# Total kidney volume in autosomal dominant polycystic kidney disease: intraobserver and interobserver agreement of two methods with MRI

**Elif GÜNDOĞDU*, Çağatay CİHAN, Celal YAZICI**

Department of Radiology, Faculty of Medicine, Eskişehir Osmangazi University, Eskişehir, Turkiye

***Correspondence:** elif_basbay@hotmail.com

ORCIDs:

Elif GÜNDOĞDU: https://orcid.org/0000-0002-1729-6958

Çağatay CİHAN : https://orcid.org/0000-0002-8327-1302

Celal YAZICI: https://orcid.org/0000-0003-2376-1227

**Acknowledgment/disclaimers/conflict of interest**

**Conflict of interest:** The authors have no conflicts of interest to declare.

**Funding:** The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

**Informed consent**

The study was approved by the Ethics Committee of the Faculty of Medicine of Eskişehir Osmangazi University (Date: 22.12.2021 No:E-25403353-050.99-266323). The study was conducted in accordance with the principles of the Helsinki Declaration. Datasets were evaluated retrospectively. Therefore, approval and informed consent were not necessary and were waived by our local institutional review board.

**Total kidney volume in autosomal dominant polycystic kidney disease: intraobserver and interobserver agreement of two methods with MRI**


## Abstract

**Background/Aim:** Total kidney volume (TKV) is a parameter used in both treatment decision and follow-up in autosomal dominant polycystic kidney disease (ADPKD) patients. In this study, it was aimed to evaluate intraobserver and interobserver agreement of the ellipsoid formula (EF) and manual boundary tracing method (MBTM) used in TKV measurement of ADPKD patients in different levels of experience radiologists, and also to evaluate the correlation between the EF and MBTM which is considered the gold standard for TKV.

**Materials and methods:** The magnetic resonance imaging (MRI) of 55 ADPKD patients who underwent abdomen MRI between January 2017 and November 2021 for evaluating TKV were evaluated retrospectively. Measurements for TKV were performed by three independent observers (observer 1, an abdominal imaging radiologist with 5 years of experience; observer 2, a fourth-year radiology resident; observer 3, a second-year radiology resident). To assess intraobserver variability, all observers repeated the measurements again at two week intervals. The ICC was used to assess intraobserver and interobserver variability. Comparison of two methods was performed by linear regression for all three observers.

**Results:** The ICC (95% CI) indicated excellent agreement between the observers for both two methods (among all observers, $p<0.001$). Excellent intraobserver agreement was found between all observer measurements either EF or MBTM based on ICC (95% CI) ($p<0.001$). High correlations were observed for two methods in all 3 observers on linear regression analysis (For first observer r=0.992, p<0.001; for second observer r=0.975, p<0.001; for third observer r=0.989, p<0.001).

**Conclusion:** Both of methods (EF and MBTM) using for measurement of TKV provided excellent intra and interobserver reproducibility. The EF is as accurate and precise as the MBTM. It can be preferred in radiology departments with heavy workload because it is a reliable method for rapid and easy assessment independent of experience.

**Keywords:** Autosomal dominant polycystic kidney disease, total kidney volume, magnetic resonance imaging, manual boundary tracing method, ellipsoid formula

## 1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a genetic and systemic disease characterized by multiple cysts developing in the kidneys and progressive loss of kidney functions with an increase in total kidney volume (TKV) [1,2]. Currently, there is no definitive treatment for this disease [3]. Some preventive measures such as salt restriction, weight control, increasing fluid intake are the first step in treatment. However, some antihypertensive agents, especially angiotensin converting enzyme inhibitors, and lipid-lowering agents are used in the treatment of the disease [4]. The vasopressin-2 receptor antagonist (tolvaptan), which is effective on the pathophysiological mechanism responsible for cyst formation, is one of the pharmacological agents that has been used recently [5]. The Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and its Outcomes (TEMPO) 3:4 and 4:4 studies show that the use of tolvaptan slows renal disease progression in patients with advanced ADPKD, and there is a decrease in TKV in patients receiving tolvaptan after 3 years of follow-up [6,7]. In the TEMPO 3:4 study, it was stated that it would be appropriate for the patient group aged 18-55 years with a estimated glomerular filtration rate (eGFR) above 60 ml/min and a TKV above 750 ml to receive tolvaptan treatment [6]. TKV is used in both treatment decision and follow-up in ADPKD patients.

