

Supplementary Table 1. All patients' baseline information						
Variable	Internal training	Temporal validation	External validation	Statistic	P value	
Occult high-volume CLNM: Negative	257 (54.7%)	110 (54.5%)	78 (54.9%)	0.008	0.996	
Occult high-volume CLNM: Positive	213 (45.3%)	92 (45.5%)	64 (45.1%)			
Age (years)	47.00 (37.00, 55.00)	47.00 (38.25, 56.00)	48.00 (37.25, 55.00)	1.092	0.579	
Sex: Female	336 (71.5%)	136 (67.3%)	111 (78.2%)	4.832	0.089	
Sex: Male	134 (28.5%)	66 (32.7%)	31 (21.8%)			
Hashimoto: No	465 (98.9%)	201 (99.5%)	141 (99.3%)	0.585	0.746	
Hashimoto: Yes	5 (1.1%)	1 (0.5%)	1 (0.7%)			
Hypertension: No	389 (82.8%)	162 (80.2%)	116 (81.7%)	0.637	0.727	
Hypertension: Yes	81 (17.2%)	40 (19.8%)	26 (18.3%)			
Hyperlipidemia: No	464 (98.7%)	201 (99.5%)	142 (100.0%)	2.504	0.286	
Hyperlipidemia: Yes	6 (1.3%)	1 (0.5%)	0 (0.0%)			
Diabetes: No	435 (92.6%)	195 (96.5%)	135 (95.1%)	4.320	0.115	
Diabetes: Yes	35 (7.4%)	7 (3.5%)	7 (4.9%)			
Coronary disease: No	470 (100.0%)	202 (100.0%)	141 (99.3%)	4.738	0.094	
Coronary disease: Yes	0 (0.0%)	0 (0.0%)	1 (0.7%)			
Other comorbidity: No	469 (99.8%)	202 (100.0%)	142 (100.0%)	0.733	0.693	
Other comorbidity: Yes	1 (0.2%)	0 (0.0%)	0 (0.0%)			
Prior neck surgery: No	470 (100.0%)	202 (100.0%)	142 (100.0%)			
Prior radiotherapy: No	470 (100.0%)	202 (100.0%)	142 (100.0%)			
Prior RFA: No	470 (100.0%)	202 (100.0%)	142 (100.0%)			
WBC (×10 ⁹ /L)	5.80 (5.10, 6.90)	6.00 (5.03, 7.00)	5.90 (5.00, 7.17)	0.123	0.940	
Neutrophils (×10 ⁹ /L)	3.30 (2.80, 4.10)	3.25 (2.20, 4.20)	3.35 (2.60, 4.35)	0.235	0.889	
Lymphocytes (×10 ⁹ /L)	2.00 (1.60, 2.30)	2.10 (1.70, 2.50)	2.10 (1.60, 2.30)	3.087	0.214	
Monocytes (×10 ⁹ /L)	0.32 (0.27, 0.39)	0.33 (0.26, 0.42)	0.33 (0.27, 0.42)	0.624	0.732	
RBC (×10 ¹² /L)	4.65 (4.35, 5.01)	4.66 (4.34, 5.02)	4.66 (4.36, 5.02)	0.022	0.989	
Hemoglobin (g/L)	137.00 (129.00, 148.00)	138.50 (130.00, 148.00)	135.50 (127.00, 148.00)	0.669	0.716	
CEA (ng/mL)	1.50 (1.03, 2.15)	1.54 (1.04, 2.12)	1.44 (1.02, 2.00)	0.570	0.752	
Tg (ng/mL)	19.18 (7.33, 38.04)	20.62 (8.48, 44.32)	18.70 (7.60, 40.18)	0.630	0.730	
Calcitonin (pg/mL)	2.00 (2.00, 3.30)	2.00 (2.00, 2.60)	2.00 (1.78, 2.89)	0.688	0.709	
Total cholesterol (mmol/L)	4.81 (4.25, 5.67)	4.84 (4.22, 5.58)	4.97 (4.28, 5.67)	0.429	0.807	
Triglycerides (mmol/L)	1.19 (0.86, 1.71)	1.19 (0.89, 1.83)	1.20 (0.91, 1.71)	0.491	0.782	
LDL-C (mmol/L)	3.12 (2.56, 3.82)	3.15 (2.60, 3.75)	3.29 (2.62, 3.88)	1.140	0.566	
HDL-C (mmol/L)	1.35 (1.12, 1.62)	1.33 (1.10, 1.60)	1.31 (1.09, 1.60)	0.441	0.802	
FFG (mmol/L)	5.30 (4.99, 5.73)	5.27 (4.96, 5.73)	5.32 (4.97, 5.71)	0.185	0.911	
TSH (mIU/L)	1.93 (1.31, 2.67)	1.91 (1.17, 2.69)	1.92 (1.26, 2.54)	0.468	0.791	
