
Utility of the Aortic-Lesion-Attenuation-Difference (ALAD) and Peak Early-Phase Enhancement Ratio (PEER) to differentiate benign from malignant renal masses

Amanda E. Kahn, BS,¹ Steven J. Lomax, MD,¹ Essa M. Bajalia, BS,¹
Colleen T. Ball, MS,² David D. Thiel, MD¹

¹Department of Urology, Mayo Clinic, Jacksonville, Florida, USA

²Division of Biomedical Statistics and Informatics, Mayo Clinic, Jacksonville, Florida

KAHN AE, LOMAX SJ, BAJALIA EM, BALL CT, THIEL DD. Utility of the Aortic-Lesion-Attenuation-Difference (ALAD) and Peak Early-Phase Enhancement Ratio (PEER) to differentiate benign from malignant renal masses. *Can J Urol* 2020;27(4): 10278-10284.

Introduction: To evaluate the utility of the Aorta-Lesion-Attenuation-Difference (ALAD) and Peak Early-phase Enhancement Ratio (PEER) on contrast-enhanced computed tomography (CT) to differentiate between the appearances of chromophobe renal cell carcinoma, clear cell renal cell carcinoma, and oncocytoma.

Material and methods: ALAD and PEER values were retrospectively measured by a reviewer from 119 patients with surgically resected renal masses (chromophobe renal cell carcinoma n = 29, clear cell renal cell carcinoma n = 28, and oncocytoma n = 62). The ALAD value is expressed as: $ALAD = \text{Hounsfield Units aorta} - \text{Hounsfield Units mass}$. PEER is expressed as $(\text{Hounsfield Units contrast tumor} - \text{Hounsfield Units non-contrast tumor}) / (\text{Hounsfield Units$

$\text{contrast cortex} - \text{Hounsfield Units non-contrast cortex})$.

Results: The ALAD median was 27.6 for oncocytomas, 68.5 for chromophobe renal cell carcinoma, and 55.4 for clear cell renal cell carcinoma. A significant difference between ALAD values of oncocytoma and chromophobe renal cell carcinoma was observed in the nephrographic (area under the ROC curve 0.92) and excretory phases (area under the ROC curve 0.95). The PEER median was 0.74 for oncocytomas and 0.37 for chromophobe renal cell carcinoma. The PEER values significantly differed while comparing oncocytomas and chromophobe renal cell carcinoma in the nephrographic and excretory phases.

Conclusions: Preoperative contrast-enhanced CT ALAD and PEER values both significantly differentiate between chromophobe renal cell carcinoma and oncocytoma. PEER may be more effective in contrast-enhanced CT scans lacking distinct phases.

Key Words: x-ray computed, benign, carcinoma, renal cell, chromophobe renal cell carcinoma, oncocytoma, tomography

Introduction

A byproduct of the increase in incidentally detected renal masses on imaging is the unnecessary excision of benign masses secondary to the unreliability of contrast-enhanced imaging to differentiate benign oncocytoma from malignancy (typically renal cell carcinoma).¹⁻⁵ The most troublesome differentiation is between chromophobe renal cell carcinoma (chRCC) and benign oncocytic masses.⁵

In order to address the problematic differentiation between oncocytoma and chRCC, two different imaging-based approaches have been developed. Dhyani et al introduced the idea of measuring the Aorta-Lesion-Attenuation-Difference (ALAD) as a method to characterize renal masses.⁶ The ALAD value represents the difference in detected Hounsfield units (HU) between the aorta and the region of interest (ROI) on specific phases of contrast-enhanced CT (CECT). Similarly, Amin et al introduced a new measure called the peak early-phase enhancement ratio (PEER) of the tumor: cortex.⁷ The PEER value measures the difference in HU between the renal cortex and the ROI of the lesion. In this study, we attempt to evaluate the utility of the ALAD and PEER values to differentiate benign from malignant pathology of renal masses.