Magnetic resonance imaging (MRI) is accepted as the gold standard method for TKV measurement in the literature [8,9]. TKV volume can be calculated in two ways in MRI: ellipsoid formula (EF) and manual boundary tracing method (MBTM). The EF is a generally accepted practical volume measurement method of spherical or oval shaped structures that is frequently used in daily radiology practice. The MBTM is a standard volume measurement method that can be used to measure the volume of any shaped organ, but requires a longer time [10]. Although MBTM for TKV is the gold standard technique, it is a time-consuming method and also requires special software [10]. Due to these disadvantages, it is difficult to implement in practice. The EF, on the other hand, is less time consuming, does not require special software, and is therefore a method preferred by radiologists in daily practice. Repeatability is one of the most important parameters that determine the reliability of different measurement methods. Therefore, in this study, it was aimed to investigate the intraobserver and interobserver agreement of the EF and MBTM used in TKV measurement of patients with ADPKD in radiologists with different experience levels. In addition, since the MBTM for TKV is considered the gold standard, the correlation of the EF with this method was also evaluated.

## 2. Materials and methods

The study was approved by the Ethics Committee of the Faculty of Medicine of Eskişehir Osmangazi University (Date: 22.12.2021 No:E-25403353-050.99-266323). The study was conducted in accordance with the principles of the Helsinki Declaration. All image data used in this study were obtained from routine imaging at our institution. Datasets were evaluated retrospectively. Therefore, approval and informed consent were not necessary and were waived by our local institutional review board.

### 2.1.Study participants

The MRI of ADPKD patients who underwent abdomen MRI between January 2017 and November 2021 for evaluating TKV were evaluated retrospectively. Patients with MRI in which it was not possible to evaluate TKV due to motion artifacts (n=2) or an inappropriate MRI (n=3 not whole kidney in imaging area) were excluded from the study. The MRI scans of the remaining 55 patients were included in the study.

### 2.2.Image acquisition, analysis and interpretation

All MRI scans were performed on a 3 T (General Electric) MRI device using a 48-channel body coil. Contrast material was not used in any of the patients. Axial plane T1 weighted gradient echo, T2 weighted single shot fast spin echo sequences in the axial, coronal and sagittal planes were obtained. The images were evaluated by radiologists using a dedicated workstation (Advantage WorkStation AW 4.7 software, GE Healthcare, WI, USA). The measurements were performed by three independent observers (observer 1, an abdominal imaging radiologist with 5 years of experience; observer 2, a fourth-year radiology resident; observer 3, a second-year radiology resident) who both performed two measurements for each parameter from which the average values were obtained. To assess intraobserver variability, both observers repeated the measurements again at two week intervals. The volumes of the right and left kidneys were calculated separately and then TKV was found by summing them (Total 110 kidney in 55 patients, all patients had two kidney, no patient had solitary kidney). T2 weighted single shot fast spin echo sequences were used for all measurements.

For MBTM, both kidney boundaries were manually drawn on axial plane one-by-one on each slice (Figure 1). Kidney volumes were calculated from the set of contiguous images by summing the products of the area measurements within the kidney boundaries and slice thickness. Kidney volume was obtained by automatically with software.

The recommendation of the Mayo Clinic was used for the EF (π/6 x Lenght (Coronal Lenght +Sagittal Length)/2 × Depth × Width) (Mayo Clinic (2013). Imaging classification of ADPKD: A simple model for selecting patients for clinical trials [online]. Website https://www.mayo.edu/research/documents/pkd-center-adpkd-classification/doc-20094754 [accessed 28 01 2023). Parameters are obtained from the 4 measurements with using the axial, coronal, and sagittal planes. For each kidney, length was measured as the average maximal longitudinal diameter measured in the coronal and sagittal plane. Width was obtained from the transversal image at maximum transversal diameter, and depth was measured from the same image perpendicular to the width measurement (Figure 2).

## 2.3.Statistical analysis

SPSS software v. 22.0 (IBM Corp.) was used for statistical analysis. Normality analysis was performed by the Shapiro-Wilk test. The mean, standard deviation (SD), minimum and maximum values were obtained as descriptive statistics of continuous data, and frequency (percentage) values for discrete data. The intraclass correlation coefficient (ICC) was used to assess intraobserver and interobserver variability. Based on the 95% confidence interval (CI) of the ICC estimate, values less than 0.5, 0.5 to 0.75, 0.75 to 0.9, and greater than 0.90 indicate poor, moderate, good, and excellent reliability, respectively. Comparison of two methods for TKV was performed by linear regression for all three observers.

