RFE	5	N_estimators = 20, Min_samples leaf = 3	0.628	
	Lasso	6	N_estimators = 45, Min_samples leaf = 3	0.719	
	Tree- based	37	N_estimators = 30, Min_samples leaf = 2	0.723	
	F score	25	N_estimators = 10, Learning_rate = 1	0.790	
	MI	25	N_estimators = 25, Learning_rate = 2	0.746	
AdaBoost	RFE	15	N_estimators = 15, Learning_rate = 1	0.722	
	Lasso	38	N_estimators = 35, Learning_rate = 0.05	0.733	
	Tree- based	31	N_estimators = 20, Learning_rate = 2	0.816	0.761 (0.691, 0.827)
L-SVM	F score	25	C = 0.03	0.799	

	MI	25	C = 1	0.714	
	RFE	20	C = 0.008	0.830	0.803 (0.718, 0.879)
	Lasso	25	C = 0.2	0.816	
	Tree- based	34	C = 0.8	0.736	
	F score	60	C = 2, gamma = 0.005	0.782	
	MI	70	C =2, gamma = 0.006	0.783	
R-SVM	RFE	15	C = 0.001, gamma = 0.02	0.804	
	Lasso	25	C = 1, gamma = 0.01	0.817	0.753 (0.658, 0.839)
	Tree- based	34	C = 0.9, gamma = 0.01	0.754	
	F score	50	NA	0.761	
	MI	80	NA	0.818	0.768 (0.673, 0.856)
LDA	RFE	20	NA	0.763	
	Lasso	12	NA	0.798	
	Tree- based	33	NA	0.794	

PT = peritumoral T2 hyperintense, AUC = area under the receiver operating characteristic curve, CI = confidence interval, , kNN = k-nearest neighbor, NB = na Bayes, RF = random forest, Ada = adaptive boosting, L-SVM = linear support vector machine, R-SVM = radial basis function support vector machine, LDA = linear discriminant analysis, MI = mutual information, RFE = recursive feature elimination, Lasso = least absolute shrinkage and selection operator

**Supplementary Table S3.** Detailed diagnostic performance of different combinations of five featureselection and seven classification methods, using combined mask

Classifier	Feature selection method	Optimal feature number	Optimal hyperparameters	Mean AUC in the training set	AUC (95% CI) in the test set
	F score	25	K = 7	0.719	
	MI	20	K = 9	0.781	
kNN	RFE	20	K = 6	0.782	0.738 (0.648, 0.822)
	Lasso	35	K = 6 0.772		
	Tree- based	97	K = 9	0.727	
	F score	25	NA	0.657	
	MI	20	NA	0.695	
NB	RFE	20	NA	0.753	0.713 (0.616, 0.804)
	Lasso	34	NA	0.677	
	Tree- based	100	NA	0.669	
	F score	20	N_estimators = 15, Min_samples leaf = 5	0.862	
	MI	120	N_estimators = 20, Min_samples leaf = 4	0.853	
RF	RFE	20	N_estimators = 25, Min_samples leaf = 2	0.866	
	Lasso	45	N_estimators = 45, Min_samples leaf = 4	0.883	0.780 (0.687, 0.862)
	Tree- based	96	N_estimators = 30, Min_samples leaf = 1	0.857	
	F score	250	N_estimators = 25, Learning_rate = 2	0.918	
	MI	65	N_estimators = 20 Learning_rate = 2	0.910	
AdaBoost	RFE	60	N_estimators = 20, Learning_rate = 0.5	0.910	
	Lasso	44	N_estimators = 35, Learning_rate = 0.1	0.899	
	Tree- based	96	N_estimators = 20, Learning_rate = 1	0.926	0.890 (0.823, 0.947)
L-SVM	F score	120	C = 0.1	0.929	

	MI	130	C = 0.4	0.899	
	RFE	70	C = 0.05	0.932	0.886 (0.822, 0.940)
	Lasso	34	C = 1.2	0.928	
	Tree- based	110	C = 1	0.901	
	F score	45	C = 2, gamma = 0.005	0.908	
	MI	20	C = 0.05, gamma = 0.04	0.900	
R-SVM	RFE	30	C = 3, gamma = 0.02	0.925	0.827 (0.749, 0.898)
	Lasso	8	C = 1, gamma = 0.06	0.883	
	Tree- based	250	C = 2, gamma = 0.002	0.883	
	F score	55	NA	0.860	
	MI	40	NA	0.830	
LDA	RFE	40	NA	0.941	
	Lasso	34	NA	0.945	0.883 (0.816, 0.941)
	Tree- based	98	NA	0.760	