Accepted for publication June 2020

Address correspondence to Dr. David D. Thiel, Department of Urology, Mayo Clinic Florida, 4500 San Pablo Road, Jacksonville, FL 32224 USA

Materials and methods

Patient selection

We examined 826 patients who underwent radical or partial nephrectomy for renal masses. We isolated all pathologically confirmed chRCC and oncocytomas followed by narrowing the cohort to patients who had a preoperative CECT available ($n = 91$) for evaluation. We added ccRCC patients by matching for tumor size with the chRCC cohort ($n = 28$) for ALAD evaluation. Following IRB approval, preoperative CECT scans from the 119 patients were evaluated and ALAD and PEER values were calculated.

Data collection

Patient demographic data was collected regarding patient's age, sex, body mass index (BMI), and MAP score of the tumor kidney.⁸ The patient's renal mass size, presence of central scar, tumor homogeneity, and calcifications were noted. MAP score was categorized as 0-3 or 4-5 and renal mass size was categorized as < 2 cm, 2-4 cm, or > 4 cm. Categorization was based on previously studied risk of malignant renal masses.^{4,9} CD117 immunostain results were also noted from the pathology report.

Radiographic measurements

The ALAD value was retrospectively measured from CECT by a single reviewer blinded to pathology results. To calculate the ALAD value, HU of the aorta and the renal mass were measured on the same plane of CECT. A circular ROI, identical to the diameter of the aorta, was used to measure the HU of the renal mass, Figure 1a and Figure 1b. The ALAD value is expressed by the following equation: $ALAD = HU_{aorta} - HU_{mass}$. We evaluated ALAD's performance in the nephrographic and excretory phases, and also on CECTs that lacked distinct phases ("not specific").

Measurements to calculate the PEER value were gathered by using a ROI around 1 centimeter in diameter to measure the HU of the renal lesion on preoperative CECT in patients with oncocytoma or chRCC ($n = 91$). Next, the renal cortex adjacent to the tumor was carefully outlined in an elliptical like shape to obtain the HU of the cortex as shown in Figure 1a and Figure 1b. The lesion and the cortex were measured in either the nephrographic, excretory, or "not specific" phases. The same measurements of the lesion and cortex were taken again on a non-contrast CT. To calculate the PEER value, the HU measurements of the lesion without contrast were subtracted from the HU measurements of the lesion with contrast.⁷ Similarly, the HU measurements of the cortex without contrast were subtracted from the HU

