

Supplementary files:

2.1. Patients

Through a search of our institutional database for medical records and pathological results from January 2013 to June 2016, data for all patients with histologically confirmed adrenal adenoma or pheochromocytoma who underwent surgical resection were collected. All patients had detailed medical records and pathological results and none of them received tumor-related therapy before undergoing CT scanning.

Inclusion criterion was AI identified during an imaging examination performed for reasons other than the evaluation of adrenal glands. The exclusion criteria were (1) no preoperational CT images available; (2) existing unenhanced CT scan displaying a fat-rich adenoma for patients with adrenal adenoma, (3) adrenal lesion showing enhancement of greater than 100 HU on a CT scan for patients with pheochromocytoma; (4) no enhancement found in the lesion for patients with adrenal adenoma; and (5) CT performed on other machines other than 320-MDCT scanner (Aquilion ONE, Toshiba, Otawara, Japan).

2.4. Texture analysis analysis

QTA features extraction was performed by using texture analysis software (MaZda Version 4.6, Institute of Electronics, Technical University of Lodz, Poland) [17]. For each patient, fellowship-trained radiologist selected the representative axial image on which the lesion has the largest cross-sectional area from the preoperative CT images. These images were transferred from PACS to a personal computer and were

anonymized using DicomWorks software (version 1.3.5). Each image was input into the texture analysis software (MaZda Version 4.6, Institute of Electronics, Technical University of Lodz, Poland) [17], and the tumor was manually contoured by the radiologist and saved as a region of interest (ROI) file for subsequent texture analysis (Supplementary figure 1). Contouring was performed carefully to cover the maximum extent of the tumor without exceeding the lesion border to avoid contamination from adjacent normal adrenal tissues or fat. During contouring on the unenhanced CT images, the corresponding contrast-enhanced CT images were used as references in cases where the margin of the adrenal lesion was difficult to define on unenhanced images.

Prior to the texture analysis, CT image were normalized between $\mu \pm 3\sigma$, where μ was the mean value of gray levels inside the ROI and σ was the standard deviation (SD) of the gray levels inside the ROI. This normalization procedure is able to minimize interscanner effects in MR imaging texture analyses and is thought to also reduce interscanner variation in other imaging modalities, such as CT [18]. For each ROI file, MaZda software can automatically generate 377 parameters, including a gray level histogram, gradient, run-length matrix, co-occurrence matrix, autoregressive model and wavelet transform analysis.

Intraobserver (reader 1 twice) and interobserver (reader 1 v reader 2) reproducibility evaluation, could be find in the Supplement files.

Following the calculation of Texture analysis features, feature selection was performed. Given that this analysis produced many features, only a subset was

selected for further analysis to minimize the likelihood of over-fitting. The 30 features with the highest discriminative abilities for classification were selected automatically based on the combination of three methods: Fisher coefficient (Fisher), mutual information measure (MI), and classification of error probability (POE) combined with average correlation coefficients (ACCs). Feature analysis was carried out using the B11 (version 3.3) application of MaZda. A linear discriminant analysis (LDA) was run for the features selected. As a supervised feature transformation method, LDA is able to produce new feature vectors, which are also referred to as most discriminating factors (MDFs). MDFs are optimized for both maximum between-class scatter and minimum within-class scatter [19]. LDA classification results were represented graphically as the relationships between the MDFs. The number of MDF axes is one less than the number of output classes.

Wilcoxon rank sum tests and ROC curves analyses were performed to compare the differences in the 30 selected features between sPHEO and lipid-poor adenoma. Each feature was considered to be positive or negative based on its value. We used the number of positive features to predict the accuracy of differentiation.

Supplementary table S1 Scanning parameters for the CT scans

Modality	Toshiba 320-MDCT
Tube current	160 mAs
Tube voltage	120 kV
Rotation time	0.5 s
Detector collimation	64 × 0.625 mm
Field of view	350 × 350 mm
Reconstruction matrix	512 × 512

Supplementary table S2 Difference analysis of 30 features between LPA and sPHEO (medians and interquartile ranges, Wilcoxon rank sum test)

Features	LPA	sPHEO	Z	P value
Horzl_RLNon	536.43(308.25-	2773.61(2096.66-		
Uni	932.64)	4543.79)	6.118	<0.001
GeoW6	0.03(0.02-0.04)	0.01(0.01-0.02)	6.062	<0.001
GeoEI	3.86(2.6-5.14)	9.35(8.31-12.87)	6.048	<0.001
GeoM2x	41.93(28.97-78.68)	266.83(206.81-414.61)	6.083	<0.001
GeoRb	24.18(17.93-31.09)	55.38(49.15-75.04)	6.048	<0.001
GeoRc1	27.96(21.44-37.46)	64.12(56.96-85.74)	6.055	<0.001
GeoSpol	27.96(21.44-37.46)	64.12(56.96-85.74)	6.055	<0.001