FT4 (pmol/L)	16.34 (15.00, 17.66)	16.34 (15.09, 17.86)	16.19 (14.84, 17.70)	0.530	0.767	
FT3 (pmol/L)	5.10 (4.78, 5.45)	5.12 (4.78, 5.44)	5.03 (4.71, 5.53)	0.135	0.935	
TgAb (IU/mL)	10.00 (10.00, 40.47)	10.00 (10.00, 30.08)	12.32 (10.00, 29.76)	0.399	0.819	
TPOAb (IU/mL)	2.92 (2.00, 17.92)	2.92 (2.00, 23.70)	4.04 (2.00, 16.31)	0.172	0.918	
ALT (U/L)	17.00 (12.00, 24.00)	17.00 (12.00, 26.75)	16.00 (12.00, 23.00)	0.982	0.612	
AST (U/L)	18.00 (15.00, 22.00)	18.00 (15.00, 22.00)	17.00 (15.00, 21.00)	1.177	0.555	
GGT (U/L)	19.00 (14.00, 30.00)	21.00 (14.00, 34.00)	19.00 (13.00, 29.00)	1.779	0.411	
ALP (U/L)	69.00 (57.00, 82.00)	70.00 (56.25, 83.75)	71.00 (58.25, 85.07)	1.246	0.536	
TbIL (μmol/L)	9.60 (7.30, 12.52)	9.20 (6.50, 12.50)	9.35 (7.33, 12.81)	1.477	0.478	
Albumin (g/L)	46.00 (44.00, 48.00)	46.00 (44.00, 47.75)	46.00 (45.00, 48.00)	2.012	0.366	
BUN (mmol/L)	4.79 (4.00, 5.70)	4.90 (4.21, 5.90)	4.60 (4.00, 5.70)	4.455	0.108	
Creatinine (μmol/L)	60.50 (53.00, 69.00)	59.00 (53.00, 71.75)	59.00 (53.00, 70.00)	0.439	0.803	
Uric acid (μmol/L)	318.00 (262.50, 383.00)	315.00 (265.50, 372.75)	301.50 (256.00, 367.75)	2.078	0.354	
Vertical location: Upper	78 (16.6%)	28 (13.9%)	31 (21.8%)	6.560	0.363	
Vertical location: Middle	227 (48.3%)	100 (49.5%)	72 (50.7%)			
Vertical location: Lower	111 (23.6%)	50 (24.8%)	23 (16.2%)			
Vertical location: Isthmus	54 (11.5%)	24 (11.9%)	16 (11.3%)			
Horizontal location: Left lobe	201 (42.8%)	89 (44.1%)	65 (45.8%)	5.901	0.207	
Horizontal location: Isthmus	17 (3.6%)	1 (0.5%)	3 (2.1%)			
Horizontal location: Right lobe	252 (53.6%)	112 (55.4%)	74 (52.1%)			
Boundary: Clear	150 (31.9%)	78 (38.6%)	49 (34.5%)	2.842	0.242	
Boundary: Unclear	320 (68.1%)	124 (61.4%)	93 (65.5%)			
Contour: Smooth	25 (5.3%)	18 (8.9%)	13 (9.2%)	7.354	0.118	
Contour: Ill-defined	88 (18.7%)	31 (15.3%)	17 (12.0%)			
Contour: Irregular	357 (76.0%)	153 (75.7%)	112 (78.9%)			
Irregular margin: Jagged	276 (58.7%)	116 (57.4%)	81 (57.0%)	2.965	0.813	
Irregular margin: Angular	65 (13.8%)	24 (11.9%)	17 (12.0%)			
Irregular margin: Lobulated	69 (14.7%)	39 (19.3%)	25 (17.6%)			
Irregular margin: Spiculated	60 (12.8%)	23 (11.4%)	19 (13.4%)			
Halo sign: Absent	401 (85.3%)	160 (79.2%)	118 (83.1%)	3.826	0.148	
Halo sign: Present	69 (14.7%)	42 (20.8%)	24 (16.9%)			
Composition: Predominantly cystic	2 (0.4%)	3 (1.5%)	2 (1.4%)	5.758	0.218	
Composition: Predominantly solid	23 (4.9%)	17 (8.4%)	8 (5.6%)			
Composition: Solid	445 (94.7%)	182 (90.1%)	132 (93.0%)			
Echogenicity: Anechoic	1 (0.2%)	3 (1.5%)	2 (1.4%)	12.566	0.128	
Echogenicity: Hyperechoic	2 (0.4%)	2 (1.0%)	0 (0.0%)			