## 3. Results

The study included 55 patients, of whom 26 (47.2%) were female and 29 (52.7%) were male. The mean age of the patients participating in the study was 47.36 ± 12.28 (25-80) years. The descriptive statistics of TKV calculated using the EF and MBTM, and measured by the first, second and third observers are given in Table 1.

ICC (95% CI) indicated excellent agreement between the observers for both two methods (among all observers, $p<0.001$). Moreover, excellent intraobserver agreement was found between all observer measurements either EF or MBTM on ICC (95% CI) ($p<0.001$). Table 2 and 3 shows detailed information about intraobserver and interobservers agreement.

Linear regression analysis was performed for all three observers to assess the correlation of measurement methods. High correlations were observed for two methods in all 3 observers (For first observer $r=0.992$, $p<0.001$; for second observer $r=0.975$, $p<0.001$; for third observer $r=0.989$, $p<0.001$) (Figure 3).

## 4. Discussion

In this study, we evaluated the intraobserver and interobserver agreement levels and the correlation between the two methods (EF and MBTM) for determine TKV in ADPKD patients in radiologists with different experience levels. We found that both the EF and MBTM had excellent intraobserver and interobserver agreement. The correlation of the EF with the MBTM, which is considered the gold standard for TKV, was also very high.

In the literature, there are some studies using different radiological methods to calculate TKV volume in ADPKD patients [9]. Ultrasonography (USG); despite its advantages such as being cheap, easily accessible and not containing ionizing radiation, it is not a precise and accurate method that can be used for this purpose [11,12]. Despite the advantage of short time of computed tomography (CT) application, its use in practice is limited (except in patients who cannot undergo MRI) due to ionizing radiation exposure, which poses a problem especially with repetitive examinations, and the difficulty in using iodinated contrast material in patients with impaired renal function [12]. MRI is the most appropriate imaging method used for this purpose because of its high soft tissue contrast resolution and the ability to easily identify renal borders and cysts without the need for contrast material. In the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) study, it was found that there was differences in TKV in measurements made with contrast and non-contrast T1-weighted images [13]. Today, T2-weighted sequences have replaced T1-weighted sequences due to the risk of nephrogenic systemic fibrosis of gadolinium-containing contrast agents and the rapid acquisition of T2-weighted sequences in parallel with recent technological developments. In our study, we also performed TKV measurements on T2-weighted sequences.

The gold standard method for TKV is MBTM performed on MR images [10]. In the literature, studies on this subject have shown that this method has high reproducibility rates. However, it is a time consuming method and requires a specialized workstation [14]. Due to their heavy workload, radiologists need a less time-consuming and accurate method that can be applied in daily practice. For this purpose, studies have been conducted to evaluate whether the EF can be used due to the short evaluation time compared to the MBTM.

In their study, Higashihara et al. found that intra and interobserver reliabilities in standard TKV and in TKV calculated with EF were highly reliable [14]. Irazabal and co-authors maintain that TKV calculated with the EF is strongly correlated with TKV calculated by the stereological method ($R^2$=0.979) [15]. In our study we found a strongly correlation for all three observers regardless of experience, like this study (For first observer r=0.992, p<0.001; for second observer r=0.975, p<0.001; for third observer r=0.989, p<0.001). In addition to this study, we also found that the intraobserver and interobserver agreement of the EF was excellent and independent of experience. Cohen et al. stated the while intraobserver agreement was excellent with the semiautomatic MR volumetric method, the interobserver agreement was quite good [16]. They suggested that the reason why the interobserver agreement is lower than the intraobserver  agreement is that the reader experiences are different and the workstation formal education is insufficient. We found excellent intra and interobserver agreement with both MBTM and EF, and we therefore think that this is independent of experience. Sharma et al. ,in their study with expert and beginner level observers, they found high intraobserver variability in the beginer operator and reported that the measurements should be made by the expert operator [17]. Kidney volumes were performed on T1-

weighted images in this study. Kidney cysts and their borders are more difficult to distinguish on T1-weighted images than on T2-weighted images. Therefore, fast T2-weighted sequences have been used for this purpose in recent studies. The high intraobserver variability of the beginner operator may be due to this. Also, the operators in this study are not radiologists. Non-radiologist operators may not be as familiar with MR images as radiologists. This may be another reason for the inconsistency with our study.

