# MRI-Based Kidney Volume Measurement in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Comparison of T2-Weighted, IDEAL, and Post-Contrast T1-Weighted Sequences

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*Objective*: To compare kidney volume (KV) measurements between, single-shot T2-weighted (sshT2W), IDEAL, and post contrast T1-weighted (T1W) images of autosomal dominant polycystic kidney disease (ADPKD) patients.

*Materials and Methods*: KVs of ADPKD patients presenting at the nephrologic clinic between January 2014 and April 2015 were segmented from coronal sshT2W images, opposed phase IDEAL images, and post-gadolinium T1W images. Measurements were performed independently by three readers using a method involving manual segmentation with image thresholding. The mean KV differences between the evaluated magnetic resonance imaging (MRI) pulse sequences were compared using paired t-tests. Associations between KV and estimated glomerular filtration rate (eGFR) were determined by Pearson correlation coefficient (r). Inter-reader agreement in kidney volumetry was evaluated by intraclass correlation coefficient (ICC) for each comparison.

**Results**: For the cohort of 28 ADPKD patients, the total kidney volume (TKV) and total cyst volume (TCV) measured on sshT2W images were significantly higher than those on post-contrast T1W and opposed phase IDEAL images. The mean differences were the smallest between sshT2W and post-contrast T1W images. The processing times for the sshT2W sequence were significantly less than for the other sequences. KVs showed significant negative correlation with renal function on all evaluated MR sequences. High levels of agreement between all pairings of the three readers were found for all measurements.

*Conclusion*: Non-gadolinium MRI sequences, especially sshT2W sequences, are of sufficient quality for KV measurement in ADPKD, revealing the same negative correlation with eGFR as the other sequences, the smallest mean difference with post-contrast T1W images, and requiring less processing time.

Keywords: ADPKD, MRI, Volume measurement, DIXON, T2W, Post contrast T1W

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Autosomal dominant polycystic kidney disease (ADPKD) is the most common form of polycystic kidney disease, and is a hereditary kidney disorder that occurs worldwide and in all races, affecting 1:400 to

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1:1,000 individuals<sup>(1,2)</sup>. ADPKD is characterized by the slow progressive development of innumerable renal cysts, which lead to tremendous renal enlargement that ultimately progresses to renal failure, which usually occurs by the fifth or sixth decade of life. The disease accounts for 2.5% of end-stage renal disease (ESRD) in the United States<sup>(3)</sup>, and approximately 50% of patients need dialysis or transplantation by the age of 70 years<sup>(4)</sup>. The renal function of most patients is maintained within the normal range for decades, despite the progressive growth of cysts. This is because of compensatory hyperfiltration by

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residual healthy nephrons<sup>(3)</sup>. Once a critical renal size is reached, renal dysfunction and a sharply decreased glomerular filtration rate (GFR) occur. A baseline total kidney volume (TKV) above 1,500 mL is associated with rapidly declining GFR (by 4.33±8.07 mL/minute/ year)<sup>(5)</sup>. Renal function starts to decline in the late course of the disease, after serious irreversible damage to non-cystic parenchyma has already occurred, and at which stage the kidneys are usually massively enlarged with little recognizable normal parenchyma on imaging studies. Thus, late therapeutic intervention usually fails to demonstrate any potential benefit when individuals with established renal insufficiency are treated, because residual healthy nephrons have been completely replaced by the relentless growth of cysts<sup>(3,6)</sup>. The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) was developed to establish reliable measures of disease progression over a relatively short period of time in early-stage ADPKD patients with intact renal function. The CRISP cohort study revealed a negative correlation between renal structure (parenchyma and cyst volume) and renal function (GFR), and confirmed the notion that significant growth of cysts and renal enlargement occur prior to renal function impairment<sup>(7)</sup>. The study also concluded that renal and cyst volume measurements on magnetic resonance imaging (MRI) were reliable and accurate in patients with ADPKD. TKV growth has been confirmed as a clinically meaningful surrogate marker for predicting the decline of renal function in ADPKD<sup>(6,8)</sup>.