 $\overline{AUC}$  = area under the receiver operating characteristic curve, CI = confidence interval, , kNN = k-nearest neighbor, NB = naïve Bayes, RF = random forest, Ada = adaptive boosting, L-SVM = linear support vector machine, R-SVM = radial basis function support vector machine, LDA = linear discriminant analysis, MI = mutual information, RFE = recursive feature elimination, Lasso = least absolute shrinkage and selection operator Supplementary Table S4. Importance score of radiomics features used for seven machine learning

classifiers

Features	kNN	NB	RF	AdaB	L-	R-	LDA	Total
CE mask with T2 image firstorde	1.00	0.42	0.22	00St			0.46	4.25
r Median	1.00	0.42	0.32	0.10	1.00	1.00	0.40	4.55
CE mask with T2 image firstorde	NS	0.54	1.00	0.87	0.55	0.40	0.08	3.44
r 10Percentile	110	0.01	1.00	0.07	0.55	0.10	0.00	5.11
periT2 mask with T2 image shap	0.74	NS	NS	0.79	0.43	0.08	0.09	2.13
e Maximum2DDiameterRow								
periT2_mask_with_T2_image_firsto	0.60	NS	NS	0.61	0.66	NS	NS	1.86
rder_Median								
periT2_mask_with_T2_image_shap	NS	NS	NS	0.61	0.34	0.76	0.05	1.76
e_Flatness								
periT2_mask_with_T2_image_glsz	NS	NS	NS	0.34	0.22	0.84	0.16	1.56
m_GrayLevelNonUniformity								
periT2_mask_with_T2_image_glsz	0.67	0.08	NS	0.34	0.07	0.24	0.00	1.40
m_SizeZoneNonUniformity	0.55	0.00	210	0.00	0.01	0.00	0.11	1.25
CE_mask_with_12_image_firstorde	0.77	0.38	NS	0.00	0.01	0.08	0.11	1.35
r_InterquartileRange	NC	NC	NC	0.22	0.01	NC	1.00	1.22
CE_mask_with_CE_image_gicm_id	INS	INS	NS	0.32	0.01	IN S	1.00	1.33
CE_mask_with_CE_image_glrlm_L	NS	NS	NS	0.00	0.45	0.20	0.63	1.28
owGrayLevelRunEmphasis								
CE_mask_with_T2_image_glszm_	NS	0.04	0.18	1.00	NS	NS	NS	1.22
GrayLevelNonUniformity								
CE_mask_with_T2_image_firstorde	NS	0.04	0.59	0.47	NS	NS	NS	1.11
r_Skewness								
CE_mask_with_CE_image_firstord	0.60	NS	0.27	0.00	0.00	0.16	NS	1.03
er_10Percentile	NG	1.00	NG	NG	NG	NG	NG	1.00
CE_mask_with_12_image_firstorde	NS	1.00	NS	NS	NS	NS	NS	1.00
r_MeanAbsoluteDeviation	NC	NC	NC	0.00	0.27	0.04	0.58	0.08
CE_IIIask_witii_CE_IIIiage_giciii_iii	113	IND	IND	0.00	0.57	0.04	0.38	0.98
CE mask with CE image glcm A	NS	NS	NS	0.00	0.00	NS	0.94	0.94
utocorrelation	145	145	110	0.00	0.00	110	0.71	0.71
CE mask with T2 image firstorde	0.11	NS	0.14	0.00	0.03	0.44	0.20	0.91
r Mean								
CE_mask_with_CE_image_firstord	NS	NS	0.82	0.00	0.07	NS	NS	0.88
er_Median								
CE_mask_with_T2_image_glcm_Di	NS	NS	0.82	NS	NS	NS	NS	0.82
fferenceAverage								
CE_mask_with_CE_image_glrlm_S	NS	NS	NS	0.50	0.00	0.08	0.23	0.81
hortRunLowGrayLevelEmphasis								
periT2_mask_with_T2_image_glrl	NS	NS	0.77	NS	0.03	NS	NS	0.80
m_RunVariance	210	210	0.55	210	0.00	210	210	0.55
peril2_mask_with_12_image_glrl	NS	NS	0.77	NS	0.00	NS	NS	0.77
m_LowGrayLevelRunEmphasis	NC	NC	0.41	0.00	0.04	0.22	NC	0.77
CE_IIIask_with_CE_IIIage_girinf_L	113	INS	0.41	0.00	0.04	0.52	112	0.77
periT2 mask with T2 image firsto	NS	0.08	NS	0.68	0.00	NS	NS	0.77
rder Skewness		0.00	TAD.	0.00	0.00	611		0.77
CE mask with CE image glszm	NS	NS	0.45	0.00	0.03	0.16	0.07	0.71
LowGrayLevelZoneEmphasis				0.00	0.05	0.10	0.07	0.71
CE mask with CE image glcm D	NS	NS	NS	0.00	NS	NS	0.71	0.71
	-		-		1			