In recent years, there have been studies conducted with artificial intelligence (AI) applications for automatic kidney segmentation in ADPKD patients. Kline et al. found that the AI segmentation system they developed performed equally with the readers [18]. Goel et al. stated that the model-assisted segmentation, which they developed with the deep learning method, requires 51% less time than the manual contour determination method without model support [19]. These studies with AI are very promising for the future; but still, full stomach, full bladder, hemorrhagic renal cysts and cysts located at the liver borders are the cause of significant failure [19]. We think that the validity and widespread using of these studies, which are obtained with AI application, will take time. It seems that radiologists will spend time measuring volume in ADPKD patients in the near future, as they do today. We did not record the evaluation times for the MBTM and EF, but the average time for the MBTM in the literature is between 28 and 90 minutes [20]. On the other hand, 5-7 minutes are reported for the EF [21]. The MBTM requires 4-18 times more time than the EF. According to the results of our study, the EF is a time-effective method that can be used safely by radiologists with different levels of experience. We can also speculate that the EF is more preferable among radiologists due to the increasing workload and the

MBTM being the tedious contouring task. Of course, the most important issues are repeatability and accuracy. The result of our study may relieve radiologists in this preferences.

The most important limitation of the study is its retrospective nature. Obtaining data from a single center is another limitation. In our study, all MRI examinations were performed on a 3 T MRI device. Three-tesla scanners have a higher magnetic feld strength and provide higher signal to noise ratio, thus better image quality and cyst contrast [21]. In order for the results of our study to be valid at 1.5 T, it may be necessary to support studies with MRI devices with this magnetic field strength.

In conclusion, both of methods (MBTM and EF) using in this study provided excellent intra and interobserver reproducibility. The EF is as accurate and precise as the MBTM and it is a reliable method for rapid and easy assessment independent of experience. It can be preferred in radiology departments with heavy workload.

## Conflict of interest

The authors have no conflicts of interest to declare.

## References

1. Grantham JJ, Geiser JL, Evan AP. Cyst formation and growth in autosomal dominant polycystic kidney disease. Kidney International 1987; 31 (5): 1145-1152. https://doi.org/10.1038/ki.1987.121
2. Chebib FT, Torres VE. Autosomal Dominant Polycystic Kidney Disease: Core Curriculum 2016. American Journal of  Kidney Diseases 2016; 67 (5): 792–810. https://doi.org/10.1053/j.ajkd.2015.07.037

3. Igarashi P, Somlo S. Genetics and pathogenesis of polycystic kidney disease. Journal of the American Society of Nephrology 2002; 13 (9): 2384–2398. https://doi.org/10.1097/01.asn.0000028643.17901.42
4. Chapman AB, Devuyst O, Eckardt KU, Gansevoort RT, Harris T et al. Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney International 2015; 88 (1): 17–27. https://doi.org/10.1038/ki.2015.59
5. Torres VE, Chapman AB, Devuyst O, Gansevoort RT, Grantham JJ et al. Tolvaptan in patients with autosomal dominant polycystic kidney disease. The New England Journal of Medicine 2012; 367 (25): 2407–2418. https://doi.org/10.1056/NEJMoa1205511
6. Torres VE, Meijer E, Bae KT, Chapman AB, Devuyst O et al. Rationale and design of the TEMPO (Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and its Outcomes) 3-4 Study. American Journal of Kidney Diseases 2011; 57 (5): 692–699. https://doi.org/10.1053/j.ajkd.2010.11.029
7. Torres VE, Chapman AB, Devuyst O, Gansevoort RT, Perrone RD et al. Multicenter, open-label, extension trial to evaluate the long-term efficacy and safety of early versus delayed treatment with tolvaptan in autosomal dominant polycystic kidney disease: the TEMPO 4:4 Trial. Nephrology Dialysis Transplantation 2018; 33 (3): 477–489. https://doi.org/10.1093/ndt/gfx043