Gadolinium-based contrast media (GBCM) is commonly used to improve discrimination of the renal cysts from the renal parenchymal background<sup>(9)</sup>. Nephrogenic systemic fibrosis (NSF) is an acquired idiopathic multisystemic fibrotic disease with the potential for increased mortality, and for which there is not a consistently effective treatment or prevention regimen. This potentially fatal disorder appears to be strongly associated with intravenous administration of GBCM in patients undergoing dialysis and those with severe to end-stage chronic kidney disease without dialysis or acute kidney injury<sup>(10-13)</sup>. Thus, increasing the clinician's and radiologist's awareness and assurance of a valid clinical indication for contrast administration is important.

MRI has been increasingly used for volume measurement in ADPKD, because of the high resolution of 3D images with excellent tissue contrast, and the facts that is free from exposure to ionizing radiation and does not require administration of iodinated contrast medium<sup>(14)</sup>. Specific MRI acquisition techniques with appropriate image segmentation methods have been developed for volume measurement. The majority of published studies have estimated kidney volume by manual contouring of the kidney on the MR images with thresholding methods, which is the most common and simplest approach<sup>(5,7)</sup>. The present study is the first to determine the kidney volume profile of ADPKD patients in Thai or Asian population and is also the first to introduce opposed phase IDEAL (iterative decomposition of water and fat with echo asymmetry and least-squares estimation; the Dixon method) for quantitative kidney volume measurement. The goal of the present study was to compare kidney volume measurement on single-shot T2-weighted (sshT2W), IDEAL, and post contrast T1-weighted (T1W) sequences from patients with ADPKD, and to determine the correlation between renal function (GFR) and renal volume on these MRI pulse sequences.

### **Materials and Methods**

## Study design and population

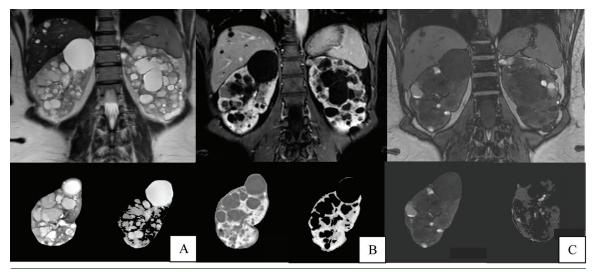
The authors' Institutional Ethics Committee on Human Rights Related to Research Involving Human Subjects approved the present study. The need to obtain informed consent was waived because the analysis used anonymous data obtained after each patient agreed to treatment by written consent. The data collection was from twenty-eight consecutive asymptomatic adult patients with a diagnosis of ADPKD from a nephrology clinic who underwent a 3-T MRI for kidney volume measurement purpose between January 1, 2014 and April 30, 2015. The exclusion criteria included contraindications to MRI [e.g., cardiac devices, aneurysm clips, ear, cochlear implant, metallic structures in body, pregnancy (especially in first trimester), unable to lay in a supine position in the MRI machine, and claustrophobia] and any other active medical conditions that could influence renal function.

### Magnetic resonance imaging

All renal MRI examinations were performed on a 3.0-T MRI scanner (Ingenia MR system; Philips, Best, Netherlands). A phased-array surface coil was positioned with its center over the inferior costal margin, which was estimated as the upper border of the kidney. The field of view was maintained between 34 and 40 cm. The MRI protocol included sshT2W, IDEAL, non-contrast enhanced T1W, and dynamic contrast enhanced MRI sequences (Table 1).

