

A multimodal deep learning framework with contrastive learning and multi-instance learning for endometrial cancer preoperative risk stratification

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Supplementary information

Dataset of our's UNet3D

Our dataset comprises MRI data from 325 patients at the Sun Yat-sen University Cancer Center, totaling 1,300 MRI images with sequences including T1CA, T1CS, T2A, and T2S per patient. These data were randomly partitioned into training and validation sets at an 8:2 ratio, yielding 1,040 images for training and 260 for validation.

Training and testing of our's UNet3D

For 3D MRI volumes, images were first resampled to a resolution of (0.8 mm/pixel, 0.8 mm/pixel, 2.0 mm/pixel), followed by intensity normalization via min-max scaling to the [0.0, 1.0] range. During training, we implemented online data augmentation through random cropping and padding to standardize input dimensions to $256 \times 256 \times 32$ voxels, whereas during inference, center-cropping with padding achieved identical dimensional consistency. The neural architecture employed is depicted in Figure 1. This 3D network constitutes a modest adaptation of the original 2D UNet, extending 2D layers into 3D layers while reducing the input channel dimension from 64 to 32 to conserve GPU memory. Optimization utilizes a composite loss function equally weighting cross-entropy and Dice loss (1:1 ratio). Training proceeds for 100 epochs using the Adam optimizer with an initial learning rate of $2e-3$, following a cosine annealing schedule terminating at zero learning rate. The model demonstrating optimal validation metrics was retained for downstream experimental evaluation.

As illustrated in Figure 2, our UNet3D predictions demonstrate effective tumor region segmentation. The achieved Dice coefficient of 0.639 on the validation set suffices for experimental requirements, as the primary objective of this segmentation network focuses on capturing dominant tumor interfaces rather than pixel-perfect boundaries.

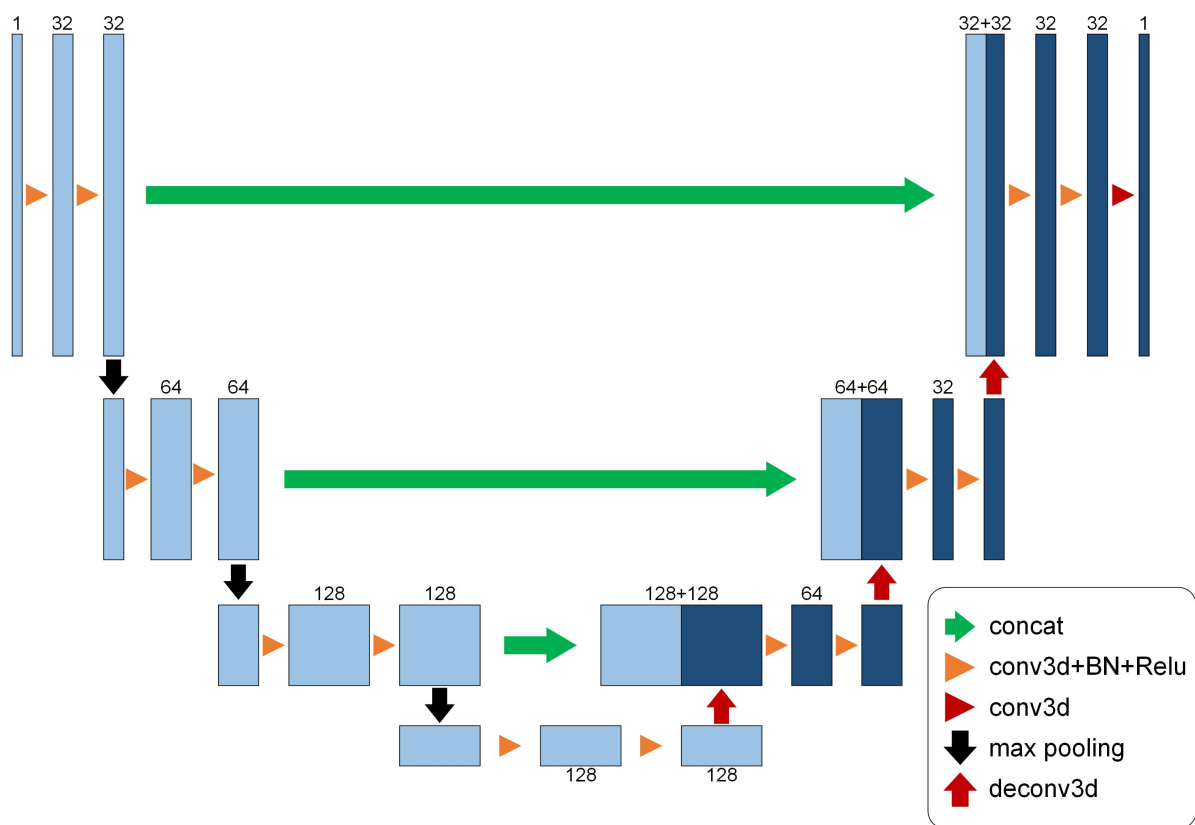


Figure 1. The network architecture of our's UNet3D.