8. Cavoli GL, Finazzo F, Mongiovi R, Bono L, Ferrantelli A et al. The imaging of total kidney volume in ADPKD. Brazilian Journal of Nephrology 2020; 42 (3): 384–385. https://doi.org/10.1590/2175-8239-JBN-2019-0218
9. Magistroni R, Corsi C, Martí T, Torra R. A Review of the Imaging Techniques for Measuring Kidney and Cyst Volume in Establishing Autosomal Dominant Polycystic Kidney Disease Progression. American Journal of Nephrology 2018; 48 (1): 67–78. https://doi.org/10.1159/000491022
10. Ozkurt S, Dogan I, Ozcan O, Fidan N, Bozaci I et al. Correlation of serum galectin-3 level with renal volume and function in adult polycystic kidney disease. International Urology and Nephrology 2019; 51 (7): 1191–1197. https://doi.org/10.1007/s11255-019-02156-8
11. O'Neill WC, Robbin ML, Bae KT, Grantham JJ, Chapman AB et al. Sonographic assessment of the severity and progression of autosomal dominant polycystic kidney disease: the Consortium of Renal Imaging Studies in Polycystic Kidney Disease (CRISP). American Journal of Kidney Diseases 2005; 46 (6): 1058–1064. https://doi.org/10.1053/j.ajkd.2005.08.026
12. Chapman AB, Wei W. Imaging approaches to patients with polycystic kidney disease. Seminars in Nephrology 2011; 31 (3): 237–244. https://doi.org/10.1016/j.semnephrol.2011.05.003
13. Chapman AB, Guay-Woodford LM, Grantham JJ, Torres VE, Bae KT et al. Renal structure in early autosomal-dominant polycystic kidney disease (ADPKD): The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) cohort. Kidney International 2003; 64 (3): 1035–1045. https://doi.org/10.1046/j.1523-1755.2003.00185.x

14. Higashihara E, Nutahara K, Okegawa T, Tanbo M, Hara H et al. Kidney volume estimations with ellipsoid equations by magnetic resonance imaging in autosomal dominant polycystic kidney disease. Nephron 2015; 129 (4): 253–262. https://doi.org/10.1159/000381476
15. Irazabal MV, Rangel LJ, Bergstralh EJ, Osborn SL, Harmon AJ et al. Imaging classification of autosomal dominant polycystic kidney disease: a simple model for selecting patients for clinical trials. Journal of the American Society of Nephrology 2015; 26 (1): 160–172. https://doi.org/10.1681/ASN.2013101138
16. Cohen BA, Barash I, Kim DC, Sanger MD, Babb JS et al. Intraobserver and interobserver variability of renal volume measurements in polycystic kidney disease using a semiautomated MR segmentation algorithm. American Journal of Roentgenology 2012; 199 (2): 387–393. https://doi.org/10.2214/AJR.11.8043
17. Sharma K, Caroli A, Quach LV, Petzold K, Bozzetto M et al. Kidney volume measurement methods for clinical studies on autosomal dominant polycystic kidney disease. PloS One 2017; 12 (5): e0178488. https://doi.org/10.1371/journal.pone.0178488
18. Kline TL, Edwards ME, Fetzer J, Gregory AV, Anaam D et al. Automatic semantic segmentation of kidney cysts in MR images of patients affected by autosomal-dominant polycystic kidney disease. Abdominal Radiology (New York) 2021; 46 (3): 1053–1061. https://doi.org/10.1007/s00261-020-02748-4
19. Goel A, Shih G, Riyahi S, Jeph S, Dev H et al. Deployed Deep Learning Kidney Segmentation for Polycystic Kidney Disease MRI. Radiology Artificial Intelligence 2022; 4 (2): e210205. https://doi.org/10.1148/ryai.210205

20. Kline TL, Edwards ME, Korfiatis P, Akkus Z, Torres VE et al. Semiautomated Segmentation of Polycystic Kidneys in T2-Weighted MR Images. AJR. American Journal of Roentgenology 2016; 207 (3): 605–613. https://doi.org/10.2214/AJR.15.15875

21. Gregory AV, Anaam DA, Vercnocke AJ, Edwards ME, Torres VE et al. Semantic Instance Segmentation of Kidney Cysts in MR Images: A Fully Automated 3D Approach Developed Through Active Learning. Journal of Digital Imaging 2021; 34 (4): 773–787. https://doi.org/10.1007/s10278-021-00452-3