Sequences	Repetition time (ms)	Echo time (ms)	ETL	Matrix	Acquisition time (second/breath hold)	Flip angle (degrees)	Slice thickness/ gab (mm)	FOV (mm)
Coronal T2W SSTSE	1,200	60	67	340×226	13	90	5/0	360
Coronal IDEAL (T1W FFE)	3.5	TE1: 1.2 TE2: 2.1	2	220×206	15	10	1.6/0	360
Coronal 3D THRIVE pre- and post-gadolinium contrast	3.0	1.4	51	208×206	13	10	1.75/0	360

ETL=echo-train length; FOV=field-of-view; T2W SSTSE=T2-weighted single-shot turbo spin echo; T1W FFE=T1-weighted fast field echo



**Figure 1.** Total kidney volume (TKV) and cyst volume measurement on coronal sshT2-weighted images of the right kidney of a 46-year-old woman with autosomal dominant polycystic kidney disease (A). TKV and parenchymal volume of the right kidney on THRIVE T1W post-gadolinium contrast enhanced MRI (3rd phase) (B) and on IDEAL (opposed phase) (C) using manual segmentation and a thresholded volumetric measurement method.

All subjects were injected with 20 to 30 mL or 0.1 mmol/kg gadobutrol (Gadovist; 1.0 mmol/mL) at a rate of 1 mL/second. The post-gadolinium dynamic imaging was acquired in three initial phases (25, 40, and 60 seconds after contrast administration), and then after delays of 3, 5, and 10 minutes, with a bolus tracking technique and fat saturation. The MRI images of all cases were uploaded into a picture archiving and communications system (PACS) under DICOM conformance (Synapse version 3.2.0, FUJIFILM Medical Systems USA's Synapse<sup>®</sup> PACS System, USA).

#### Renal volume measurements

Kidney volumes were measured by manually tracing the kidney contours using volume analysis software implemented on an Advantage Windows Workstation (4.4, GE Healthcare, Buc, France). The kidney volumes were derived from the number of pixels in the contouring region of interest multiplied by the voxel resolution which depends on the field-ofview (FOV), matrix size, and slice thickness. For the measurements of TKV, the coronal sshT2W, IDEAL (opposed phase), and THRIVE T1W post-gadolinium (third phase) sequences were used (Figure 1).

For the determination of total cyst volume (TCV), a region-based thresholding technique was applied to the coronal sshT2W sequences. In this sequence, the cysts appeared brighter than the renal parenchyma (Figure 1A). An intensity threshold was selected by the analyst and the volumes of all cysts were calculated for each kidney by multiplying the cyst areas by the section thicknesses and summing the volumes of all the sections. Parenchymal volumes (PaVs) were determined by applying a region-based thresholding technique to the coronal opposed phase IDEAL and THRIVE T1W post-gadolinium (third phase) sequences. In these sequences, the

renal parenchyma was brighter than the cysts (Figure 1B, C). An experienced radiologist selected the most appropriate intensity threshold. These measurements were obtained using the Advantage Windows workstation.

The measurements of total kidney, cyst, and PaV were each performed by an experienced radiologist, a last year radiology resident, and an experienced MRI technician. The processing time for acquiring each measurement was also recorded.

#### Statistical analysis

Means and standard deviations (SDs) or median and range were computed for all continuous data. Categorical data were summarized using frequencies and percentage. The mean volume differences between the different MRI pulse sequences were calculated using paired t-tests. Correlations between the kidney volumes measured on sshT2W, opposed phase IDEAL, and THRIVE T1 post-gadolinium imaging were calculated using Pearson's correlation coefficient (r).

Associations between renal function (estimated glomerular filtration rate [eGFR], estimated using the Chronic Kidney Disease Epidemiology Collaboration equation [CKD-EPI])<sup>(15)</sup> and kidney volume measurements obtained from sshT2W, opposed phase IDEAL, and THRIVE T1 post-gadolinium imaging were determined using Pearson correlation coefficients (r). The comparison between these correlations were determined by Z-score.