ifferenceAverage								
CE mask with T2 image glcm Di	NS	NS	NS	0.45	0.04	NS	0.20	0.69
fferenceEntropy	110	1.0	110	0.15	0.01	110	0.20	0.07
CE mask with CE image shape	0.18	0.13	0.36	0.00	NS	NS	NS	0.66
LeastAxisLength								
CE mask with CE image firstord	NS	NS	NS	0.50	0.00	0.16	NS	0.66
er Mean								
periT2 mask with T2 image glrl	NS	NS	NS	0.58	NS	0.08	NS	0.66
m ShortRunEmphasis								
periT2 mask with T2 image firsto	0.33	0.00	0.32	0.00	NS	NS	NS	0.65
rder Minimum								
CE mask with CE image glrlm R	NS	NS	NS	NS	0.29	0.32	NS	0.61
unLengthNonUniformity								
CE mask with CE image shape F	NS	NS	NS	0.58	NS	NS	NS	0.58
latness								
CE mask with CE image shape	0.12	0.17	NS	0.16	0.08	0.04	NS	0.57
Maximum2DDiameterRow								
CE mask with CE image glszm	NS	NS	NS	0.45	0.11	NS	NS	0.55
GrayLevelVariance								
CE mask with T2 image firstorde	NS	NS	0.55	0.00	0.00	NS	NS	0.55
r RobustMeanAbsoluteDeviation								
E mask with CE image glcm S	NS	NS	NS	0.00	NS	0.08	0.46	0.54
umAverage								
CE mask with CE image glcm J	NS	NS	NS	0.00	0.07	NS	0.46	0.53
ointAverage								
CE mask with T2 image firstorde	0.53	NS	NS	NS	NS	NS	NS	0.53
r Minimum	0.000	1.00	1.00	1.00	1.00	110	110	0.00
CE mask with T2 image glcm Jo	NS	NS	0.36	0.00	0.08	0.08	NS	0.52
intEnergy								
CE mask with T2 image firstorde	NS	NS	NS	NS	NS	0.48	NS	0.48
r RootMeanSquared								
CE mask with CE image glszm	NS	NS	0.45	NS	NS	NS	NS	0.45
SmallAreaHighGrayLevelEmphasis								
CE mask with T2 image glcm M	NS	NS	0.18	0.00	0.11	0.08	0.07	0.44
aximumProbability								
CE mask with CE image firstord	NS	NS	NS	NS	0.14	0.28	NS	0.42
er InterguartileRange								
periT2 mask with T2 image glrl	NS	NS	0.32	0.00	0.11	NS	NS	0.42
m RunEntropy								
CE mask with CE image firstord	0.37	0.00	0.05	NS	NS	NS	NS	0.41
er_Minimum								
periT2_mask_with_T2_image_shap	0.40	0.00	NS	NS	NS	NS	NS	0.40
e_LeastAxisLength								
CE_mask_with_T2_image_ngtdm_	NS	0.17	0.23	NS	NS	NS	NS	0.39
Strength								
periT2_mask_with_T2_image_glcm	NS	NS	0.36	0.00	0.00	NS	0.02	0.39
JointAverage								
CE_mask_with_CE_image_firstord	0.37	NS	NS	0.00	0.00	NS	NS	0.37
er_90Percentile								
CE_mask_with_T2_image_glrlm_L	NS	NS	0.36	NS	NS	NS	NS	0.36
ongRunEmphasis								
CE_mask_with_T2_image_glcm_S	NS	NS	0.36	NS	NS	NS	NS	0.36
umEntropy								
CE_mask_with_CE_image_glrlm_S	NS	NS	0.05	0.32	NS	NS	NS	0.36
hortRunHighGrayLevelEmphasis								
CE_mask_with_CE_image_glcm_J	NS	NS	NS	0.00	NS	0.36	NS	0.36
ointEnergy								