**Table 1** Descriptive statistics of TKV

| | **Observer 1**<br>**Mean±SD (cm$^3$)**<br>**Min-Max (cm$^3$)** | **Observer 2**<br>**Mean±SD (cm$^3$)**<br>**Min-Max (cm$^3$)** | **Observer 3**<br>**Mean±SD (cm$^3$)**<br>**Min-Max (cm$^3$)** |
|---|---|---|---|
| **First measurement (EF)** | 1714.85 ± 1318.65<br>365-6658 | 1935.80 ± 1437.04<br>296-7039 | 1718.42 ± 1294.40<br>370-6082 |
| **Second measurement (EF)** | 1782.75 ± 1369.74<br>350-7073 | 2008.33 ± 1563.58<br>412-7677 | 1698.42 ± 1235.79<br>328-5680 |
| **First measurement (MBTM)** | 1855.96 ± 1431.10<br>410-6971 | 1886.89 ± 1425.64<br>419-6927 | 1927.85 ± 1434.78<br>446-6956 |
| **Second measurement (MBTM)** | 1845.53 ± 1410.50<br>196-6840 | 1911.44 ± 1451.55<br>412-6970 | 1980.47 ± 1469.95<br>438-7065 |

*TKV, Total Kidney Volume; EF, Ellipsoid Formula; MBTM, manual boundary tracing method; SD, standard deviation; Min, minimum; Max, Maximum

**Table 2** ICC Statistics for intraobserver agreement

| | **ICC** | **95% Confidence Interval** | **P value** |
|---|---|---|---|
| Observer 1 (EF) | 0.98 | 0.97-0.99 | 0.0001 |
| Observer 1 (MBTM) | 0.99 | 0.99-0.99 | 0.0001 |
| Observer 2 (EF) | 0.97 | 0.96-0.98 | 0.0001 |
| Observer 2 (MBTM) | 0.99 | 0.98-0.99 | 0.0001 |
| Observer 3 (EF) | 0.99 | 0.98-0.99 | 0.0001 |
| Observer 3 (MBTM) | 0.99 | 0.99-0.99 | 0.0001 |

*ICC, Intraclass correlation coefficient; EF, Ellipsoid Formula; MBTM, manual boundary tracing method

**Table 3** ICC Statistics for interobserver agreement

| | **ICC** | **95% Confidence Interval** | **P value** |
|---|---|---|---|
| Observer 1-2 (EF) | 0.97 | 0.95-0.98 | 0.0001 |
| Observer 1-2 (MBTM) | 0.98 | 0.96-0.98 | 0.0001 |
| Observer 1-3 (EF) | 0.98 | 0.97-0.99 | 0.0001 |
| Observer 1-3 (MBTM) | 0.98 | 0.98-0.99 | 0.0001 |
| Observer 2-3 (EF) | 0.98 | 0.96-0.98 | 0.0001 |
| Observer 2-3 (MBTM) | 0.99 | 0.98-0.99 | 0.0001 |

*ICC, Intraclass correlation coefficient; EF, Ellipsoid Formula; MBTM, manual boundary tracing method