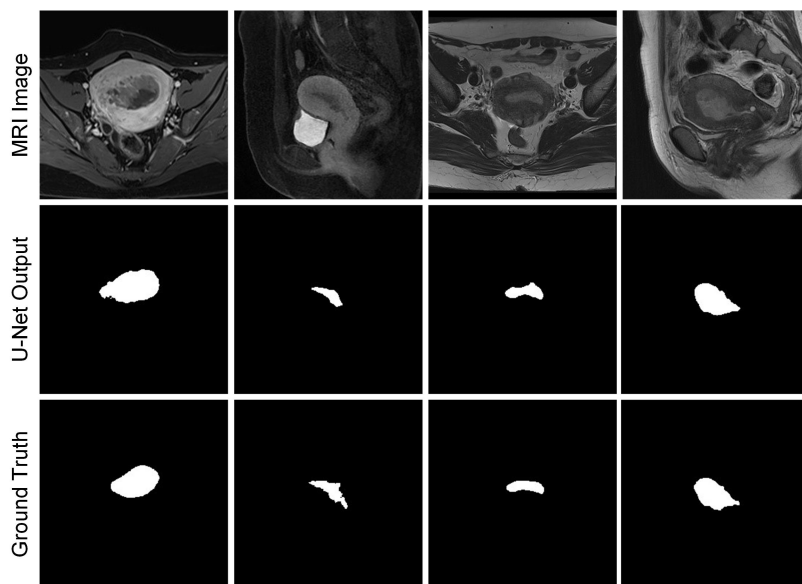


Figure 2. Our's UNet3D predicted results.