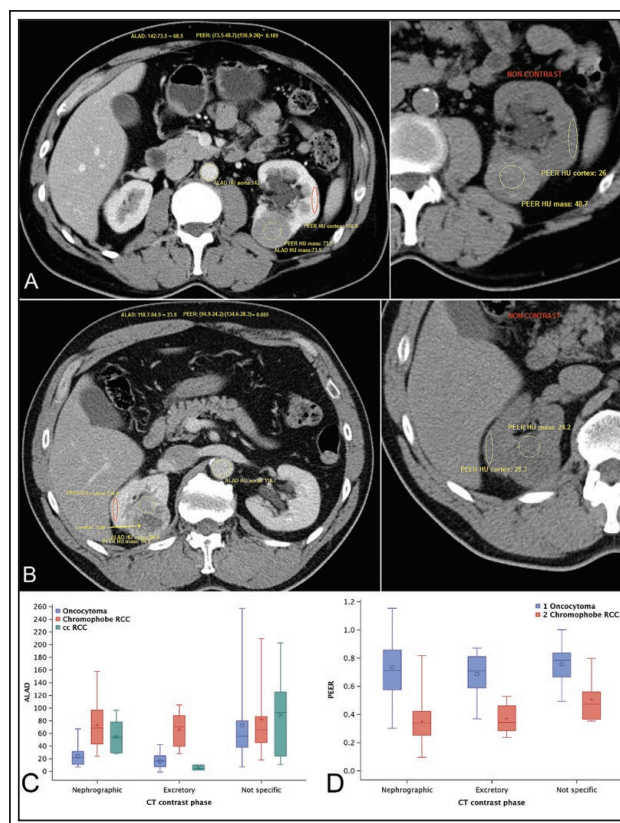


Figure 1. A) Calculation of ALAD and PEER in left renal mass. To calculate the ALAD value, Hounsfield Units (HU) of the aorta and the renal mass were measured on the same plane of CECT. $PEER = (HU_{contrast\ tumor} - HU_{non-contrast\ tumor}) : (HU_{contrast\ cortex} - HU_{non-contrast\ cortex})$. B) Calculation of ALAD and PEER in right renal mass. ALAD and PEER values calculated for right renal mass utilizing the same formula as Figure 1A. C) Distribution of aorta-lesion-attenuation-difference (ALAD) scores by renal mass pathology and CT contrast phase. D) Distribution of peak early-phase enhancement ratio (PEER) scores by renal mass pathology and CT contrast phase.

measurements of the cortex with contrast. This created a "net enhancement difference" for both the cortex and the lesion. The PEER value is the ratio of tumor net enhancement:cortex net enhancement. The calculation of the PEER value is also represented by the following equation: $(HU_{contrast\ tumor} - HU_{non-contrast\ tumor}) : (HU_{contrast\ cortex} - HU_{non-contrast\ cortex})$. If a non-contrast CT was not available, the PEER value was calculated with measurements taken from CECT and the expression was simplified accordingly. Measurements were carefully taken to avoid calcifications and central scars in lesions to avoid areas of hyper- or hypo-enhancement.

Statistical analysis

Continuous variables were summarized with the sample median, minimum, and maximum values. We constructed box plots of ALAD and PEER according to pathology and CT contrast phase. The area under the receiver operating characteristic curve (AUROCC) was estimated along with a corresponding 95% confidence interval (CI) to examine the ability of ALAD, PEER, MAP, and mass size, individually and in combination, to differentiate between malignant and benign renal masses. Likelihood ratio tests were used to compare nested models. The DeLong test¹⁰ was used to compare non-nested models (i.e., PEER versus ALAD) in the ability to differentiate chRCC from oncocytoma. P values less than 0.05 were considered statistically significant. Separately for the nephrographic, excretory, and not specific phases, we estimated the AUROCC and determined the optimal threshold for both ALAD and PEER using Youden's index.¹¹ Sensitivity, specificity, positive predictive value, and negative predictive value were estimated

based on the optimal threshold along with 95% CIs. Statistical analyses and graphics were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA).

Results

Table 1 demonstrates characteristics of the 119 patients according to renal mass pathology. Median renal mass size was 3 centimeters (range, 0.9 to 14). It was observed that every lesion with a central scar was pathologically confirmed as an oncocytoma. A total of 32 (27%) patients had calcifications in the aorta on unenhanced CT. ALAD was significantly lower among patients with oncocytoma (median 27.6) compared to those with chRCC (median 68.5, $p < 0.001$) and those with ccRCC (median 55.4, $p = 0.012$). The difference in ALAD between those with chRCC and ccRCC was not statistically significant ($p = 0.32$). PEER was significantly higher among patients with oncocytoma (median 0.74) compared to those with chRCC (median 0.37, $p < 0.001$).