Inter-reader agreement for kidney volumetry was evaluated using intraclass correlation coefficient (ICC). A p-value of less than 0.05 was considered to represent statistical significance. Stata, version 14.1 (StataCorp LP, College Station, TX, USA) was used to perform the statistical analysis.

### Results

The cohort of 28 asymptomatic ADPKD patients consisted of six men and 22 women, with a mean age of 57 years (SD 9, range 34 to 76) and mean height of 161.23 cm (SD 7.64). The mean eGFR was 73.36 mL/minute/1.73 m<sup>2</sup> (SD 23.80, range 24.80 to 104.6).

# Kidney volume measurements on the different MR sequences

The mean TKVs measured on the sshT2W, opposed phase IDEAL, and THRIVE T1W post-gadolinium images were 786.9 mL (SD 593.58), 710.04 mL (SD 554.24), and 766.59 (SD 581.29) for the left kidney, and 720.67 mL (SD 530.53), 641.85

mL (SD 464.57), and 690.93 (SD 497.97) for the right kidney, respectively.

The mean TCVs measured on sshT2W, opposed phase IDEAL images, and THRIVE T1W post-gadolinium images were 637.74 mL (SD 590.25), 431.12 mL (SD 467.16), and 548.34 (SD 526.38) for the left kidney, and 541.72 mL (SD 509.54), 390.96 mL (SD 344.96), and 467.91 (SD 420.65) for the right kidney, respectively.

The mean PaVs measured on the on sshT2W, opposed phase IDEAL, and THRIVE T1W post-gadolinium images were 149.16 mL (SD 54.88), 278.93 mL (SD 143.94), and 218.25 (SD 88.27) for the left kidney, and 178.95 mL (SD 75.58), 250.89 mL (SD 167.96), and 223.02 mL (SD 114.12) for the right kidney, respectively.

The present study showed strong positive linear relationship of TKVs and TCVs measured by different MRI sequences [Pearson's correlation coefficient (r) 0.96 to 0.99], whereas PaVs showed a weak correlation (r=0.07 to 0.79).

# Comparison of kidney volume measurements between the different MR sequences

TKV and TCV measured on the sshT2W images were significantly greater than those measured on the THRIVE T1W post-gadolinium and opposed phase IDEAL images (p<0.001). The mean TKV and TCV differences were the smallest between sshT2W images and THRIVE T1W post-gadolinium images, although the differences were still statistically significant (Table 2).

The measurements of PaV on IDEAL images were significantly higher than those on THRIVE T1W post-gadolinium and sshT2W images, although they were closer to the THRIVE images than to the sshT2W images. The PaVs measured on T2W images were lower than those of other sequences, and showed only a weak correlation with those of the other sequences (Pearson correlation (r) 0.07 to 0.24, p>0.05).

The mean image processing times for the right and left kidneys were 5.12 minutes (range 2.2 to 11.5) and 4.85 minutes (range 2.0 to 13.4), respectively for the sshT2W images, 7.9 minutes (range 2.5 to 19.1) and 8.0 minutes (range 3.1 to 14.1) for the IDEAL (opposed phase) images, and 6.54 minutes (ranges 3.2 to 11.5) and 6.82 minutes (range 2.2 to 14.6) for the THRIVE post-gadolinium (third phase) images. Across all readers, the processing times for the sshT2W were significantly less than those of the IDEAL and THRIVE T1W post-gadolinium images (p<0.05).