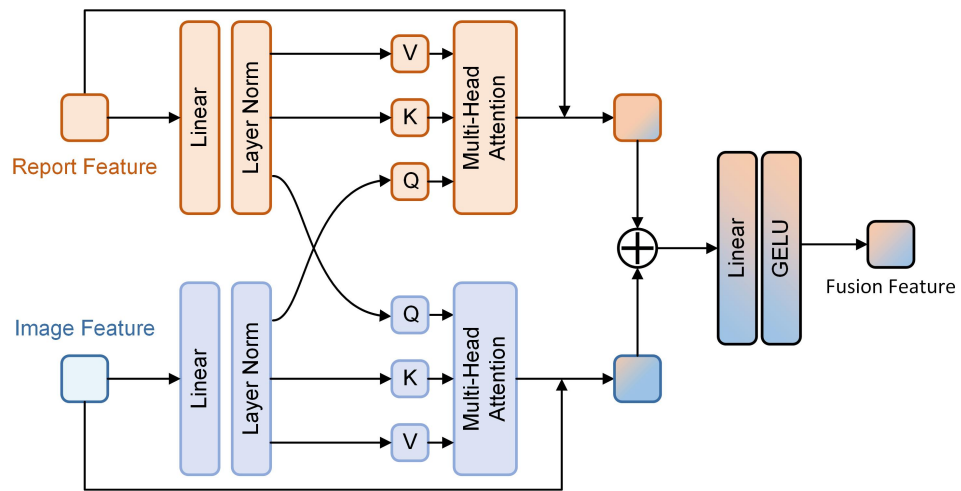


Figure 3. Bidirectional cross-attention module

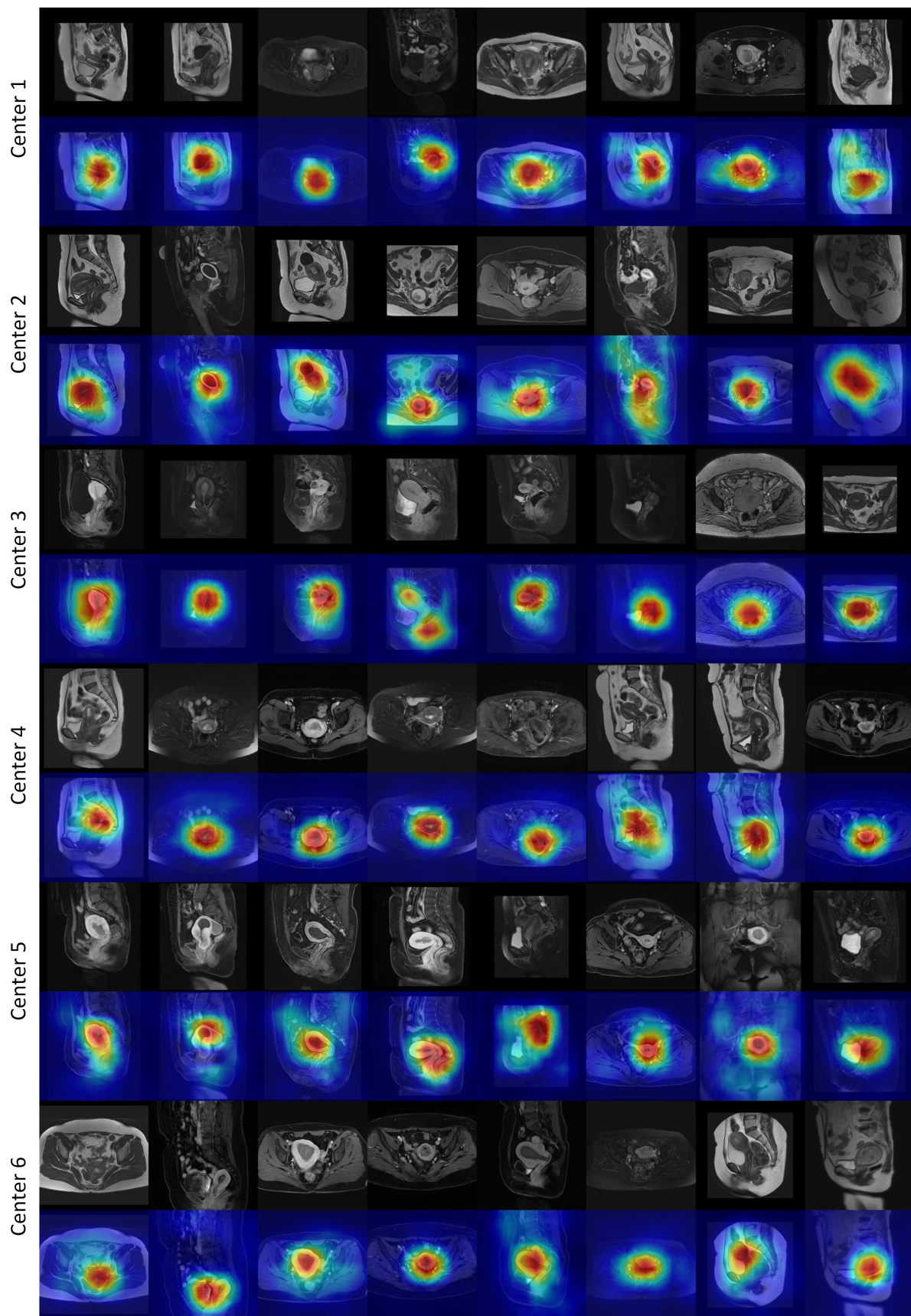


Figure 4. Region of interest (ROI) of the image encoder using Grad-CAM. Eight samples were randomly selected for each center for display.

Table 1. Performace of different methods

Dataset	Method	Precision	Recall	Accuracy	F1 score	AUC
Val	IRENE	0.789(0.701-0.871)	0.470(0.388-0.548)	0.690(0.636-0.740)	0.589(0.509-0.656)	0.778(0.727-0.828)
	MedCLIP	0.737(0.664-0.809)	0.649(0.570-0.725)	0.724(0.674-0.771)	0.690(0.628-0.746)	0.795(0.749-0.842)
	MUSK	0.752(0.675-0.827)	0.642(0.562-0.717)	0.730(0.683-0.777)	0.693(0.628-0.751)	0.797(0.749-0.844)
	MONET	0.647(0.575-0.716)	0.788(0.724-0.852)	0.696(0.646-0.746)	0.710(0.654-0.763)	0.791(0.740-0.837)
	Our's	0.670(0.607-0.736)	0.861(0.800-0.918)	0.734(0.683-0.784)	0.754(0.703-0.801)	0.827(0.782-0.871)
Test1	IRENE	0.781(0.704-0.857)	0.308(0.257-0.363)	0.593(0.553-0.635)	0.442(0.378-0.494)	0.737(0.696-0.773)
	MedCLIP	0.759(0.701-0.818)	0.502(0.448-0.562)	0.656(0.617-0.696)	0.604(0.554-0.652)	0.733(0.690-0.773)
	MUSK	0.739(0.677-0.794)	0.567(0.511-0.626)	0.669(0.631-0.709)	0.642(0.591-0.689)	0.741(0.700-0.780)
	MONET	0.709(0.655-0.763)	0.599(0.544-0.660)	0.662(0.620-0.703)	0.649(0.598-0.692)	0.736(0.693-0.775)
	Our's	0.824(0.771-0.873)	0.567(0.510-0.625)	0.711(0.676-0.749)	0.672(0.622-0.715)	0.806(0.769-0.840)
Test2	IRENE	0.669(0.592-0.742)	0.742(0.664-0.819)	0.646(0.580-0.704)	0.704(0.640-0.762)	0.684(0.610-0.757)
	MedCLIP	0.682(0.604-0.753)	0.820(0.758-0.888)	0.681(0.615-0.739)	0.745(0.679-0.796)	0.709(0.636-0.774)
	MUSK	0.700(0.616-0.773)	0.711(0.634-0.785)	0.664(0.602-0.726)	0.705(0.639-0.763)	0.706(0.635-0.771)
	MONET	0.623(0.554-0.691)	0.891(0.835-0.945)	0.633(0.571-0.695)	0.733(0.675-0.784)	0.702(0.637-0.769)
	Our's	0.626(0.561-0.698)	0.891(0.836-0.938)	0.637(0.571-0.699)	0.735(0.680-0.792)	0.768(0.706-0.829)
Test3	IRENE	0.680(0.574-0.785)	0.408(0.328-0.496)	0.622(0.560-0.676)	0.510(0.421-0.591)	0.671(0.605-0.736)
	MedCLIP	0.709(0.607-0.808)	0.488(0.397-0.568)	0.656(0.598-0.718)	0.578(0.495-0.655)	0.709(0.639-0.771)
	MUSK	0.586(0.515-0.661)	0.848(0.782-0.908)	0.637(0.579-0.691)	0.693(0.630-0.748)	0.717(0.655-0.775)
	MONET	0.573(0.497-0.646)	0.784(0.712-0.856)	0.614(0.556-0.672)	0.662(0.594-0.725)	0.706(0.642-0.769)
	Our's	0.699(0.624-0.776)	0.744(0.669-0.817)	0.722(0.664-0.780)	0.721(0.654-0.779)	0.793(0.739-0.848)
Test4	IRENE	0.857(0.643-1.000)	0.462(0.276-0.667)	0.673(0.531-0.796)	0.600(0.389-0.760)	0.753(0.603-0.879)
	MedCLIP	0.714(0.543-0.875)	0.769(0.600-0.920)	0.714(0.571-0.837)	0.741(0.600-0.857)	0.773(0.631-0.895)
	MUSK	0.619(0.455-0.762)	1.000(1.000-1.000)	0.673(0.531-0.796)	0.765(0.644-0.861)	0.774(0.626-0.890)
	MONET	0.615(0.450-0.763)	0.923(0.808-1.000)	0.653(0.510-0.776)	0.738(0.594-0.845)	0.768(0.627-0.890)
	Our's	0.686(0.528-0.833)	0.923(0.800-1.000)	0.735(0.592-0.857)	0.787(0.654-0.886)	0.863(0.738-0.953)

