

Longitudinal Multi-Modality MRI–Ultrasound Cyst-Level Analysis of Polycystic Kidney Disease in a Feline Model: A Proof-of-Concept Study

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Research Article

Keywords: Polycystic kidney disease (PKD), Magnetic resonance imaging (MRI), Ultrasound imaging, Cyst-level analysis, Cyst coalescence

Posted Date: September 29th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-8667717/v2>

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Additional Declarations: The authors declare potential competing interests as follows: The author (Naruhiko Nakanishi, PhD; Takeru Lab) is the owner of the study subject (Aiko) and is the inventor on multiple patent applications filed with the Japan Patent Office (August 6, 2025). These interests did not influence the study design, data analysis, interpretation of results, or the conclusions presented. The author declares no other competing interests.

Longitudinal Multi-Modality MRI–Ultrasound Cyst-Level Analysis of Polycystic Kidney Disease in a Feline Model: A Proof-of-Concept Study

Naruhiko Nakanishi^{1,*}

Abstract

Polycystic kidney disease (PKD) in Persian cats is commonly monitored using total kidney volume (TKV); however, this kidney-level metric does not capture heterogeneity in individual cyst dynamics. Here, a standardized longitudinal imaging framework integrating volumetric magnetic resonance imaging (MRI) with serial ultrasound (US) is presented, enabling cyst-level analysis in a feline PKD model followed over two years. MRI-based volumetry quantified individual cyst growth rates and identified structural coalescence events, defined as the persistent loss of visible boundaries between adjacent cysts without implying luminal communication. Serial US provided high-frequency temporal context and supported MRI-defined trends, rather than replacing MRI-based structural assessment. The analysis revealed marked asymmetric progression, with significant enlargement and coalescence of right-sided cysts, while left-sided cysts remained stable. This dual-modality approach demonstrates the feasibility of integrating volumetric MRI with serial ultrasound for longitudinal cyst-level analysis, enabling the identification of asymmetric progression and cyst-level structural remodeling that may be overlooked by kidney-level volumetrics alone. Although based on a single case, this study demonstrates the feasibility of a standardized MRI–ultrasound workflow and provides a methodological framework for future validation in larger cohorts.

Keywords: Polycystic kidney disease (PKD); Magnetic resonance imaging (MRI); Ultrasound imaging; Cyst-level analysis; Cyst coalescence

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Introduction

Autosomal Dominant Polycystic Kidney Disease (ADPKD) in Humans and Polycystic Kidney Disease (PKD) in Cats: Commonalities and Translational Potential.

Autosomal dominant polycystic kidney disease (ADPKD) in humans and polycystic kidney disease (PKD) in cats are both hereditary disorders characterized by the progressive enlargement of renal cysts that eventually compromise renal function. In human ADPKD, quantitative imaging biomarkers such as total kidney volume (TKV) have been validated as predictors of disease progression, with magnetic resonance imaging (MRI) serving as the gold standard for volumetric assessment and ultrasound (US) widely used for routine monitoring because of its accessibility and lower cost [1-3].

From a historical perspective, the landmark CRISP study conducted at the Mayo Clinic established MRI-based total kidney volume (TKV) as the first validated imaging biomarker for ADPKD progression [3, 4]. Building upon the foundation, this work extends the imaging-based framework to a feline PKD model, integrating MRI with ultrasound to capture both volumetric progression and high-frequency temporal trends.

Recent clinical reports further reinforce TKV as a principal surrogate endpoint for progression and therapeutic monitoring in ADPKD [5]. Beyond TKV, recent reviews emphasize additional imaging markers such as cyst complexity and parenchymal heterogeneity [6], and highlight the need for novel biomarkers to refine risk stratification and therapeutic monitoring [7]. Moreover, pediatric ADPKD cohorts have demonstrated that advanced MRI features may offer early indicators of progression across age groups [8]. Recent multicenter evidence further shows that MRI-based total kidney volume assessment can stratify pediatric ADPKD patients into specific risk categories, underscoring its prognostic utility for early intervention [9]. From a translational perspective, practical frameworks such as “Size Matters” clearly underscore TKV’s role as a robust clinical endpoint while calling for multi-modality integration [10]. These developments have been consolidated in the most recent KDIGO 2025 ADPKD Guideline, which explicitly supports standardized imaging biomarkers and data sharing initiatives [11].