	Left kidn	ey (mL)		Right kidney (mL)		
	Mean difference (mL)	SE	p-value	Mean difference (mL)	SE	p-value
TKV difference						
THRIVE post Gd - sshT2W	-20.31	7.27	0.009*	-29.74	10.39	0.008*
THRIVE post Gd - IDEAL	56.55	6.76	< 0.001*	49.08	13.31	0.001*
sshT2W - IDEAL	76.86	10.10	< 0.001*	78.82	20.09	0.001*
TCV difference						
THRIVE post Gd - sshT2W	-89.40	24.16	0.001*	-73.81	29.05	0.017*
THRIVE post Gd - IDEAL	117.22	22.31	< 0.001*	76.95	22.71	0.002*
sshT2W - IDEAL	206.63	35.86	< 0.001*	150.76	43.08	0.002*
PaV difference						
THRIVE post Gd - sshT2W	69.10	21.20	0.003*	44.07	23.13	0.067
THRIVE post Gd - IDEAL	-60.67	20.56	0.006*	-27.87	19.84	0.172
sshT2W - IDEAL	-129.77	28.43	< 0.001*	-71.94	31.50	0.030*

SE=standard error; Gd=gadolinium; sshT2W=single-shot T2-weighted

\* p<0.05

Table 3. Pearson correlation (r) between kidney volume
measured by different MRI sequences and eGFR

MRI sequence/variable	Correlation coefficients (r)	p-value	
Total kidney volume			
Coronal T2 ssh	-0.35	< 0.001*	
Coronal IDEAL	-0.33	< 0.001*	
Coronal THRIVE post-gadolinium	-0.33	< 0.001*	
Total cyst volume			
Coronal T2 ssh	-0.33	< 0.001*	
Coronal IDEAL	-0.26	< 0.001*	
Coronal THRIVE post-gadolinium	-0.29	0.001*	
Parenchyma volume			
Coronal T2 ssh	-0.16	0.041*	
Coronal IDEAL	-0.40	< 0.001*	
Coronal THRIVE post-gadolinium	-0.43	< 0.001*	

MRI=magnetic resonance imaging; ssh=single-shot

\* p<0.05

# Relationships between kidney volume measurements and renal function

The Pearson correlation coefficients between TKV and kidney function (eGFR) were negative for all the evaluated MR sequences [Pearson's correlation coefficient (r) -0.16 to -0.43]. The differences between these correlations were not statistically significant in both comparison between different the MRI sequences and the type of kidney volumes, Z=0.015 to 1.058, p>0.29 to 0.99 (Table 3, 4).

Statistically significant correlations between TKV and eGFR support the view of MR image derived TKV being a clinically meaningful surrogate marker in ADPKD patients. TCV and PaV also demonstrated statistically significant negative correlations with eGFR (Figure 2).

### Reproducibility of MRI kidney volumetry

For the TKV measurements, the ICCs across all reader pairings were between 0.98 and 1.00 for all the evaluated MR sequences, representing excellent agreement. For TCV measurements, the ICCs were between 0.97 and 0.99 across all reader pairings, again representing excellent agreement. The ICCs for PaV measurements were between 0.41 and 0.67 for sshT2W images, representing moderate agreement, between 0.68 and 0.92 for opposed phase IDEAL images, representing good agreement, and between 0.80 and 0.92 for THRIVE T1W post-gadolinium images, representing excellent agreement. Accuracy and precision were high over the entire range of measured kidney volumes, indicating similar reliability in the measurement of low and high kidney volumes.

### Discussion

Volumetric studies of the kidneys of patients with ADPKD have been performed by different imaging modalities<sup>(16-18)</sup>. The main goal for evaluating the process of disease progression in human ADPKD should be the differentiation of cysts from

Kidney volume/MRI sequences	Z-score	p-value	Kidney volume/MRI sequences	Z-score	p-value
Total kidney volume (TKV)			Coronal T2 ssh		
THRIVE post Gd vs. sshT2W	0.043	0.97	TKV vs. TCV	0.054	0.97
THRIVE post Gd vs. IDEAL	0.015	0.99	TKV vs. PaV	0.699	0.48
sshT2W vs. IDEAL	0.058	0.95	PaV vs. TCV	0.644	0.52
Total cyst volume (TCV)			Coronal IDEAL		
THRIVE post Gd vs. sshT2W	0.176	0.86	TKV vs. TCV	0.258	0.80
THRIVE post Gd vs. IDEAL	0.086	0.93	TKV vs. PaV	0.277	0.78
sshT2W vs. IDEAL	0.262	0.79	PaV vs. TCV	0.536	0.59
Parenchyma volume (PaV)			Coronal THRIVE post-gadolinium		
THRIVE post Gd vs. sshT2W	1.058	0.29	TKV vs. TCV	0.187	0.85
THRIVE post Gd vs. IDEAL	0.136	0.89	TKV vs. PaV	0.397	0.69
sshT2W vs. IDEAL	0.920	0.36	PaV vs. TCV	0.585	0.56