Table 2. Different metrics in the ablation study1

Dataset	Method	Precision	Recall	Accuracy	F1 score	AUC
Val	Report Only	0.829(0.750-0.899)	0.576(0.494-0.654)	0.743(0.693-0.793)	0.680(0.609-0.746)	0.786(0.734-0.834)
	Image Only	0.659(0.589-0.731)	0.728(0.660-0.795)	0.693(0.639-0.743)	0.692(0.631-0.747)	0.752(0.696-0.805)
	Report+Image	0.676(0.607-0.742)	0.762(0.690-0.828)	0.715(0.668-0.762)	0.717(0.656-0.770)	0.800(0.747-0.850)
	Contrastive Loss	0.727(0.654-0.795)	0.742(0.671-0.808)	0.746(0.696-0.793)	0.734(0.679-0.789)	0.814(0.763-0.859)
	Our's	0.670(0.607-0.736)	0.861(0.800-0.918)	0.734(0.683-0.784)	0.754(0.703-0.801)	0.827(0.782-0.871)
Test1	Report Only	0.737(0.681-0.792)	0.581(0.526-0.641)	0.673(0.635-0.709)	0.650(0.598-0.695)	0.752(0.714-0.791)
	Image Only	0.768(0.709-0.821)	0.505(0.449-0.562)	0.662(0.620-0.702)	0.610(0.558-0.657)	0.744(0.701-0.785)
	Report+Image	0.839(0.779-0.899)	0.433(0.375-0.496)	0.660(0.620-0.696)	0.571(0.511-0.624)	0.775(0.736-0.813)
	Contrastive Loss	0.798(0.747-0.849)	0.574(0.516-0.635)	0.702(0.665-0.738)	0.668(0.620-0.716)	0.794(0.756-0.831)
	Our's	0.824(0.771-0.873)	0.567(0.510-0.625)	0.711(0.676-0.749)	0.672(0.622-0.715)	0.806(0.769-0.840)
Test2	Report Only	0.677(0.593-0.754)	0.672(0.585-0.746)	0.633(0.571-0.699)	0.675(0.607-0.740)	0.688(0.619-0.756)
	Image Only	0.677(0.595-0.761)	0.656(0.569-0.738)	0.628(0.562-0.690)	0.667(0.594-0.731)	0.701(0.635-0.764)
	Report+Image	0.689(0.610-0.772)	0.727(0.650-0.802)	0.659(0.597-0.721)	0.707(0.640-0.763)	0.728(0.662-0.789)
	Contrastive Loss	0.709(0.634-0.780)	0.781(0.714-0.850)	0.695(0.637-0.752)	0.743(0.685-0.796)	0.746(0.680-0.809)
	Our's	0.626(0.561-0.698)	0.891(0.836-0.938)	0.637(0.571-0.699)	0.735(0.680-0.792)	0.768(0.706-0.829)
Test3	Report Only	0.709(0.608-0.805)	0.448(0.361-0.531)	0.645(0.583-0.699)	0.549(0.454-0.619)	0.711(0.651-0.771)
	Image Only	0.601(0.528-0.669)	0.832(0.769-0.895)	0.653(0.595-0.714)	0.698(0.638-0.753)	0.747(0.683-0.806)
	Report+Image	0.669(0.579-0.754)	0.696(0.618-0.776)	0.687(0.629-0.745)	0.682(0.614-0.742)	0.773(0.718-0.826)
	Contrastive Loss	0.677(0.595-0.757)	0.688(0.602-0.772)	0.691(0.633-0.749)	0.683(0.613-0.742)	0.786(0.732-0.841)
	Our's	0.699(0.624-0.776)	0.744(0.669-0.817)	0.722(0.664-0.780)	0.721(0.654-0.779)	0.793(0.739-0.848)
Test4	Report Only	0.704(0.519-0.870)	0.731(0.545-0.885)	0.694(0.571-0.816)	0.717(0.560-0.844)	0.771(0.641-0.899)
	Image Only	0.810(0.619-0.955)	0.654(0.440-0.828)	0.735(0.612-0.857)	0.723(0.571-0.851)	0.761(0.615-0.879)
	Report+Image	0.833(0.654-0.963)	0.769(0.600-0.926)	0.796(0.673-0.898)	0.800(0.645-0.902)	0.829(0.695-0.932)
	Contrastive Loss	0.833(0.680-0.963)	0.769(0.600-0.920)	0.796(0.673-0.898)	0.800(0.667-0.915)	0.844(0.728-0.947)
	Our's	0.686(0.528-0.833)	0.923(0.800-1.000)	0.735(0.592-0.857)	0.787(0.654-0.886)	0.863(0.738-0.953)