Advanced methods now include segmentation, radiomics, and integration between modalities, facilitated by open-source platforms such as 3D Slicer [12, 13]. Deep learning frameworks for ultrasound-based kidney segmentation have also been proposed, achieving robust performance in heterogeneous clinical data sets [14]. More recently, ultrasound localization microscopy (ULM)

has emerged as a super-resolution technique capable of visualizing renal microvasculature and hemodynamics with unprecedented detail, demonstrating early diagnostic utility in hypertensive nephrosclerosis [15].

In feline PKD, the genetic basis (PKD1 mutations) and epidemiology are well established [16, 17], and feasibility of longitudinal imaging has been demonstrated [18]. Comparative human studies further confirm that US can approximate MRI-derived TKV with acceptable accuracy [19, 20], while new proposals emphasize abdominal imaging features beyond volume alone, incorporating cyst complexity and parenchymal heterogeneity [6]. In addition, deep learning-based segmentation approaches have been successfully applied to polycystic liver disease, highlighting the broader applicability of automated imaging frameworks to multi-organ cystic conditions [21]. Automated segmentation approaches are also being developed for patients with PKD [22], and recent deep learning frameworks further extend these analyses to broader abdominal MRI features in ADPKD [23, 24]. Recent work has also introduced fully automated semantic segmentation of kidney cysts in MR images of ADPKD patients, achieving performance comparable to interobserver variability and enabling reliable quantification of cyst burden [25]. Despite these advances, the mechanisms governing the rate and pattern of cyst progression in feline PKD remain incompletely understood [26].

MRI and Ultrasound Integration for Cyst-Level Dynamics: Overcoming Kidney-Level Volumetrics in Asymmetric Progression and Structural Coalescence Detection..

Previous PKD studies, both veterinary and human, have largely relied on kidney-level volumetrics, overlooking the heterogeneity of individual cyst dynamics. Comparative analyses have shown that ultrasound-based measurements can approximate MRI-derived total kidney volume (TKV) with acceptable accuracy, enabling multimodal assessment for disease monitoring and risk stratification [19, 20]. However, longitudinal cyst-level analyses—quantifying changes such as growth, regression, and structural coalescence—have not been systematically conducted in either veterinary or human studies. The study by Caroli, A. and Kline, T.L. addressed this gap by proposing standardized and reproducible MRI-ultrasound integration strategies for cyst-oriented imaging, thereby extending multimodal imaging concepts previously emphasized in human ADPKD research [6].

Research Aim. This study addresses the current lack of systematic, longitudinal MRI-ultrasound integration in feline PKD by presenting a proof-of-concept framework for cyst-level imaging

analysis. Specifically, this methodology focuses on cyst-level analysis rather than traditional kidney-level volumetrics (TKV), enabling characterization of cyst progression patterns, morphological changes suggestive of structural coalescence, and asymmetric progression between the left and right kidneys. By combining serial ultrasound measurements with volumetric MRI references, this study evaluates the feasibility of a standardized multimodal imaging workflow that integrates temporal accessibility with volumetric precision, providing a methodological basis for future validation studies in cystic kidney diseases.

A Proof-of-Concept Framework for Future Translational Imaging Studies. Beyond its veterinary relevance, this study presents a proof-of-concept analytical framework for longitudinal cyst-level imaging in feline PKD. Although developed from a single case, the proposed workflow may provide methodological insights for future studies of cystic kidney diseases, including human ADPKD, after appropriate validation. Such future investigations may be evaluated within established imaging biomarker frameworks, including those advocated by the KDIGO 2025 guideline [11].

Results

Evaluation of Renal Cyst Progression with MRI and Ultrasound and Identification of Asymmetric Progression. MRI volumetric analysis showed a 48.7% increase in maximal right kidney cyst volume over one year, while the left kidney remained stable or decreased. This asymmetric progression was identified within the present longitudinal framework and requires further validation in larger cohorts [27].

The reproducibility of MRI-based TKV (total kidney volume) measurements, which were used to track kidney enlargement, has been validated through multi-center trials [28, 29], further supporting the robustness of MRI as a tool for assessing kidney progression.

Ultrasound imaging corroborated the asymmetric trend observed by MRI, with the right kidney showing a general tendency toward enlargement while the left kidney remained relatively stable. In this study, “directional concordance” was defined as agreement between imaging modalities in the direction of temporal change (increase or decrease), irrespective of absolute quantitative differences. Given the limited spatial resolution and higher measurement variability of US, these results are interpreted only as supportive evidence of directional trends rather than precise quantitative estimates.

Comparative studies demonstrate that 3D and ellipsoid ultrasound can approximate MRI-based TKV with reasonable accuracy [19, 20], and recent analyses further confirm the robustness of US–MRI concordance in clinical ADPKD cohorts [20].