Table 4. Comparison between correlation coefficients of kidney volume and renal function by different MRI sequences

MRI=magnetic resonance imaging; Gd=gadolinium; sshT2W=single-shot T2-weighted

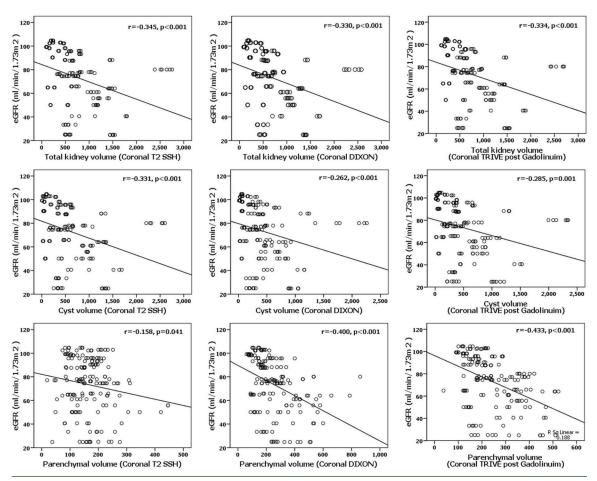
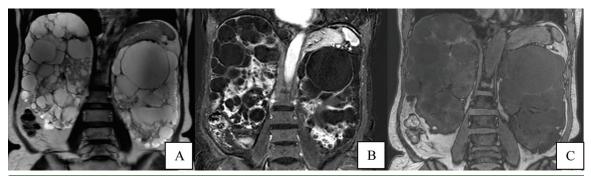


Figure 2. Relationships between kidney volume measurements on the evaluated MR sequences and eGFR in the 28 patients with autosomal dominant polycystic kidney disease.



**Figure 3.** Coronal sshT2-weighted MRI (A), THRIVE T1W post-gadolinium contrast-enhanced MRI (3rd phase) (B), and IDEAL (opposed phase) images (C) of a 68-year-old woman with autosomal dominant polycystic kidney disease with co-existing innumerable liver cysts.

normal renal tissue, which then makes accurate volumetry possible<sup>(7)</sup>. Although there was no renal dysfunction population and we could not determine the real renal functional part in our study, the present study demonstrated that current available MRI techniques and region-based thresholding volume measurement methods allowed renal and cyst volume to be accurately and reliably measured in ADPKD individuals with significant structural involvement. This volumetric analysis of the kidneys avoids the potential pitfalls of operator-dependent techniques, or impossibility to visualize the entire large kidneys in the single acquisition when ultrasonographic methods are employed. Furthermore, MR-based acquisition also avoids the risk of radiation induced carcinogenesis in patients undergoing serial examinations<sup>(19)</sup>, and the risk of iodinated contrast-induced renal toxicity in patients with preexisting kidney disease<sup>(20)</sup>. With superior soft-tissue contrast resolution to the other imaging modalities, MRI maintains high accuracy and precision<sup>(6,21)</sup> without exposing the patient to ionizing radiation or iodinated contrast material, which have additional costs to the health care system, particularly when serial surveillance imaging is required.