Table 3. Different metrics in the ablation study2

Dataset	Method	Precision	Recall	Accuracy	F1 score	AUC
Val	Early Fusion	0.825(0.750-0.893)	0.623(0.543-0.701)	0.759(0.708-0.803)	0.709(0.642-0.767)	0.814(0.768-0.860)
	Late Fusion	0.867(0.791-0.930)	0.517(0.434-0.595)	0.734(0.687-0.781)	0.647(0.575-0.713)	0.812(0.765-0.856)
	Our's	0.670(0.607-0.736)	0.861(0.800-0.918)	0.734(0.683-0.784)	0.754(0.703-0.801)	0.827(0.782-0.871)
Test1	Early Fusion	0.783(0.731-0.834)	0.599(0.537-0.654)	0.703(0.665-0.740)	0.678(0.630-0.718)	0.798(0.763-0.833)
	Late Fusion	0.796(0.736-0.851)	0.498(0.444-0.557)	0.671(0.633-0.711)	0.613(0.560-0.665)	0.791(0.754-0.829)
	Our's	0.824(0.771-0.873)	0.567(0.510-0.625)	0.711(0.676-0.749)	0.672(0.622-0.715)	0.806(0.769-0.840)
Test2	Early Fusion	0.746(0.669-0.819)	0.758(0.684-0.832)	0.717(0.659-0.770)	0.752(0.690-0.809)	0.749(0.682-0.812)
	Late Fusion	0.714(0.639-0.787)	0.742(0.669-0.820)	0.686(0.624-0.743)	0.728(0.669-0.782)	0.759(0.697-0.817)
	Our's	0.626(0.561-0.698)	0.891(0.836-0.938)	0.637(0.571-0.699)	0.735(0.680-0.792)	0.768(0.706-0.829)
Test3	Early Fusion	0.726(0.634-0.823)	0.552(0.464-0.642)	0.683(0.625-0.738)	0.627(0.552-0.688)	0.762(0.699-0.818)
	Late Fusion	0.692(0.615-0.773)	0.720(0.641-0.792)	0.710(0.652-0.764)	0.706(0.632-0.766)	0.784(0.727-0.835)
	Our's	0.699(0.624-0.776)	0.744(0.669-0.817)	0.722(0.664-0.780)	0.721(0.654-0.779)	0.793(0.739-0.848)
Test4	Early Fusion	0.697(0.531-0.848)	0.885(0.731-1.000)	0.735(0.612-0.857)	0.780(0.656-0.886)	0.843(0.733-0.939)
	Late Fusion	0.692(0.500-0.846)	0.692(0.519-0.870)	0.673(0.551-0.796)	0.692(0.537-0.820)	0.789(0.642-0.916)
	Our's	0.686(0.528-0.833)	0.923(0.800-1.000)	0.735(0.592-0.857)	0.787(0.654-0.886)	0.863(0.738-0.953)

Table 4. MRI acquisitions. T1CA = Axial T1 contrast-enhanced; T1CS = Sagittal T1 contrast-enhanced; T2A = Axial T2-weighted; T2S = Sagittal T2-weighted.

Center	Sequence	Repetition time	Echo time	Slice thickness	Acquisition matrix
Center 1	T1CA	3.8 ms	1.8 ms	5 mm	288×244
	T1CS	3.9 ms	1.8 ms	4 mm	288×244
	T2A	5900.0 ms	110.0 ms	6 mm	320×250
	T2S	3350.0 ms	130.0 ms	6 mm	300×225
Center 2	T1CA	3.5 ms	1.2 ms	4 mm	320×142
	T1CS	3.5 ms	1.2 ms	4 mm	320×150
	T2A	4000.0 ms	82.0 ms	5 mm	320×256
	T2S	3800.0 ms	105.0 ms	5 mm	384×307
Center 3	T1CA	470.0 ms	10.0 ms	4 mm	320×256
	T1CS	450.0 ms	10.0 ms	4 mm	348×272
	T2A	3500.0 ms	129.0 ms	5 mm	384×269
	T2S	3550.0 ms	80.0 ms	6 mm	288×224
Center 4	T1CA	1.4 ms	4.5 ms	4 mm	320×234
	T1CS	4.0 ms	1.5 ms	3 mm	320×320
	T2A	1000.0 ms	95.0 ms	5 mm	320×203
	T2S	3270.0 ms	95.0 ms	5 mm	384×187
Center 5	T1CA	3.5 ms	1.6 ms	5 mm	256×192
	T1CS	6.4 ms	3.2 ms	5 mm	256×192
	T2A	5900.0 ms	125.0 ms	6 mm	320×250
	T2S	6000.0 ms	130.0 ms	6 mm	320×256
Center 6	T1CA	4.9 ms	1.8 ms	5 mm	379×345
	T1CS	4.5 ms	1.8 ms	5 mm	300×272
	T2A	4925.0 ms	80.0 ms	5 mm	320×300
	T2S	3140.0 ms	85.0 ms	4 mm	284×265