135dr_RLNon Uni	555.5(316.78-996.05)	2897.03(2226.85- 5075.97)	6.076 <0.001
45dgr_RLNon Uni	549.68(319.65- 1016.08)	2899.6(2233.86-4796.73)	6.027 <0.001
Vertl_RLNonU ni	538.13(305.08- 971.42)	2849.92(2189.71- 4972.07)	6.069 <0.001
GeoW13	0.05(0.04-0.08)	0.02(0.02-0.03)	6.007 <0.001
S(5,5)SumAve rg	64.16(63.08-65.59)	63.55(63.2-64.16)	2.021 0.043
S(5,-5)Entropy GeoEI2	2.7(2.49-2.89) 23.37(11.09-41.54)	3.04(2.97-3.11) 134.3(105.9-251.81)	6.083 <0.001 6.041 <0.001
Vertl_GLevNo nU	12.4(7.58-23.01)	92.6(53.7-142.29)	6.041 <0.001
Horzl_GLevNo nU	11.96(7.58-23.19)	90.04(53.14-140.92)	6.034 <0.001
135dr_GLevN onU	12.42(7.76-24.03)	94.05(54.4-144.29)	6.027 <0.001
WavEnHL_s-3	418.34(282.8-608.43)	182.07(124.05-257.21)	6.138 <0.001
S(0,5)SumAve rg	64.39(63.35-65.23)	63.75(63.29-64.09)	2.263 0.024
S(5,-5)Correlat	0.06(-0.08-0.15)	0.12(0.07-0.22)	2.603 0.009

GeoMaver	13.82(10.64-18.3)	31.87(28.28-42.41)	6.055 <0.001
GeoD1	11.34(8.02-15.53)	26.71(23.66-37.42)	6.000 <0.001
GeoEr	9.57(7.59-12.62)	21.69(19.35-28.79)	6.041 <0.001
GeoFmin	24(17.4-33)	55(50.55-80.13)	6.028 <0.001
GeoS	25.28(19.22-33.59)	56.57(51.49-81)	5.875 <0.001
GeoUg	240.35(179.17-316.31)	557.13(485.1-744.75)	6.041 <0.001
GeoRc2	76.51(57.03-100.69)	177.34(154.41-237.06)	6.041 <0.001
GeoUI	240.35(179.17-316.31)	557.13(485.1-744.75)	6.034 <0.001
GeoMmin	10.85(6.99-15.01)	25.7(22.49-34.69)	5.917 <0.001
GeoNc	82(62-109)	188(163-250.5)	5.869 <0.001

Supplementary table S3 ROC curves of 30 features used in differentiating LPA and sPHEO

Features	Cutoff point	Area under the ROC curve	Concordance rate	P value
Horzl_RLNonUni	1074.562	0.885(0.820-0.951)	0.852	0.931
GeoW6	0.021	0.882(0.816-0.948)	0.852	0.931
GeoEI	5.907	0.881(0.814-0.947)	0.852	0.931

GeoM2x	90.676	0.883(0.816-0.95)	0.824	0.966
GeoRb	35.282	0.881(0.814-0.947)	0.852	0.931
GeoRc1	40.173	0.881(0.815-0.948)	0.843	0.931
GeoSpol	40.173	0.881(0.815-0.948)	0.843	0.931
135dr_RLNonUni	1473.258	0.883(0.816-0.949)	0.861	0.897
45dgr_RLNonUni	1453.959	0.880(0.812-0.947)	0.861	0.897
Vertl_RLNonUni	1127.620	0.882(0.816-0.949)	0.852	0.931
GeoW13	0.035	0.878(0.811-0.945)	0.852	0.931
S(5,5)SumAverg	64.292	0.627(0.523-0.731)	0.583	0.828
S(5,-5)Entropy	2.924	0.883(0.815-0.951)	0.824	0.897
GeoEI2	54.699	0.88(0.814-0.947)	0.852	0.931
Vertl_GLevNonU	25.885	0.88(0.816-0.945)	0.833	0.966
Horzl_GLevNonU	25.625	0.88(0.815-0.945)	0.833	0.966
135dr_GLevNonU	26.092	0.88(0.815-0.945)	0.833	0.966
WavEnHL_s-3	269.465	0.887(0.823-0.95)	0.796	0.828
S(0,5)SumAverg	64.349	0.643(0.539-0.746)	0.620	0.862
S(5,-5)Correlat	0.004	0.664(0.562-0.765)	0.546	0.931
GeoMaver	21.405	0.881(0.814-0.948)	0.852	0.897
GeoD1	17.353	0.878(0.811-0.945)	0.852	0.931
GeoEr	15.344	0.88(0.813-0.948)	0.861	0.897
GeoFmin	36.026	0.88(0.813-0.946)	0.852	0.931

GeoS	36.179	0.87(0.801-0.939)	0.843	0.931
GeoUg	383.850	0.88(0.812-0.948)	0.861	0.897
GeoRc2	122.183	0.88(0.812-0.948)	0.861	0.897
GeoUI	383.850	0.88(0.812-0.948)	0.861	0.897
GeoMmin	16.306	0.873(0.804-0.941)	0.843	0.931
GeoNc	129.500	0.879(0.811-0.947)	0.852	0.931

Supplementary table S4 Predictive effect of the number of positive features

Tumor	Predictive value		Total
	LPA	sPHEO	
LPA	64	15	79
sPHEO	1	28	29
Total	65	43	108

Supplementary figure S1 Representative CT images of lipid-poor adrenal adenoma and sPHEO. Pre-enhanced (A), arterial (B) and portal venous (C) contrast-enhanced CT images show a left pathologically-proven lipid-poor adrenal adenoma (arrow) that measures 39HU on pre-enhanced phase, 73HU on arterial phase and 120 HU on portal venous phase. Pre-enhanced (D), arterial (E) and portal venous (F) contrast-enhanced

CT images show a left pathologically-proven sPHEO (arrow) that measures 46HU on pre-enhanced phase, 69HU on arterial phase and 92 HU on portal venous phase. (G)

A manually defined ROI is drawn in the lipid-poor adrenal adenoma area. (H) A manually defined ROI is drawn in the sPHEO area.