The present study results demonstrate that renal volume measurements on all of the evaluated MR pulse sequences (sshT2W, opposed phase IDEAL images, and THRIVE T1W post-gadolinium) provided the same significant negative correlations with renal function (eGFR). These results corroborate those of prior studies that indicated the use of gadolinium is not required for quantification of kidney size<sup>(6,7,9,22)</sup>.

The majority of published studies have estimated kidney volume by manual contouring of the kidney on the MR images, which is the most common and simplest approach<sup>(5,7,18,21)</sup>. Thresholding methods have been used to segment the cortex from cysts, with

the threshold value being obtained from analysis of a histogram of the pixel intensities of a region of interest. Local adaptation of the threshold may sometimes be necessary, because of the spatial inhomogeneity of MRI, a low contrast-to-noise ratio, and inter-subject variability. In addition, the complicated cysts with variable signal cystic content are commonly found in the ADPKD group. Thus, the selection of an appropriate threshold value is often subjective and operator dependent<sup>(23)</sup>.

The authors observed the TKV and TCV measured on sshT2W images were significantly greater than those on opposed phase IDEAL and THRIVE T1W images with gadolinium, a finding that is consistent with results reported by Bae et al<sup>(9)</sup>. This result was probably due to the requirement for multiple breath-hold scanning to cover an entire enlarged kidney on the sshT2W acquisitions. This increases the chances of incorrect registration, motion artifacts, and inhomogeneous tissue signal intensities, all of which may result in a greater imprecision in kidney volume measurement. The fluid sensitivity properties of T2W imaging resulted in numerable co-existing liver cysts being incorrectly registered as renal cysts in these ADPKD patients, and these incorrectly identified cysts were difficult to separate from the kidney volume measurement (Figure 3). Moreover, Bae et al<sup>(9)</sup> showed that manual tracing of the kidney border on images acquired without gadolinium required about 25% more time than on those with gadolinium. However, because the high kidney tissue-contrast property and the hyperintense renal cysts on T2W imaging helped delineate the kidney boundaries against the background tissue, the authors found that less processing time was required for this sequence than for the others.

PaV measurements on opposed phased IDEAL

images were significantly higher than those on THRIVE T1W post-gadolinium and sshT2W images. These higher measurements may result from the suppression of signal from tissues containing similar amounts of lipid and water and suppression of the characteristic signal void at the border between fat and non-fat tissue, termed the 'India ink artifact' (Figure 3C)<sup>(24)</sup>. This may cause over-counting of the boundaries of adjacent contiguous organs. Moreover, as opposed phase IDEAL sequences have lower signal and lower intrinsic tissue contrast than THRIVE T1W post-gadolinium images, IDEAL sequences cannot provide accurate results in patients with variable signal intensity cysts, and it may be difficult to separate cysts with T1 hypersignal from the bright PaV. Recently, the IDEAL sequence has been used and validated for volumetric quantification of pericardial and epicardial fat<sup>(25)</sup>, human brown adipose tissue<sup>(26)</sup>, and pancreatic and hepatic fat<sup>(27)</sup> as well as for the detection of diffuse liver disease, specifically steatosis and iron deposit<sup>(28)</sup>. However, this is the first study to introduce the IDEAL sequence for renal volume measurement in ADPKD. The major advantages of this sequence are that it provides uniform and reliable fat suppression throughout the body while delivering four tissue contrasts (in-phase, opposed phase, fat-only, and water-only images) during a single acquisition<sup>(29)</sup>. The authors believe that further development of specific software for the quantitative assessment of kidney volume on IDEAL sequences will provide results more accurately, especially in cases with severe cyst-burden and complicated cyst contents, which create variable signal intensity on conventional T2W imaging.

Compared with prior studies<sup>(7,9,16)</sup>, the present study kidney volume measurements using manual segmentation with image thresholding offered similarly excellent inter-reader reliabilities for TKV and TCV, with ICC between 0.97 and 1.00. However, with correlation coefficients of 0.41 to 0.92, PaV measurements by manual segmentation with image thresholding had lower reproducibility than TKV or TCV.