TABLE 1. Patient and renal mass characteristics

	Oncocytoma n = 62	chRCC n = 29	ccRCC n = 28	p value
Patient characteristics				
Median age (range), y	67 (36-83)	63 (24-81)	60 (36-72)	0.005 ^a
Sex, No. (%)				0.25 ^b
Female	21 (34%)	14 (48%)	14 (50%)	
Male	41 (66%)	15 (52%)	14 (50%)	
Median BMI (range), kg/m ²	26.9 (17.5-58.0)	27.0 (20.0-42.6)	31.7 (20.1-48.0)	0.017 ^a
MAP score of tumor kidney, No. (%)				0.17 ^b
0-3	41 (66%)	21 (72%)	24 (86%)	
4-5	21 (34%)	8 (28%)	4 (14%)	
CD117/Kit, No. (%)				0.51 ^b
Not tested/negative	55 (89%)	24 (83%)	NA	
Positive	7 (11%)	5 (17%)	NA	
Renal mass characteristics				
Median renal mass size (range), cm	2.8 (1.0-12.5)	3.0 (0.9-14.0)	3.1 (1.0-13.0)	0.14 ^a
Homogenous, No. (%)	26 (42%)	21 (72%)	11 (39%)	0.013 ^b
Central scar, No. (%)	27 (44%)	0 (0%)	0 (0%)	< 0.001 ^b
Calcification, No. (%)	22 (35%)	8 (28%)	2 (7%)	0.014 ^b
Median ALAD (range)	27.6 (-0.9-256.9)	68.5 (18.0-209.4)	55.4 (2.0-202.6)	< 0.001 ^a
Median PEER (range)	0.74 (0.30-1.15)	0.37 (0.10-0.82)	NA	< 0.001 ^c

chRCC = chromophobe renal cell carcinoma; ccRCC = clear cell renal cell carcinoma; BMI = body mass index; MAP = Mayo adhesive probability; ALAD = aorta-lesion-attenuation-difference; PEER = peak early-phase enhancement ratio. PEER was not available for 1 patient in the oncocytoma group.

^aKruskal-Wallis test; ^bFisher exact test; ^cWilcoxon rank-sum test.

Table 2 shows the AUROCC for differentiating between malignant (chRCC or ccRCC) and benign (oncocytoma) renal masses. In the nephrographic phase, the ALAD value demonstrates a strong ability to differentiate between benign and malignant lesions (AUROCC 0.91), chRCC and oncocytoma (AUROCC 0.92), and ccRCC and oncocytoma (AUROCC 0.88). In the excretory phase, the ALAD value also

demonstrates the ability to differentiate between chRCC and oncocytoma (AUROCC 0.95). When the MAP score was evaluated with the ALAD value, it was slightly more predictive than ALAD alone when differentiating between malignant RCC and oncocytoma in the excretory phase (LRT $p = 0.041$) and when differentiating between ccRCC and oncocytoma in any phase (LRT $p = 0.03$). The PEER