Table 5. Patient characteristics in the training and validation cohorts

Variables	Training cohort			Validation cohort		
	Low-risk(n=665)	Non-low-risk(n=591)	P	Low-risk(n=168)	Non-low-risk(n=151)	P
Age (mean[SD])	51.35±8.81	55.04±9.16	<0.001	51.91±9.38	54.34±9.25	0.006
BMI(mean[SD])	24.95±3.57	24.93±3.54	0.663	25.36±3.76	24.57±3.53	0.038
Menopausal status, n(%)			<0.001			<0.001
Premenopausal	342(51.43)	192(32.49)		89(53.29)	51(33.77)	
Postmenopausal	323(48.57)	399(67.51)		78(46.71)	100(66.23)	
Reproductive history, n(%)			0.354			1.000
Nulliparous	54(8.14)	39(6.61)		13(7.74)	12(7.95)	
Parous	609(91.86)	551(93.39)		155(92.26)	139(92.05)	
FIGO Stage, n(%)			<0.001			<0.001
IA	665(100.00)	2(0.34)		168(100.00)	0(0.00)	
IB	0(0.00)	103(17.43)		0(0.00)	22(14.57)	
IC	0(0.00)	20(3.38)		0(0.00)	6(3.97)	
IIA	0(0.00)	40(6.77)		0(0.00)	7(4.64)	
IIB	0(0.00)	59(9.98)		0(0.00)	14(9.27)	
IIC	0(0.00)	197(33.33)		0(0.00)	51(33.77)	
IIIA	0(0.00)	42(7.11)		0(0.00)	13(8.61)	
IIIB	0(0.00)	17(2.88)		0(0.00)	7(4.64)	
IIIC	0(0.00)	94(15.91)		0(0.00)	29(19.21)	
IVA	0(0.00)	5(0.85)		0(0.00)	1(0.66)	
IVB	0(0.00)	8(1.35)		0(0.00)	1(0.66)	
IVC	0(0.00)	4(0.68)		0(0.00)	0(0.00)	
Lymph node metastasis, n(%)			<0.001			<0.001
No	659(99.10)	487(82.40)		168(100.00)	119(78.81)	
Yes	6(0.90)	104(17.60)		0(0.00)	32(21.19)	
Differentiation status, n(%)			<0.001			<0.001
Well	330(49.62)	74(12.52)		75(44.64)	16(10.60)	
Moderate	329(49.47)	292(49.41)		92(54.76)	70(46.36)	
Poor	5(0.75)	225(38.07)		1(0.60)	65(43.05)	
Carcinoma in situ	1(0.15)	0(0.00)		0(0.00)	0(0.00)	
Depth of myometrial invasion, n(%)			<0.001			<0.001
No invasion	219(32.93)	43(7.28)		40(23.81)	10(6.62)	
Invasion<1/2	443(66.62)	235(39.76)		127(75.60)	55(36.42)	
Invasion≥1/2	3(0.45)	283(47.88)		1(0.60)	72(47.68)	
Full invasion	0(0.00)	30(5.08)		0(0.00)	14(9.27)	
Cervical invasion, n(%)			<0.001			<0.001
No	658(98.95)	489(82.74)		167(99.40)	127(84.11)	
Yes	7(1.05)	102(17.26)		1(0.60)	24(15.89)	
Ovarian invasion, n(%)			<0.001			0.283
No	656(98.65)	563(95.26)		164(97.62)	143(94.70)	
Yes	9(1.35)	28(4.74)		4(2.38)	8(5.30)	
Fallopian tube invasion, n(%)			<0.001			<0.001
No	662(99.55)	556(94.08)		168(100.00)	139(92.05)	
Yes	3(0.45)	35(5.92)		0(0.00)	12(7.95)	
Parametrial involvement, n(%)			<0.001			0.015
No	664(99.85)	569(96.28)		168(100.00)	144(95.36)	
Yes	1(0.15)	22(3.72)		0(0.00)	7(4.64)	
Lymphovascular space invasion, n(%)			<0.001			<0.001
No	660(99.25)	396(67.01)		167(99.40)	102(67.55)	
Yes	5(0.75)	195(32.99)		1(0.60)	49(32.45)	
P53, n(%)			0.439			0.279
Negative	15(5.51)	24(7.43)		9(11.84)	6(6.06)	
Positive	257(94.49)	299(92.57)		67(88.16)	93(93.94)	
ER, n(%)			<0.001			<0.001
Negative	4(0.99)	55(12.42)		1(1.02)	17(15.18)	
Positive	400(99.01)	388(87.58)		97(98.98)	95(84.82)	
Ki67, n(%)			<0.001			<0.001
Weakly positive	184(63.89)	119(36.39)		51(67.11)	28(29.17)	
Strongly positive	104(36.11)	208(63.61)		25(32.89)	68(70.83)	

Table 6. Patient characteristics in the external validation cohorts (Test1 and Test2).