CE_mask_with_T2_image_glrlm_L	NS	NS	0.32	NS	NS	NS	NS	0.32
ongRunLowGrayLevelEmphasis				2.20				
CE_mask_with_CE_image_glszm_	NS	NS	0.32	NS	NS	NS	NS	0.32
CE mask with T2 image shape I	0.19	0.12	0.00	NC	NC	NC	NC	0.20
CE_mask_with_12_image_snape_L eastAxisLength	0.18	0.15	0.00	NS	INS .	INS	INS	0.30
CE mask with T2 image firstorde	NS	NS	0.27	NS	0.03	NS	NS	0.30
r Entrony	145	145	0.27	110	0.05	145	115	0.50
neriT2 mask with T2 image glrl	NS	NS	NS	0.00	0.00	0.28	NS	0.28
m Run Length Non Uniformity	110	110	115	0.00	0.00	0.20	110	0.20
CE mask with CE image firstord	NS	NS	NS	NS	NS	0.28	NS	0.28
er RobustMeanAbsoluteDeviation	145	145	145	110	145	0.20	115	0.20
CE mask with T2 image shape	0.12	NS	NS	NS	0.08	NS	0.07	0.27
Maximum2DDiameterRow								
periT2 mask with T2 image glsz	NS	NS	NS	0.00	0.25	NS	NS	0.25
m GrayLevelVariance								
CE mask with T2 image glszm L	NS	NS	0.23	NS	NS	NS	NS	0.23
owGrayLevelZoneEmphasis								
periT2_mask_with_T2_image_glcm	NS	NS	0.23	NS	NS	NS	NS	0.23
_Correlation								
CE_mask_with_T2_image_glcm_Jo	NS	NS	0.23	0.00	NS	NS	NS	0.23
intAverage								
CE_mask_with_T2_image_glcm_Jo	NS	NS	0.23	0.00	0.00	NS	NS	0.23
intEntropy								
CE_mask_with_CE_image_ngtdm_	NS	NS	0.23	0.00	NS	NS	NS	0.23
Complexity								
CE_mask_with_CE_image_glrlm_R	NS	NS	0.23	NS	NS	NS	NS	0.23
unVariance								
CE_mask_with_CE_image_glcm_C	NS	NS	0.23	NS	NS	NS	NS	0.23
lusterTendency								
periT2_mask_with_T2_image_ngtd	0.21	NS	NS	NS	NS	NS	NS	0.21
m_Complexity				110				
CE_mask_with_T2_image_shape_	NS	NS	NS	NS	NS	NS	0.21	0.21
Maximum2DDiameterSlice	NG	NG	NG	0.00	0.05	NG	0.12	0.10
CE_mask_with_12_image_glcm_Cl	NS	NS	NS	0.00	0.05	NS	0.13	0.19
CE mask with CE image alam C	NC	NC	0.19	NC	NC	NC	NC	0.19
ontrast	112	113	0.18	IND	112	112	IND	0.18
CE mask with CE image alrlm R	NS	NS	0.18	NS	NS	NS	NS	0.18
unPercentage	145	145	0.10	110	145	145	115	0.10
CE mask with T2 image glrlm R	NS	NS	0.18	NS	NS	NS	NS	0.18
unEntropy	110	110	0.10	110	110	110	1.0	0.10
CE mask with T2 image firstorde	NS	NS	0.18	0.00	NS	NS	NS	0.18
r Uniformity								
CE mask with CE image glcm J	NS	NS	0.18	NS	NS	NS	NS	0.18
ointEntropy								
CE_mask_with_CE_image_firstord	NS	NS	0.18	NS	NS	NS	NS	0.18
er_Entropy								
CE_mask_with_CE_image_glcm_	NS	NS	0.18	NS	NS	NS	NS	0.18
MaximumProbability								
CE_mask_with_CE_image_firstord	NS	NS	0.18	NS	NS	NS	NS	0.18
er_MeanAbsoluteDeviation								
CE_mask_with_CE_image_glrlm_R	NS	NS	NS	0.00	0.17	NS	NS	0.17
unLengthNonUniformityNormalize								
d								<del>.</del> .
CE_mask_with_T2_image_firstorde	NS	0.17	NS	NS	NS	NS	NS	0.17
r_Kurtosis	1		1	1	1	1	1	1