Echogenicity: Isoechoic	42 (9.0%)	4 (2.0%)	0 (0.0%)			
Echogenicity: Hypoechoic	442 (94.0%)	186 (92.1%)	133 (93.7%)			
Echogenicity: Very hypoechoic	23 (4.9%)	7 (3.5%)	7 (4.9%)			
Aspect ratio A/T: <1	187 (39.8%)	103 (51.0%)	55 (38.7%)	8.200	0.017	
Aspect ratio A/T: ≥1	283 (60.2%)	99 (49.0%)	87 (61.3%)			
Hyperechoic foci: Microcalcifications	102 (21.7%)	50 (24.8%)	44 (31.0%)	14.271	0.075	
Hyperechoic foci: Punctate echogenic foci of uncertain significance	171 (36.4%)	76 (37.6%)	44 (31.0%)			
Hyperechoic foci: Macrocalcifications	32 (6.8%)	18 (8.9%)	10 (7.0%)			
Hyperechoic foci: Peripheral calcifications	8 (1.7%)	8 (4.0%)	6 (4.2%)			
Hyperechoic foci: No hyperechoic foci	157 (33.4%)	50 (24.8%)	38 (26.8%)			
Posterior echo: Enhancement	1 (0.2%)	1 (0.5%)	0 (0.0%)	1.452	0.835	
Posterior echo: Attenuation	34 (7.2%)	16 (7.9%)	13 (9.2%)			
Posterior echo: No change	435 (92.6%)	185 (91.6%)	129 (90.8%)			
Vascularity: No obvious vascularity	446 (94.9%)	187 (92.6%)	133 (93.7%)	1.430	0.489	
Vascularity: Rich vascularity	24 (5.1%)	15 (7.4%)	9 (6.3%)			
C-TIRADS 4 subclass: 4A (low suspicion)	59 (12.6%)	28 (13.9%)	18 (12.7%)	1.914	0.752	
C-TIRADS 4 subclass: 4B (intermediate suspicion)	113 (24.0%)	40 (19.8%)	36 (25.4%)			
C-TIRADS 4 subclass: 4C (high suspicion)	298 (63.4%)	134 (66.3%)	88 (62.0%)			
Diffuse thyroid disease: No	392 (83.4%)	172 (85.1%)	125 (88.0%)	1.846	0.397	
Diffuse thyroid disease: Yes	78 (16.6%)	30 (14.9%)	17 (12.0%)			
Multifocality: No	133 (28.4%)	144 (71.3%)	97 (68.3%)	0.367	0.833	
Multifocality: Yes	339 (71.6%)	58 (28.7%)	45 (31.7%)			
Tumor max diameter (cm)	0.70 (0.50, 1.20)	0.80 (0.50, 1.20)	0.70 (0.50, 1.00)	0.796	0.672	

CLNM, central lymph node metastasis; RFA, radiofrequency ablation; WBC, white blood cell count; RBC, red blood cell count; CEA, carcinoembryonic antigen; Tg, thyroglobulin; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; TSH, thyroid-stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; TbIL, total bilirubin; BUN, blood urea nitrogen; A/T, anteroposterior/transverse; C-TIRADS 4, Chinese Thyroid Imaging Reporting and Data System 4 subclass.

Supplementary Table 2. Surgical and pathological reference standard across cohorts						
Cohort	Patients, n	Central nodes examined, median (IQR)	Central nodes examined, range	Metastatic central nodes, median (IQR)	Metastatic central nodes, range	Positive central nodes > 5, n (%)
Development cohort	470	13 (8–17)	3–38	3 (0–9)	0–26	213 (45.3%)
Temporal validation cohort	202	12 (9–18)	4–30	3 (0–8)	0–24	92 (45.5%)
External validation cohort	142	11 (7–16)	3–36	3 (0–8)	0–22	64 (45.1%)
Overall	814	12 (7–16)	3–38	3 (0–8)	0–26	369 (45.3%)

IQR, interquartile range.