TABLE 2. Area under the receiver operating characteristic curve

CT contrast phase/model	RCC vs. oncocytoma ^a	p value	chRCC vs. oncocytoma ^a	p value	ccRCC vs. oncocytoma ^a	p value
All CT contrast phases	n = 119		n = 91		n = 90	
ALAD	0.73 (0.64-0.83)		0.80 (0.70-0.89)		0.67 (0.54-0.80)	
MAP	0.56 (0.48-0.64)		0.53 (0.43-0.63)		0.60 (0.51-0.69)	
Tumor size	0.58 (0.49-0.67)		0.57 (0.46-0.68)		0.59 (0.48-0.70)	
ALAD+MAP	0.74 (0.66-0.83)	0.051 ^b	0.79 (0.70-0.88)	0.42 ^b	0.70 (0.59-0.81)	0.030 ^b
ALAD+tumor size	0.74 (0.65-0.83)	0.061 ^b	0.78 (0.68-0.89)	0.13 ^b	0.70 (0.57-0.82)	0.096 ^b
PEER			0.93 (0.86-0.99)	0.008 ^c		
PEER+MAP			0.93 (0.86-0.99)	0.84 ^d		
Nephrographic phase	n = 56		n = 45		n = 39	
ALAD	0.91 (0.83-0.98)		0.92 (0.85-1.00)		0.88 (0.78-0.99)	
MAP	0.55 (0.43-0.68)		0.54 (0.39-0.69)		0.70 (0.60-0.79)	
Tumor size	0.52 (0.39-0.66)		0.53 (0.37-0.68)		0.52 (0.34-0.70)	
ALAD+MAP	0.91 (0.84-0.98)	0.35 ^b	0.92 (0.85-1.00)	0.99 ^b	0.90 (0.80-0.99)	0.096 ^b
ALAD+tumor size	0.90 (0.83-0.98)	0.21 ^b	0.92 (0.83-1.00)	0.34 ^b	0.88 (0.76-1.00)	0.12 ^b
PEER			0.93 (0.85-1.00)	0.85 ^c		
PEER+MAP			0.93 (0.84-1.00)	0.51 ^d		
Excretory phase	n = 19		n = 16		n = 14	
ALAD	0.68 (0.40-0.96)		0.95 (0.84-1.00)		0.76 (0.49-1.00)	
MAP	0.64 (0.50-0.77)		0.64 (0.50-0.77)		0.64 (0.50-0.77)	
Tumor size	0.70 (0.46-0.93)		0.66 (0.36-0.97)		0.76 (0.49-1.00)	
ALAD+MAP	0.78 (0.55-1.00)	0.041 ^b	Not estimated ^e		0.85 (0.63-1.00)	0.17 ^b
ALAD+tumor size	0.78 (0.56-1.00)	0.13 ^b	0.96 (0.88-1.00)	0.51 ^b	0.91 (0.73-1.00)	0.15 ^b
PEER			0.96 (0.88-1.00)	0.76 ^c		
PEER+MAP			Not estimated ^e			
Phase "not specific"	n = 34					
ALAD	0.60 (0.42-0.77)		0.58 (0.32-0.83)		0.61 (0.39-0.82)	
MAP	0.56 (0.43-0.69)		0.65 (0.56-0.75)		0.51 (0.35-0.67)	
Tumor size	0.58 (0.45-0.72)		0.52 (0.31-0.73)		0.61 (0.46-0.77)	
ALAD+MAP	0.59 (0.42-0.77)	0.32 ^b	0.70 (0.50-0.91)	0.036 ^b	0.64 (0.44-0.84)	0.81 ^b
ALAD+tumor size	0.63 (0.45-0.80)	0.26 ^b	0.56 (0.28-0.84)	0.81 ^b	0.66 (0.46-0.86)	0.16 ^b
PEER			0.90 (0.73-1.00)	0.002 ^c		
PEER+MAP			0.93 (0.82-1.00)	0.15 ^d		

RCC = renal cell carcinoma; chRCC = chromophobe renal cell carcinoma; ccRCC = clear cell renal cell carcinoma; ALAD = aorta-lesion-attenuation-difference; MAP = Mayo adhesive probability score; PEER = peak early-phase enhancement ratio. ^aArea under the receiver operating characteristic curve and 95% confidence interval is given; ^bP values result from the likelihood ratio test comparing the given model to the model with only ALAD; ^cP values result from comparing the model with ALAD only to the model with PEER only using the DeLong method; ^dP values result from the likelihood ratio test comparing the given model to the model with only PEER; ^eNot estimated due to only 3 patients with MAP >3 and all 3 had chromophobe RCC.

value also demonstrates a strong ability to differentiate between chRCC and oncocytoma in the nephrographic phase (AUROCC 0.93) and in the excretory phase (AUROCC 0.96). Among the 12 patients with CD117+ masses, PEER performed with 100% accuracy in our retrospective cohort; PEER ranged from 0.58 to 1.05 among those with oncocytoma (n = 7) and 0.10 to 0.45 among those with chRCC (n = 5).

On “not specific” CECT, the ALAD value appears ineffective in differentiating between benign and malignant lesions (AUC 0.60), chRCC and oncocytoma (AUROCC 0.58), and ccRCC and oncocytoma (AUROCC 0.61). The PEER value demonstrated stronger predictive ability than ALAD on “not specific” CECT when differentiating between chRCC and oncocytoma (AUC 0.90 versus 0.58, DeLong $p = 0.002$).

We did not find strong evidence of either MAP score or mass size improving the ability of PEER to differentiate between malignant and benign lesions; nor did mass size improve the ability of ALAD to differentiate between benign and

malignant pathologies. When differentiating between chromophobe RCC and oncocytoma among all CT phases, PEER (AUROCC 0.93, 95% CI 0.86-0.99) performed better than ALAD (AUROCC 0.80, 95% CI 0.70-0.89) ($p = 0.008$, Table 2). Our data also suggests that the ability of ALAD to differentiate between malignant and benign lesions is dependent on CT contrast phase, Figure 1c, whereas the ability of PEER to differentiate between chromophobe RCC and oncocytoma is consistent across all CT contrast phases, Figure 1d.