CE_mask_with_CE_image_glcm_S	NS	NS	NS	0.00	0.16	NS	0.01	0.16
umEntropy	210	210	210	NG	0.00	0.1.6	210	0.1.6
CE_mask_with_T2_image_glcm_ln	NS	NS	NS	NS	0.00	0.16	NS	0.16
CE mask with T2 image firstorde	NS	NS	NS	NS	0.13	NS	NS	0.13
r Range	110	110	110	110	0.15	115	110	0.12
CE_mask_with_CE_image_glrlm_	NS	NS	NS	0.00	0.00	NS	0.13	0.13
HighGrayLevelRunEmphasis								
CE_mask_with_T2_image_glszm_	NS	NS	NS	0.00	NS	NS	0.13	0.13
HighGrayLevelZoneEmphasis								
CE_mask_with_CE_image_shape_ MinorAxisI ength	NS	0.13	NS	NS	NS	NS	NS	0.13
CE mask with T2 image glszm S	0.12	NS	NS	NS	NS	NS	NS	0.12
izeZoneNonUniformity								
periT2 mask with T2 image shap	NS	NS	NS	0.00	0.08	0.04	NS	0.12
e Maximum3DDiameter								
CE mask with CE image firstord	NS	NS	NS	0.00	0.12	NS	NS	0.12
er_Maximum								
periT2_mask_with_T2_image_firsto	0.11	0.00	NS	NS	NS	NS	NS	0.11
rder_MeanAbsoluteDeviation								
periT2_mask_with_T2_image_glsz	NS	NS	NS	0.00	0.09	NS	NS	0.09
m_GrayLevelNonUniformityNorma								
lized								
CE_mask_with_T2_image_glrlm_S	NS	NS	0.09	NS	NS	NS	NS	0.09
hortRunEmphasis								
periT2_mask_with_T2_image_shap	NS	NS	NS	0.00	0.05	0.00	0.04	0.09
e_VoxelVolume								
CE_mask_with_T2_image_glcm_Id	NS	NS	NS	0.00	NS	NS	0.09	0.09
periT2_mask_with_T2_image_ngtd	0.00	0.08	NS	0.00	NS	NS	NS	0.08
m_Strength								
CE_mask_with_T2_image_firstorde	NS	NS	NS	NS	0.00	NS	0.07	0.07
r_Energy								
periT2_mask_with_T2_image_shap	NS	NS	NS	0.00	0.07	0.00	NS	0.07
e_MeshVolume								
CE_mask_with_T2_image_glszm_S	NS	NS	NS	0.00	0.07	NS	NS	0.07
izeZoneNonUniformityNormalized								
CE_mask_with_CE_image_glcm_D	NS	NS	NS	0.00	0.00	NS	0.05	0.05
ifferenceEntropy								
CE_mask_with_T2_image_glcm_S	NS	NS	NS	NS	0.04	NS	NS	0.04
umSquares								
CE_mask_with_CE_image_firstord	NS	NS	NS	0.00	0.03	NS	0.01	0.03
er_RootMeanSquared				_		_		
CE_mask_with_CE_image_shape_S	NS	NS	NS	0.00	0.00	NS	0.03	0.03
urfaceVolumeRatio				_		_		
CE_mask_with_T2_image_shape_S	NS	NS	NS	0.00	NS	NS	0.03	0.03
urfaceVolumeRatio								
CE_mask_with_CE_image_firstord	NS	NS	NS	0.00	0.03	NS	NS	0.03
er_Skewness								
periT2_mask_with_T2_image_glsz	NS	NS	NS	NS	0.03	NS	NS	0.03
m_ZoneEntropy								
periT2_mask_with_T2_image_glcm	NS	NS	NS	0.00	0.00	NS	0.02	0.02
_SumAverage								
CE_mask_with_T2_image_shape_E	NS	NS	NS	NS	0.01	NS	NS	0.01
longation		2.25						
CE_mask_with_T2_image_glcm_Id	NS	NS	NS	0.00	0.01	NS	NS	0.01
m	110	110	110	0.00	0.01	110	110	0.01
peri12_mask_with_12_image_glrl	NS	NS	NS	0.00	0.01	NS	NS	0.01