Hashimoto: Yes	3 (1.2%)	2 (0.9%)		
Hypertension: No	206 (80.2%)	183 (85.9%)	2.320	0.128
Hypertension: Yes	51 (19.8%)	30 (14.1%)		
Hyperlipidemia: No	254 (98.8%)	210 (98.6%)	0.000	1.000
Hyperlipidemia: Yes	3 (1.2%)	3 (1.4%)		
Diabetes: No	236 (91.8%)	199 (93.4%)	0.231	0.631
Diabetes: Yes	21 (8.2%)	14 (6.6%)		
Coronary disease: No	257 (100.0%)	213 (100.0%)		
Other comorbidity: No	256 (99.6%)	213 (100.0%)	0.000	1.000
Other comorbidity: Yes	1 (0.4%)	0 (0.0%)		
Prior neck surgery: No	257 (100.0%)	213 (100.0%)		
Prior radiotherapy: No	257 (100.0%)	213 (100.0%)		
Prior RFA: No	257 (100.0%)	213 (100.0%)		
WBC (×10 ⁹ /L)	5.80 (5.10, 6.80)	6.00 (5.00, 7.00)	26114.000	0.391
Neutrophils (×10 ⁹ /L)	3.30 (2.80, 4.00)	3.40 (2.90, 4.20)	26563.000	0.582
Lymphocytes (×10 ⁹ /L)	1.90 (1.60, 2.30)	2.00 (1.70, 2.40)	24643.500	0.062
Monocytes (×10 ⁹ /L)	0.32 (0.27, 0.40)	0.31 (0.26, 0.38)	28674.000	0.374
RBC (×10 ¹² /L)	4.61 (4.33, 4.97)	4.74 (4.40, 5.05)	23980.500	0.021
Hemoglobin (g/L)	137.00 (129.00, 147.00)	138.00 (130.00, 149.00)	25928.500	0.325
CEA (ng/mL)	1.52 (1.05, 2.14)	1.49 (1.03, 2.15)	27234.000	0.926
Tg (ng/mL)	18.41 (6.48, 34.10)	20.06 (9.38, 43.51)	25213.500	0.141
Calcitonin (pg/mL)	2.00 (2.00, 3.48)	2.00 (1.85, 3.11)	28967.000	0.267
Total cholesterol (mmol/L)	4.75 (4.18, 5.57)	4.94 (4.29, 5.81)	24665.500	0.065
Triglycerides (mmol/L)	1.18 (0.84, 1.71)	1.21 (0.90, 1.71)	26548.500	0.575
LDL-C (mmol/L)	3.11 (2.56, 3.69)	3.17 (2.62, 3.98)	25376.500	0.174
HDL-C (mmol/L)	1.34 (1.12, 1.57)	1.38 (1.12, 1.63)	26488.000	0.547
FFPG (mmol/L)	5.31 (5.00, 5.76)	5.30 (4.96, 5.68)	28857.500	0.311
TSH (mIU/L)	1.80 (1.19, 2.66)	2.01 (1.49, 2.67)	23975.500	0.021
FT4 (pmol/L)	16.24 (14.92, 17.66)	16.42 (15.09, 17.65)	26308.000	0.469
FT3 (pmol/L)	5.13 (4.81, 5.43)	5.10 (4.73, 5.46)	27679.000	0.834
TgAb (IU/mL)	10.00 (10.00, 49.79)	12.51 (10.00, 32.26)	27125.500	0.858
TPOAb (IU/mL)	2.46 (2.00, 17.26)	3.56 (2.00, 17.98)	26059.000	0.353
ALT (U/L)	17.00 (12.00, 22.00)	17.00 (13.00, 26.00)	25408.000	0.180
AST (U/L)	18.00 (15.00, 21.00)	18.00 (16.00, 22.00)	26206.500	0.426
GGT (U/L)	19.00 (14.00, 31.00)	19.00 (14.00, 29.00)	26883.000	0.739
ALP (U/L)	66.00 (55.80, 82.00)	71.00 (58.00, 82.00)	25894.000	0.314
TbIL (μmol/L)	9.70 (7.30, 12.52)	9.50 (7.30, 12.50)	27753.000	0.794
Albumin (g/L)	46.00 (44.00, 48.00)	46.00 (45.00, 48.00)	25193.000	0.135
BUN (mmol/L)	4.70 (3.90, 5.70)	4.80 (4.00, 5.70)	26834.000	0.715
Creatinine (μmol/L)	59.00 (52.00, 69.00)	61.00 (55.00, 70.00)	24186.500	0.030
Uric acid (μmol/L)	318.00 (256.00, 375.00)	318.00 (271.00, 390.00)	25567.500	0.219
Vertical location: Upper	47 (18.3%)	31 (14.6%)	3.510	0.319
Vertical location: Middle	129 (50.2%)	98 (46.0%)		
Vertical location: Lower	55 (21.4%)	56 (26.3%)		
Vertical location: Isthmus	26 (10.1%)	28 (13.1%)		
Horizontal location: Left lobe	120 (46.7%)	81 (38.0%)	4.029	0.133