Automated segmentation using 3D Slicer facilitated reproducible delineation of cyst structures. Similar approaches using deep learning have shown high agreement with expert manual measurements, supporting the robustness of volumetric analysis in ADPKD [30–32].

Recent reviews emphasize that imaging biomarkers beyond TKV, such as cyst complexity and parenchymal heterogeneity, may further refine disease monitoring [6].

MRI-Based Volume and Morphology Assessment. MRI-based volumetric and morphological analyses were performed to quantify cyst growth and structural changes over time.

MRI Acquisition. A female Persian cat diagnosed with polycystic kidney disease (PKD), referred to as “Aiko” in this study, underwent two MRI scans conducted one year apart. Figures 1 and 2 present composite T2-weighted MRI images ($TE = 600$ ms) acquired in November 2023 and November 2024, respectively. Each MRI volume consisted of 100 axial slices with a matrix size of 576×576 pixels and an in-plane resolution of 0.2604 mm per pixel. The slice thickness was 0.5 mm.

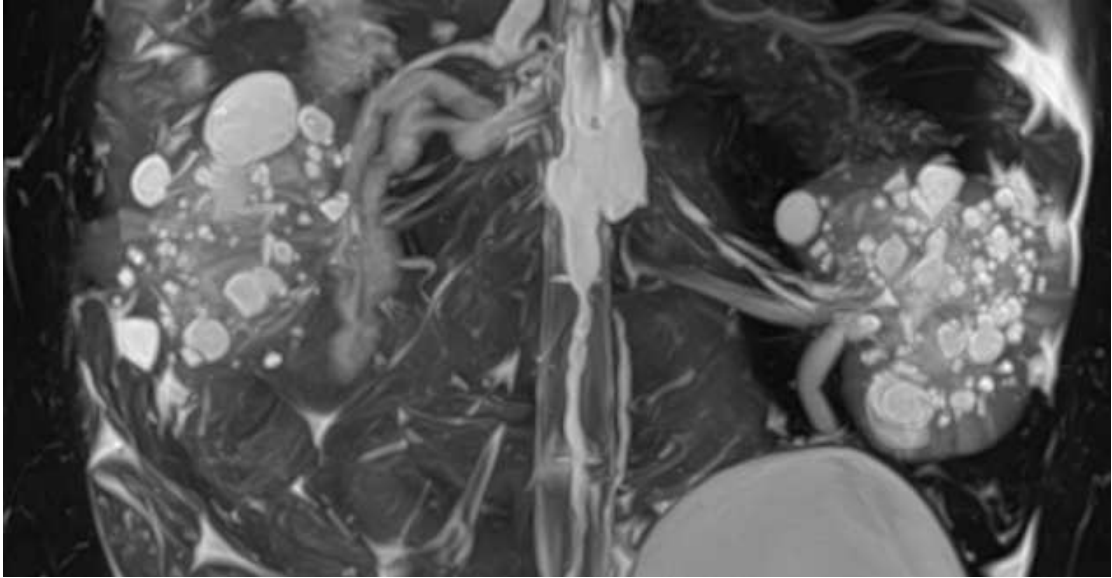


Figure 1: T2-weighted MRI image acquired in November 2023 ($TE = 600$ ms). This baseline MRI dataset served as the reference dataset for subsequent cyst segmentation and longitudinal comparison. The standardized acquisition and analysis workflow provides a methodological basis for future investigations of cyst-level imaging analysis in larger cohorts.