m_GrayLevelNonUniformity								
periT2_mask_with_T2_image_firsto rder_90Percentile	NS	NS	NS	NS	0.01	NS	NS	0.01

Features with zero total score were not included.

kNN = k-nearest neighbor, NB = naïve Bayes, RF = random forest, ADA = adaptive boosting, L-SVM = linear support vector machine, R-SVM = radial basis function support vector machine, LDA = linear discriminant analysis, CE = contrast-enhancing, NS = not selected for this classifier.

	AdaBoost	L-SVM	LDA	DNN	Human 1	Human 2
AdaBoost	1.0	0.607	0.644	0.742	0.17	0.421
L-SVM	0.607	1.0	0.631	0.685	0.238	0.466
LDA	0.644	0.631	1.0	0.663	0.285	0.546
DNN	0.742	0.685	0.663	1.0	0.311	0.479
Human 1	0.17	0.238	0.285	0.311	1.0	0.505
Human 2	0.421	0.466	0.546	0.479	0.505	1.0

**Supplementary Table S5.** Kappa statistics representing inter-rater agreement between various classifying methods

AdaBoost = adaptive boosting, L-SVM = linear support vector machine, R-SVM = radial basis function support vector machine, LDA = linear discriminant analysis.

**Supplementary Table S6.** Comparison of magnetic resonance imaging parameters of patients in the training cohort (from our institution) and those in the external validation cohort (from another tertiary medical center).

Pulse Sequence	Our institution	External validation set		
T2-weighted image				
Repetition Time (ms)	3000-9000	3000		
Echo Time (ms)	80–120	80–120		
Matrix	$256 \times 256$	$256 \times 256$		
Section thickness (mm)	5	4–7		
Field of view	220–240	230–240		
Contrast-enhanced T1-weighted image				
Repetition Time (ms)	6.3–8.3	6.4–10.1		
Echo Time (ms)	2.9–4	2.8-4.8		
Matrix	$256 \times 256$ or $192 \times 192$	$512 \times 512$		
Section thickness (mm)	1	0.5		
Field of view	224–240	224–230		

## Supplementary Table S7. Details of feature selection and classification method

	Acronym	Feature selection method
1	F score	F score
2	MI	Mutual information
3	RFE	Recursive feature elimination
4	LASSO	Least absolute shrinkage and selection operator
5	Tree-based	Tree-based

	Acronym	Classification method
1	kNN	k-nearest neighbor
2	NB	Naïve Bayes
3	RF	Random forest
4	AdaBoost	Adaptive boosting
5	L-SVM	Support vector machine using linear kernel
6	R-SVM	Support vector machine using radial basis function kernel
7	LDA	Linear discriminant analysis

#### Feature selection methods

## 1. F score<sup>1</sup>

The F score is a univariate feature selection method. It is based on F-test estimate the degree of linear dependency between two random variables. It is to find a subset of features, such that in the data space spanned by the selected features, the distances between data points in different classes are as large as possible, while the distances between data points in the same class are as small as possible.

## 2. MI (Mutual information)<sup>2</sup>

The MI method measures arbitrary dependencies between random variables. It is suitable for assessing the information content of features in complex classification tasks, where methods based on linear relations are prone to mistakes

#### **3.** RFE (Recursive feature elimination)<sup>3</sup>

The RFE selects features by recursively considering smaller and smaller sets of features. The estimator is trained on an initial set of features and weights are assigned to each. Then the features whose absolute weights are the smallest are eliminated from the current features in a backwards elimination manner. This procedure is recursively repeated until the desired number of features is reached

#### 4. LASSO (Least absolute shrinkage and selection operator)<sup>4</sup>

The LASSO performs two tasks: regularization and feature selection. The LASSO minimizes the residual sum of squares subject to the sum of the absolute value of the coefficients being less than a constant. Because of the nature of this constraint it tends to produce some coefficients that are exactly 0 and hence gives interpretable models.