Variables	Test1 cohort			Test2 cohort		
	Low-risk(n=264)	Non-low-risk(n=289)	P	Low-risk(n=98)	Non-low-risk(n=128)	P
Age (mean[SD])	51.54±8.38	54.62±8.75	<0.001	54.29±7.63	55.91±7.95	0.124
BMI(mean[SD])	25.20±4.46	24.20±3.59	0.014	24.55±3.35	24.98±3.41	0.477
Menopausal status, n(%)			<0.001			0.514
Premenopausal	145(54.92)	103(35.64)		30(30.61)	33(25.78)	
Postmenopausal	119(45.08)	186(64.36)		68(69.39)	95(74.22)	
Reproductive history, n(%)			0.763			0.782
Nulliparous	21(7.95)	20(6.92)		3(3.06)	6(4.69)	
Parous	243(92.05)	269(93.08)		95(96.94)	122(95.31)	
FIGO Stage, n(%)			<0.001			<0.001
IA	263(99.62)	0(0.00)		98(100.00)	0(0.00)	
IB	1(0.38)	87(30.10)		0(0.00)	28(21.88)	
IC	0(0.00)	3(1.04)		0(0.00)	2(1.56)	
IIA	0(0.00)	11(3.81)		0(0.00)	7(5.47)	
IIB	0(0.00)	34(11.76)		0(0.00)	15(11.72)	
IIC	0(0.00)	78(26.99)		0(0.00)	31(24.22)	
IIIA	0(0.00)	23(7.96)		0(0.00)	4(3.12)	
IIIB	0(0.00)	6(2.08)		0(0.00)	4(3.12)	
IIIC	0(0.00)	41(14.19)		0(0.00)	35(27.34)	
IVA	0(0.00)	0(0.00)		0(0.00)	0(0.00)	
IVB	0(0.00)	4(1.38)		0(0.00)	1(0.78)	
IVC	0(0.00)	2(0.69)		0(0.00)	1(0.78)	
Lymph node metastasis, n(%)			0.002			<0.001
No	130(49.24)	182(62.98)		98(100.00)	94(73.44)	
Yes	134(50.76)	107(37.02)		0(0.00)	34(26.56)	
Differentiation status, n(%)			<0.001			<0.001
Well	153(57.95)	55(19.03)		3(3.06)	28(21.88)	
Moderate	93(35.23)	144(49.83)		27(27.55)	46(35.94)	
Poor	5(1.89)	82(28.37)		68(69.39)	54(42.19)	
Carcinoma in situ	13(4.92)	8(2.77)		0(0.00)	0(0.00)	
Depth of myometrial invasion, n(%)			<0.001			<0.001
No invasion	93(35.23)	7(2.42)		10(10.20)	4(3.12)	
Invasion<1/2	171(64.77)	263(91.00)		88(89.80)	59(46.09)	
Invasion≥1/2	0(0.00)	18(6.23)		0(0.00)	60(46.88)	
Full invasion	0(0.00)	1(0.35)		0(0.00)	5(3.91)	
Cervical invasion, n(%)			<0.001			<0.001
No	260(98.48)	260(89.97)		93(94.90)	99(77.34)	
Yes	4(1.52)	29(10.03)		5(5.10)	29(22.66)	
Ovarian invasion, n(%)			0.005			0.031
No	263(99.62)	276(95.50)		98(100.00)	120(93.75)	
Yes	1(0.38)	13(4.50)		0(0.00)	8(6.25)	
Fallopian tube invasion, n(%)			<0.001			0.041
No	262(99.24)	264(91.35)		97(98.98)	118(92.19)	
Yes	2(0.76)	25(8.65)		1(1.02)	10(7.81)	
Parametrial involvement, n(%)			0.005			0.209
No	263(99.62)	276(95.50)		98(100.00)	124(96.88)	
Yes	1(0.38)	13(4.50)		0(0.00)	4(3.12)	
Lymphovascular space invasion, n(%)			<0.001			<0.001
No	253(95.83)	161(55.71)		94(95.92)	74(57.81)	
Yes	11(4.17)	128(44.29)		4(4.08)	54(42.19)	
P53, n(%)			0.362			0.111
Negative	3(1.69)	9(3.66)		5(6.76)	16(15.84)	
Positive	175(98.31)	237(96.34)		69(93.24)	85(84.16)	
ER, n(%)			0.009			0.003
Negative	1(0.45)	13(4.73)		7(9.21)	30(28.04)	
Positive	222(99.55)	262(95.27)		69(90.79)	77(71.96)	
Ki67, n(%)			<0.001			0.004
Weakly positive	156(70.91)	117(44.15)		42(76.36)	41(50.00)	
Strongly positive	64(29.09)	148(55.85)		13(23.64)	41(50.00)	

Table 7. Patient characteristics in the external validation cohorts (Test3 and Test4).