The high accuracy and reproducibility of the authors' method should allow monitoring of the changes that occurred within a short time interval in early ADPKD. TKV measurements were acquired by manually tracing the kidney contours of all relevant areas in each image slice and then summing the volumes of each slice, with this forming the initial value, before cyst and parenchyma volumes were measured after application of thresholding. In addition, the present study results demonstrated same statistically significant correlations between TKV and kidney function (eGFR). Therefore, the present results support the view of MRI derived TKV as a clinically meaningful image-based surrogate biomarker for following ADPKD progression in early stage disease<sup>(6,8,30-34)</sup>.

### Limitation

Several limitations to the present study warrant mention. First, the small sample size is the most important limitation. This resulted from the specific MRI protocol for ADPKD patients, which did not include severe or end-stage CKD patients because they would be at high risk from gadolinium administration. Second, the present study covered the initial experience of a single-institution and the results may not be widely applicable. Third, the limited experience of the three readers and the measurement software, which involved manual segmentation and image thresholding, may result in increased processing time and errors. Finally, the authors were unable to compare the kidney volume measurements with kidney specimens, which would have provided a gold standard measurement, and hence, could not determine the most useful MR sequence for providing accurate quantitative renal volume profiles (cyst, parenchyma, and total volume).

Despite these limitations, to the best of the authors' knowledge, the present study is the first to evaluate the kidney volume profile of ADPKD patients in Thai or Asian population and the first to introduce opposed phase IDEAL for quantitative kidney volume measurement. These initial results require further validation before the techniques can be widely applied in routine ADPKD patient care to determine which patients will have a potential benefit from new therapeutic interventions.

# Conclusion

The kidney volumes measured on the evaluated MR sequences, both non-gadolinium and gadoliniumenhanced sequences, together with manual segmentation and the image threshold method, showed significantly inverse relationships with renal function, with excellent inter-reader reproducibility. They could be considered to provide reliable kidney volume measurement. The authors suggest the consistent use of non-gadolinium-enhanced sequences for ADPKD patients, especially the use of sshT2W images to measure TKV and TCV, as these measurements revealed the smallest mean differences from THRIVE T1W post-gadolinium images, while requiring less processing time than the other MR sequences.

### What is already known of this topic?

TKV growth has been confirmed as a clinically meaningful surrogate marker for predicting the decline of renal function in ADPKD. MRI has been increasingly used for volume measurement in ADPKD, because of the high resolution of 3D images with excellent tissue contrast, and the facts that is free from exposure to ionizing radiation and does not require administration of iodinated contrast medium. However, methods for volume estimation with designed MRI images have just recently been introduced in the clinics and are still under development

# What this study adds?

This study is the first to determine initial kidney volume profile of ADPKD patients in Thai and Asian population by different MRI sequences and to determine the correlation between renal function (GFR) and renal volume. Renal volume measurements on all evaluated MR pulse sequences (sshT2W, opposed phase IDEAL, and T1W with gadolinium) with manual segmentation and the image thresholding technique were significantly negatively correlated with renal function (eGFR) and offered similar excellent inter-reader reliabilities for TKV and TCV, with correlation coefficients between 0.97 and 1.00.

SshT2W MRI together with the manual segmentation and image thresholding method can be considered for reliable kidney volume measurement in ADPKD, with the sshT2W showing the smallest mean differences from T1W post-gadolinium images and requiring less processing time. Faster and more accurate volumetric procedures for the quantitatively separate cysts and renal parenchyma in ADPKD are challenged. A close collaboration between clinicians and image-processing researchers as well as carefully designed studies to validate the accuracy of volumetry by these new MRI techniques are needed. The major goal of these development is for improve ADPKD patients care before ineluctably ultimate progression to renal failure.

# **Conflicts of interest**

The authors declare no conflict of interest.

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