### 5. Tree-based<sup>5</sup>

The tree-based algorithm utilizes a tree structure to model relationships among the features and the potential outcomes. A standard CART algorithm is used to select the split predictor that maximizes the split-criterion gain over all possible splits of all predictors. Finding the optimal size of the tree helps improve predictive accuracy through the reduction of overfitting.

### **Classification methods**

## 1. kNN (k-nearest neighbor)<sup>6</sup>

The kNN algorithm assigns to unclassified observation (incoming test sample) the class/category/label of the nearest sample (using metric) in training set. The letter k is a variable term implying that any number of nearest neighbors could be used.

#### 2. NB (Naïve Bayes)<sup>7</sup>

The NB model assumes that observations have a multivariate distribution, given class membership, but the predictor and features composing the observation are independent.

#### 3. RF (Random forest)<sup>8</sup>

The RF model uses ensembles of trees, where each tree in the ensemble is grown in accordance with a random parameter. Final predictions are obtained by aggregating over the ensemble. As the base constituents of the ensemble are tree-structured predictors, and since each of these trees is constructed using an injection of randomness.

#### 4. AdaBoost (Adaptive boosting)9

The ADA is a general method for generating a strong classifier out of a set of weak classifiers. It works even when the classifiers come from a continuum of potential classifiers (such as neural networks, linear discriminants, etc.).

## 5. L-SVM (Support vector machine using linear kernel)<sup>10</sup>

The L-SVM model constructs a hyperplane separating data into two classes. The optimal hyperplane maximizes a margin surrounding itself, which creates boundaries for positive and negative classes.

## 6. R-SVM (Support vector machine using radial basis function kernel)<sup>10</sup>

The R-SVM is a nonlinear version of L-SVM with Gaussian kernel function that projects original features onto a higher dimensional space via a nonlinear mapping function where it becomes linearly separable.

#### 7. LDA (Linear discriminant analysis)<sup>11</sup>

The LDA model searches for the vectors in the underlying space that best discriminate among classes (rather than those that best describe the data). Given a number of independent features relative to which the data is described, LDA creates a linear combination of these which yields the largest mean differences between the desired classes. The goal is to maximize the between-class measure while minimizing the within-class measure.



### Supplementary Figure S8. Multi-input DNN implemented for deep learning

#### References

- 1 Gu, Q., Li, Z. & Han, J. Generalized fisher score for feature selection. *arXiv preprint arXiv:1202.3725* (2012).
- 2 Battiti, R. Using mutual information for selecting features in supervised neural net learning. *IEEE Transactions on neural networks* **5**, 537-550 (1994).
- 3 Guyon, I., Weston, J., Barnhill, S. & Vapnik, V. Gene selection for cancer classification using support vector machines. *Machine learning* **46**, 389-422 (2002).
- 4 Tibshirani, R. Regression shrinkage and selection via the lasso. *Journal of the Royal Statistical Society: Series B (Methodological)* **58**, 267-288 (1996).
- 5 Loh, W. Y. Classification and regression trees. *Wiley Interdisciplinary Reviews: Data Mining and Knowledge Discovery* **1**, 14-23 (2011).
- 6 Cover, T. & Hart, P. Nearest neighbor pattern classification. *IEEE transactions on information theory* **13**, 21-27 (1967).
- 7 Friedman, J., Hastie, T. & Tibshirani, R. *The elements of statistical learning*. Vol. 1 (Springer series in statistics New York, 2001).
- 8 Biau, G. Analysis of a random forests model. *Journal of Machine Learning Research* **13**, 1063-1095 (2012).
- 9 Rojas, R. AdaBoost and the super bowl of classifiers a tutorial introduction to adaptive boosting.
   Freie University, Berlin, Tech. Rep (2009).
- 10 Cristianini, N. & Shawe-Taylor, J. *An introduction to support vector machines and other kernelbased learning methods.* (Cambridge university press, 2000).
- 11 Martínez, A. M. & Kak, A. C. Pca versus lda. *IEEE transactions on pattern analysis and machine intelligence* 23, 228-233 (2001).