Youden’s index was used to determine optimal thresholds of ALAD and PEER to differentiate between oncocytoma and chRCC in our cohort, Table 3. For the ALAD value, the optimal threshold was 43 in the nephrographic phase, 28 in the excretory phase, and 66 in the not specific phase although ALAD did not prove to be a useful diagnostic tool in the not specific phase (AUC 0.58). For the PEER value, the threshold was 0.485 in the nephrographic phase, 0.528 in the excretory phase, and 0.560 in the not specific phase.

TABLE 3. ALAD and PEER in specific phases

ALAD threshold	Nephrographic phase	Excretory phase	Phase not specific
n	45	16	30
chRCC	17	5	7
Oncocytoma	28	11	23
<i>chRCC vs. oncocytoma</i>			
ALAD threshold ^a	43	28	66
Sensitivity (95% CI), %	82 (69-91)	100 (81-100)	71 (54-84)
Specificity (95% CI), %	93 (82-97)	82 (58-94)	57 (39-73)
PPV (95% CI), %	88 (75-94)	71 (47-88)	33 (19-51)
NPV (95% CI), %	90 (77-96)	100 (81-100)	87 (70-95)
PEER threshold	Nephrographic phase	Excretory phase	Phase not specific
n	44	16	30
chRCC	17	5	7
Oncocytoma	27	11	23
<i>chRCC vs. oncocytoma</i>			
PEER threshold ^a	0.485	0.528	0.560
Sensitivity (95% CI), %	88 (76-95)	100 (81-100)	86 (69-94)
Specificity (95% CI), %	93 (81-97)	73 (48-88)	91 (76-97)
PPV (95% CI), %	88 (76-95)	63 (39-82)	75 (57-87)
NPV (95% CI), %	93 (81-97)	100 (81-100)	95 (82-99)

chRCC = chromophobe renal cell carcinoma; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value

^aThe threshold was determined by taking the value with the highest Youden’s index. Youden’s index = sensitivity + specificity – 1, where sensitivity and specificity are expressed as proportions ranging from 0 to 1.

Discussion

Modern imaging has proven unreliable at differentiating benign oncocytic neoplasms from RCC.⁵ Oncocytoma and chRCC arise from the same cell within the distal nephron, causing an overlap in imaging characteristics making them nearly indistinguishable on imaging.^{5,12} Attempts to use imaging characteristics such as the presence of a central scar, well differentiated margins, and similar hyper-enhancement patterns on contrast-enhanced imaging have noted varied results.^{5,12}

Dhyani et al developed the ALAD concept to assist in differentiating malignant from benign renal masses that appear on CECT.⁶ This group evaluated an initial cohort of 79 renal masses that was composed of 23 chRCC lesions and 56 oncocytic lesions that were confirmed by biopsy. They also evaluated a validation cohort of 36 surgically resected lesions. They found a significant difference in enhancement between chRCC and oncocytomas in the nephrographic, early excretory, and excretory phases on CECT. This study concluded that in the nephrographic phase on CECT, the ALAD value has the potential to differentiate between benign and malignant renal masses if biopsy is indeterminate. They determined an ALAD threshold of 25.5 to best represent their results; ALAD values greater than 25.5 were chRCC masses while ALAD values less than 25.5 were oncocytic masses. More recently, Grajo et al sought to validate ALAD's ability to discriminate between oncocytomas and all subtypes of RCC: chromophobe, clear cell, and papillary.¹³ They evaluated 227 lesions (22 oncocytoma, 9 angiomyolipoma, 11 chRCC, 37 papillary RCC, 148 ccRCC) in excretory and nephrographic phases on CECT. They determined the nephrographic phase as the most effective in differentiating between oncocytoma and chRCC (AUC 0.98).¹³