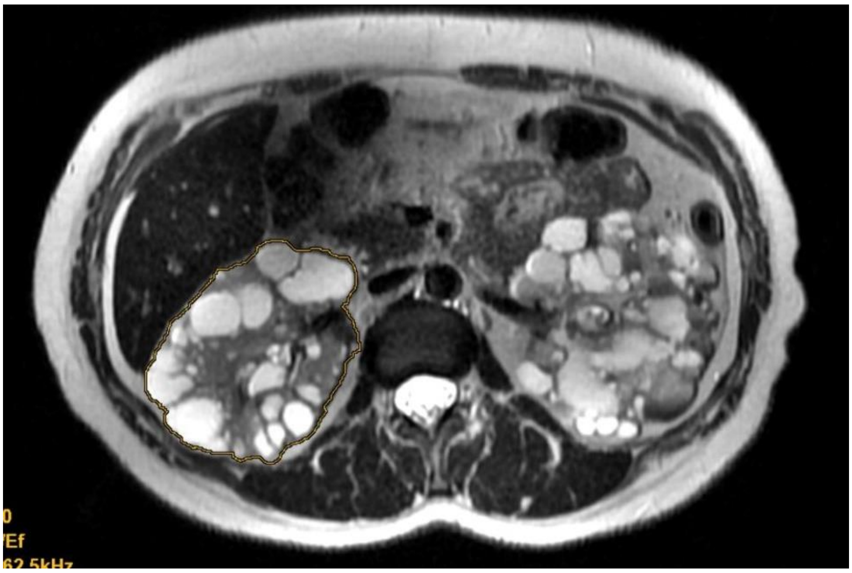


**Figure 1:** MBTM for TKV of ADPKD: kidney boundaries manually drawn on axial plane T2 weighted MRI

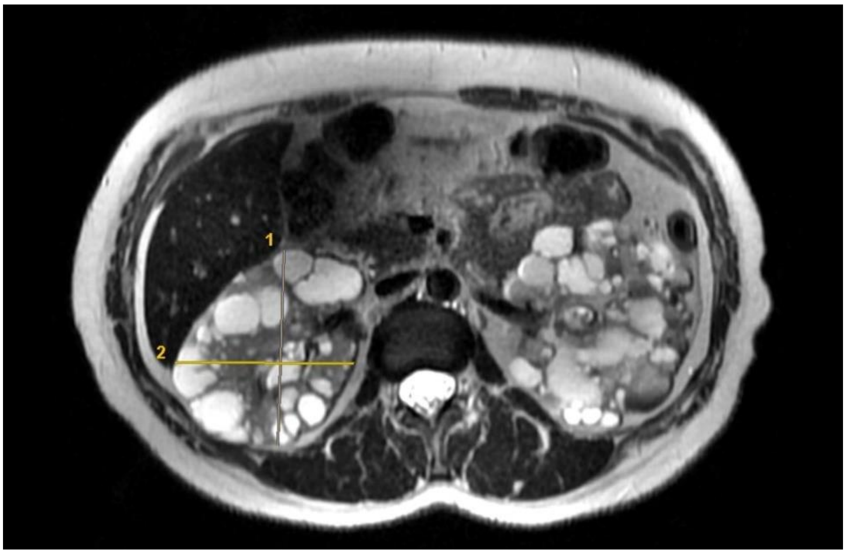
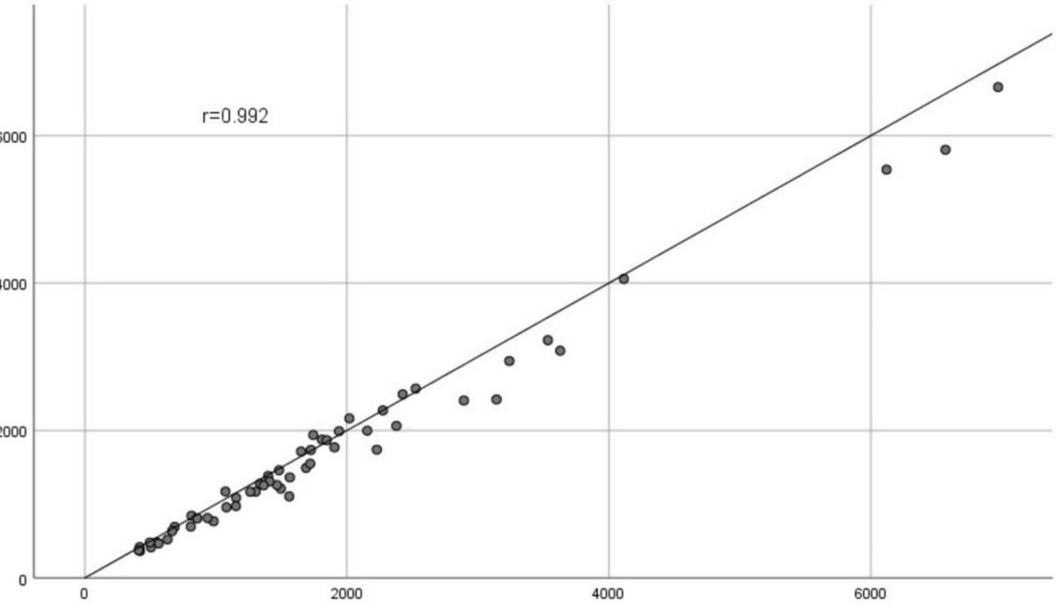
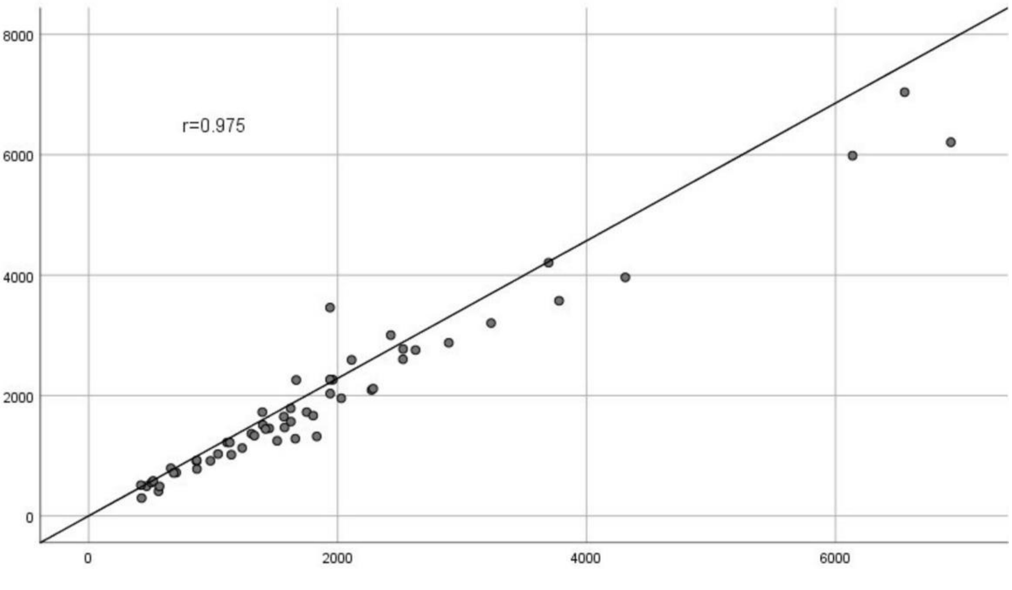