Variables	Test3 cohort			Test4 cohort		
	Low-risk(n=134)	Non-low-risk(n=125)	1.000	Low-risk(n=23)	Non-low-risk(n=26)	P
Age (mean[SD])	54.68±9.13	55.03±9.27	0.95	54.04±10.36	57.50±9.40	0.236
BMI(mean[SD])	25.67±4.15	24.67±3.84	0.082	27.35±3.96	26.31±4.04	0.383
Menopausal status, n(%)			0.172			0.546
Premenopausal	52(38.81)	60(48.00)		9(39.13)	7(26.92)	
Postmenopausal	82(61.19)	65(52.00)		14(60.87)	19(73.08)	
Reproductive history, n(%)			0.664			0.693
Nulliparous	15(11.19)	11(8.80)		1(4.35)	3(11.54)	
Parous	119(88.81)	114(91.20)		22(95.65)	23(88.46)	
FIGO Stage, n(%)			<0.001			<0.001
IA	132(98.51)	2(1.60)		23(100.00)	0(0.00)	
IB	1(0.75)	39(31.20)		0(0.00)	8(30.77)	
IC	0(0.00)	1(0.80)		0(0.00)	1(3.85)	
IIA	1(0.75)	13(10.40)		0(0.00)	1(3.85)	
IIB	0(0.00)	8(6.40)		0(0.00)	2(7.69)	
IIC	0(0.00)	24(19.20)		0(0.00)	6(23.08)	
IIIA	0(0.00)	11(8.80)		0(0.00)	2(7.69)	
IIIB	0(0.00)	7(5.60)		0(0.00)	1(3.85)	
IIIC	0(0.00)	19(15.20)		0(0.00)	5(19.23)	
IVA	0(0.00)	1(0.80)		0(0.00)	0(0.00)	
IVB	0(0.00)	0(0.00)		0(0.00)	0(0.00)	
IVC	0(0.00)	0(0.00)		0(0.00)	0(0.00)	
Lymph node metastasis, n(%)			<0.001			0.023
No	133(99.25)	106(84.80)		23(100.00)	19(73.08)	
Yes	1(0.75)	19(15.20)		0(0.00)	7(26.92)	
Differentiation status, n(%)			<0.001			0.007
Well	77(57.46)	42(33.60)		6(26.09)	2(7.69)	
Moderate	56(41.79)	55(44.00)		17(73.91)	16(61.54)	
Poor	1(0.75)	28(22.40)		0(0.00)	8(30.77)	
Carcinoma in situ	0(0.00)	0(0.00)		0(0.00)	0(0.00)	
Depth of myometrial invasion, n(%)			<0.001			0.386
No invasion	24(17.91)	3(2.40)		3(13.04)	1(3.85)	
Invasion<1/2	107(79.85)	44(35.20)		20(86.96)	23(88.46)	
Invasion≥1/2	3(2.24)	72(57.60)		0(0.00)	1(3.85)	
Full invasion	0(0.00)	6(4.80)		0(0.00)	1(3.85)	
Cervical invasion, n(%)			<0.001			1.000
No	134(100.00)	112(89.60)		17(73.91)	19(73.08)	
Yes	0(0.00)	13(10.40)		6(26.09)	7(26.92)	
Ovarian invasion, n(%)			0.113			0.913
No	134(100.00)	121(96.80)		21(91.30)	25(96.15)	
Yes	0(0.00)	4(3.20)		2(8.70)	1(3.85)	
Fallopian tube invasion, n(%)			0.221			0.951
No	134(100.00)	122(97.60)		22(95.65)	26(100.00)	
Yes	0(0.00)	3(2.40)		1(4.35)	0(0.00)	
Parametrial involvement, n(%)			0.447			1.000
No	134(100.00)	123(98.40)		22(95.65)	25(96.15)	
Yes	0(0.00)	2(1.60)		1(4.35)	1(3.85)	
Lymphovascular space invasion, n(%)			<0.001			0.451
No	134(100.00)	108(86.40)		19(82.61)	18(69.23)	
Yes	0(0.00)	17(13.60)		4(17.39)	8(30.77)	
P53, n(%)			0.056			0.848
Negative	6(25.00)	2(5.13)		2(9.52)	1(3.85)	
Positive	18(75.00)	37(94.87)		19(90.48)	25(96.15)	
ER, n(%)			0.006			0.280
Negative	2(8.00)	18(42.86)		0(0.00)	3(12.00)	
Positive	23(92.00)	24(57.14)		22(100.00)	22(88.00)	
Ki67, n(%)			0.043			0.519
Weakly positive	15(65.22)	15(35.71)		9(42.86)	7(29.17)	
Strongly positive	8(34.78)	27(64.29)		12(57.14)	17(70.83)	