The PEER value was created by Amin et al in hopes to assist in the differentiation of CD117+ masses, which usually occurs in chRCC and oncocytomas.⁷ CD117, also known as c-kit, can be detected by immunostain on a biopsy specimen.¹⁴ This group retrospectively and prospectively tested the PEER value by evaluating renal lesions on multiphase CECT. Of the 54 lesions in the retrospective cohort, 19 were CD117+, 13 were CD117-, and 22 were untested. The median net early phase PEER value was 0.45 (range, 0.18 to 0.96) for chRCC and 0.77 (range, 0.50 to 1.00) for oncocytoma and significantly differentiated between the two pathologies ($p < 0.001$). In the prospective cohort, PEER performed exceptionally well by accurately identifying all ($n = 22$) CD117+ renal lesions as their correct pathologies by using a PEER threshold value of 0.50; PEER over 0.50 was an oncocytoma and PEER under 0.50 was chRCC.⁷

Larger renal mass size and higher MAP score have both been correlated with a higher likelihood of malignant pathology.^{4,9,15} The Mayo Adhesive Probability (MAP) score also utilizes preoperative imaging and was originally created to predict surgical difficulty.⁸ Bernstein et al found the MAP score to be a significant independent predictor of malignant pathology ($p = 0.045$); if a patient's MAP score increased by one point, their odds of malignant pathology increased by 37.4%.⁹ Kocher et al found that the MAP score was strongly associated with adherent perinephric fat ($p < 0.001$) and adherent perinephric fat was associated with the presence of renal cell carcinoma ($p = 0.04$).¹⁵ These findings motivated our evaluation of the MAP score in conjunction with ALAD and PEER.

Our evaluation of both ALAD and PEER demonstrated findings analogous with the aforementioned studies. We found that PEER (AUC 0.93) performs significantly better than ALAD (AUC 0.80) ($p = 0.008$). The utility and ease of both systems plays a role in the likelihood of use in the clinic setting. From our experience, ALAD is easier and faster to calculate. The PEER value is mathematically more involved and is slightly more time consuming to evaluate on CECT. Both values can be calculated quickly and easily with a mathematically equipped spreadsheet. We suggest the use of both ALAD and PEER when trying to differentiate between benign and malignant renal masses however we do suggest using PEER over ALAD in certain circumstances. If a biopsy has been conducted with inconclusive pathology results but is CD117+, we suggest the use of PEER. In a CD117+ renal mass, PEER performs with 100% accuracy. Our data suggests that PEER can be effective on CECT scans that lack distinct phases by examining the earliest phase available.

Our findings align well with the previously published research by Dhyani et al⁶ and Amin et al.⁷ For the ALAD value, Dhyani et al concluded that any value larger than 25.5 should be considered chRCC when ALAD is measured in the early excretory phase. Our results suggest that an ALAD value of 43 or higher in the nephrographic phase can also be predictive of malignant pathology. Amin et al determined 0.5 as an appropriate threshold for the PEER value in the earliest phase available; a lesion 0.5 or larger can be considered an oncocytoma. Our findings further identify PEER thresholds according to phase: 0.485 in the nephrographic phase, 0.528 in the excretory phase, and 0.560 in not specific phases. The determination of these thresholds suggests the PEER value is superior when evaluating an image with no specific phases.

To demonstrate clinical application, consider a patient who has a small renal mass on CECT that is

CD117+ on percutaneous biopsy with a central scar, an ALAD value of 25 and a PEER value of 0.75. We can confidently predict the mass as a benign oncocytoma. In this situation, we may recommend watchful waiting in order to preserve healthy renal parenchyma and renal function.