**Figure 2:** EF for TKV of ADPKD: The width from the axial plane image at maximum transversal diameter, and depth from the same image perpendicular to the width measurement


r=0.992
0
2000
4000
6000
0
2000
4000
6000

1


r=0.975
0
2000
4000
6000
8000
0
2000
4000
6000

2

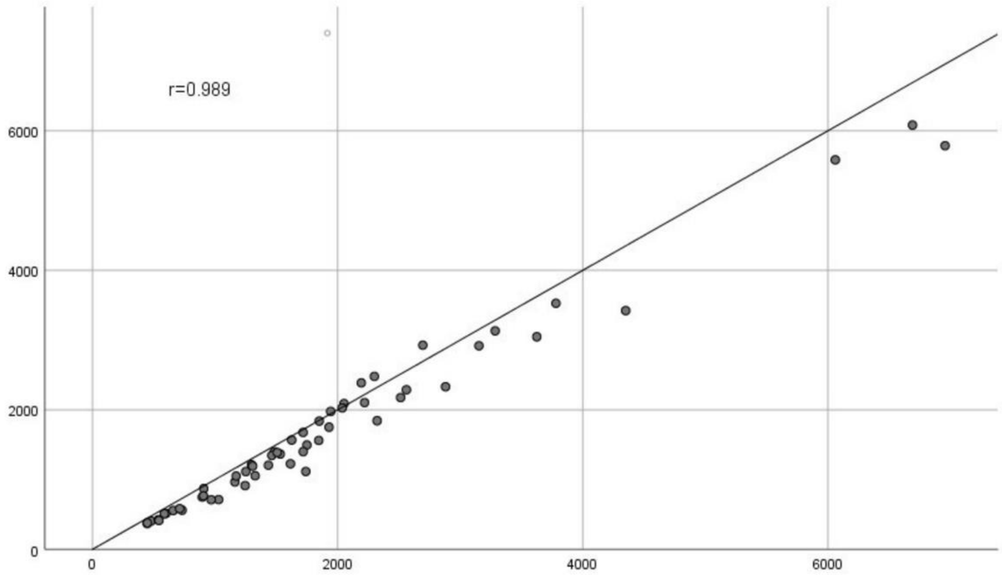



**Figure 3:** Linear regression analysis of measurement methods for all three observers A) for first observer, B) for second observer, C) for third observer