Horizontal location: Isthmus	10 (3.9%)	7 (3.3%)		
Horizontal location: Right lobe	127 (49.4%)	125 (58.7%)		
Boundary: Clear	91 (35.4%)	59 (27.7%)	2.841	0.092
Boundary: Unclear	166 (64.6%)	154 (72.3%)		
Contour: Smooth	13 (5.1%)	12 (5.6%)	0.880	0.644
Contour: Ill-defined	52 (20.2%)	36 (16.9%)		
Contour: Irregular	192 (74.7%)	165 (77.5%)		
Irregular margin: Jagged	153 (59.5%)	123 (57.7%)	2.598	0.458
Irregular margin: Angular	30 (11.7%)	35 (16.4%)		
Irregular margin: Lobulated	41 (16.0%)	28 (13.1%)		
Irregular margin: Spiculated	33 (12.8%)	27 (12.7%)		
Halo sign: Absent	227 (88.3%)	174 (81.7%)	3.583	0.058
Halo sign: Present	30 (11.7%)	39 (18.3%)		
Composition: Predominantly cystic	0 (0.0%)	2 (0.9%)	6.380	0.041
Composition: Predominantly solid	8 (3.1%)	15 (7.0%)		
Composition: Solid	249 (96.9%)	196 (92.0%)		
Echogenicity: Anechoic	0 (0.0%)	1 (0.5%)	3.263	0.515
Echogenicity: Hyperechoic	2 (0.8%)	0 (0.0%)		
Echogenicity: Isoechoic	1 (0.4%)	1 (0.5%)		
Echogenicity: Hypoechoic	240 (93.4%)	202 (94.8%)		
Echogenicity: Very hypoechoic	14 (5.4%)	9 (4.2%)		
Aspect ratio A/T: <1	90 (35.0%)	97 (45.5%)	4.951	0.026
Aspect ratio A/T: ≥1	167 (65.0%)	116 (54.5%)		
Hyperchoic foci: Microcalcifications	41 (16.0%)	61 (28.6%)	22.348	< 0.001
Hyperchoic foci: Punctate echogenic foci of uncertain significance	87 (33.9%)	84 (39.4%)		
Hyperchoic foci: Macrocalcifications	17 (6.6%)	15 (7.0%)		
Hyperchoic foci: Peripheral calcifications	4 (1.6%)	4 (1.9%)		
Hyperchoic foci: No hyperchoic foci	108 (42.0%)	49 (23.0%)		
Posterior echo: Enhancement	0 (0.0%)	1 (0.5%)	1.550	0.461
Posterior echo: Attenuation	17 (6.6%)	17 (8.0%)		
Posterior echo: No change	240 (93.4%)	195 (91.5%)		
Vascularity: No obvious vascularity	252 (98.1%)	194 (91.1%)	10.298	0.001
Vascularity: Rich vascularity	5 (1.9%)	19 (8.9%)		
C-TIRADS 4 subclass: 4A (low suspicion)	41 (16.0%)	18 (8.5%)	12.615	0.002
C-TIRADS 4 subclass: 4B (intermediate suspicion)	71 (27.6%)	42 (19.7%)		
C-TIRADS 4 subclass: 4C (high suspicion)	145 (56.4%)	153 (71.8%)		
Diffuse thyroid disease: No	217 (84.4%)	175 (82.2%)	0.287	0.592
Diffuse thyroid disease: Yes	40 (15.6%)	38 (17.8%)		
Multifocality: No	192 (74.7%)	139 (65.3%)	4.550	0.033
Multifocality: Yes	65 (25.3%)	74 (34.7%)		
Tumor max diameter (cm)	0.60 (0.40, 1.00)	0.80 (0.60, 1.30)	18825.000	< 0.001

RFA, radiofrequency ablation; WBC, white blood cell count; BCL, red blood cell count; CEA, carcinoembryonic antigen; Tg, thyroglobulin; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; TSH, thyroid-stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; TBIL, total bilirubin; BUN, blood urea nitrogen; A/T, anteroposterior/transverse; C-TIRADS 4, Chinese Thyroid Imaging Reporting and Data System 4 subclass.

Supplementary Table 4. Association between margin contour and C-TIRADS 4 subclass			
Dataset	Cramér's V	P value	
Development cohort	0.28	< 0.001	