Limitations of this study include its retrospective nature and the inherent error that is involved in the ALAD and PEER values. HU measurements of the aorta, ROI, and renal cortex must be exercised with precision and awareness. To achieve accurate values, calcifications, central scars, and areas of hyper-enhancement from metal implants must be avoided with every measurement. Because this study was executed retrospectively, the type of CT utilized was not rigorously standardized. We utilized any preoperative CECT scan available and even evaluated CECT scans with one contrasting phase. This was done in order to evaluate the breadth of application of the ALAD and PEER values. Additionally, the low number of patients with scans evaluated in the excretory phase should be considered while drawing conclusions from the statistical analysis. This study is, to our knowledge, the first to validate the PEER value in a large cohort with surgically obtained specimens. It is also the first study to compare the PEER and ALAD systems and evaluate them on CECT scans that lack specific phases.

In conclusion, both the ALAD and PEER values can successfully differentiate between chrRCC and oncocytoma from evaluation in the nephrographic or excretory phases on three-phase CECT. PEER also proved effective in CECT scans lacking distinct phases. □

6. Dhyani M, Grajo JR, Rodriguez D et al. Aorta-Lesion-Attenuation-Difference (ALAD) on contrast-enhanced CT: a potential imaging biomarker for differentiating malignant from benign oncocytic neoplasms. *Abdom Radiol (NY)* 2017;42(6):1734-1743.
7. Amin J, Xu B, Badkshian S et al. Identification and validation of radiographic enhancement for reliable differentiation of CD117(+) benign renal oncocytoma and chromophobe renal cell carcinoma. *Clin Cancer Res* 2018;24(16):3898-3907.
8. Davidiuk AJ, Parker AS, Thomas CS et al. Mayo adhesive probability score: an accurate image-based scoring system to predict adherent perinephric fat in partial nephrectomy. *Eur Urol* 2014;66(6):1165-1171.
9. Bernstein AP, Fram EB, Sankin A et al. A comparison of perinephric fat surface area and Mayo Adhesive Probability score in predicting malignancy in T1 renal masses. *Urol Oncol* 2018;36(11):499.
10. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing areas under two or more correlated receiver operating characteristics curves: a nonparametric approach. *Biometrics* 1988;44(3):837-845.
11. Youden WJ. Index for rating diagnostic tests. *Cancer* 1950;3(1):32-35.
12. Rathmell KW, Chen F, Creighton CJ. Genomics of chromophobe renal cell carcinoma: implications from a rare tumor for pancreatic studies. *Oncoscience* 2015;2(2):81-90.
13. Grajo JR, Terry RS, Ruoss J et al. Using Aorta-Lesion-Attenuation Difference (ALAD) on preoperative contrast-enhanced CT scan to differentiate between malignant and benign renal tumors. *Urology* 2019;125:123-130.
14. Pan CC, Chen PC, Chiang H. Overexpression of KIT (CD117) in chromophobe renal cell carcinoma and renal oncocytoma. *Am J Clin Pathol* 2004;121(6):878-883.
15. Kocher NJ, Kunchala S, Reynolds C, Lehman E, Nie S, Raman JD. Adherent perinephric fat at minimally invasive partial nephrectomy is associated with adverse peri-operative outcomes and malignant renal histology. *BJU Int* 2016;117(4):636-641.

References

1. Kang SK, Huang WC, Pandharipande PV, Chandarana H. Solid renal masses: what the numbers tell us. *AJR Am J Roentgenol* 2014;202(6):1196-1206.
2. Gudbjartsson T, Hardarson S, Petursdottir V, Thoroddsen A, Magnusson J, Einarsson GV. Renal oncocytoma: a clinicopathological analysis of 45 consecutive cases. *BJU Int* 2005;96(9):1275-1279.
3. Dechet CB, Bostwick DG, Blute ML, Bryant SC, Zincke H. Renal oncocytoma: multifocality, bilateralism, metachronous tumor development and coexistent renal cell carcinoma. *J Urol* 1999;162(1):40-42.
4. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: an analysis of pathological features related to tumor size. *J Urol* 2003;170(6 Pt 1):2217-2220.
5. Sasaguri K, Takahashi N. CT and MR imaging for solid renal mass characterization. *Eur J Radiol* 2018;99:40-54.