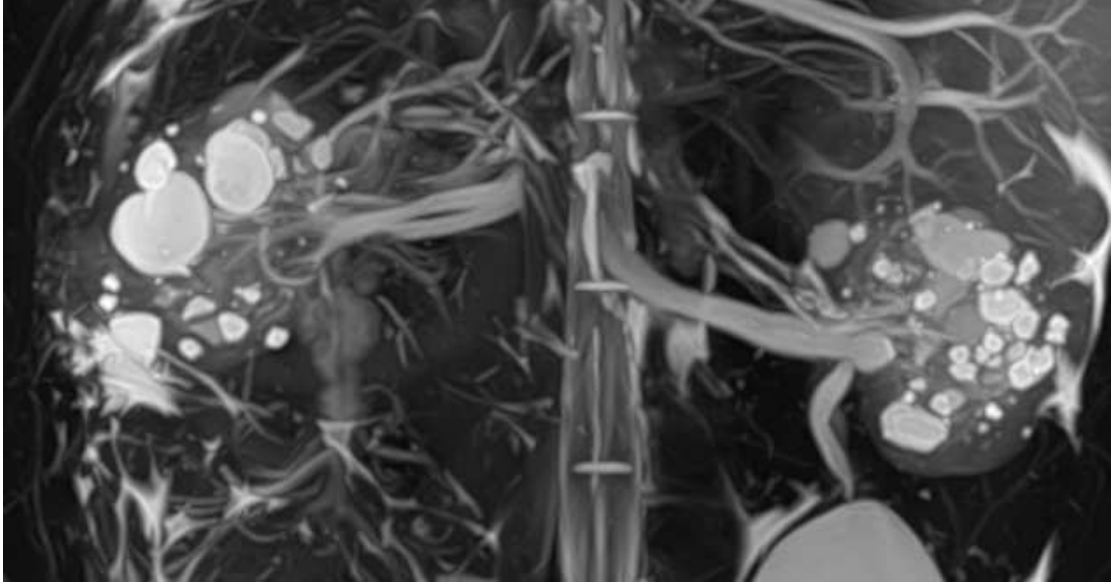


Figure 2: T2-weighted MRI image acquired in November 2024 ($TE = 600$ ms). Direct comparison with Figure 1 illustrates the longitudinal consistency of MRI acquisition and the application of the standardized analysis workflow across annual follow-up imaging. The comparison demonstrates the feasibility of applying a consistent cyst-level imaging framework over time and provides a basis for future cyst-level imaging studies in larger cohorts.

Segmentation Results from Two Time Points. Using 3D Slicer, segmentation of the polycystic kidney was performed to visualize structural changes, as illustrated in Figures 3–6.

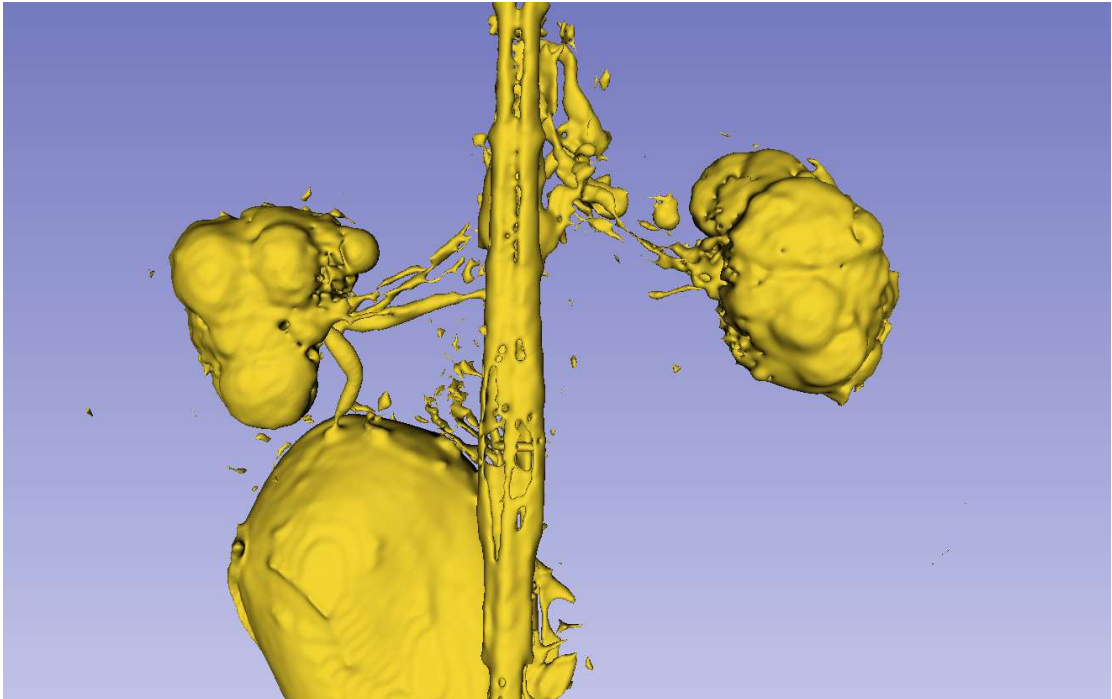


Figure 3: Renal Segmentation Results acquired in November 2023 ($TE = 100$ ms). Three-dimensional reconstruction of the renal structures was performed using the standardized segmentation workflow described in the Methods section. This visualization illustrates the application of the MRI-based segmentation workflow for structural assessment.

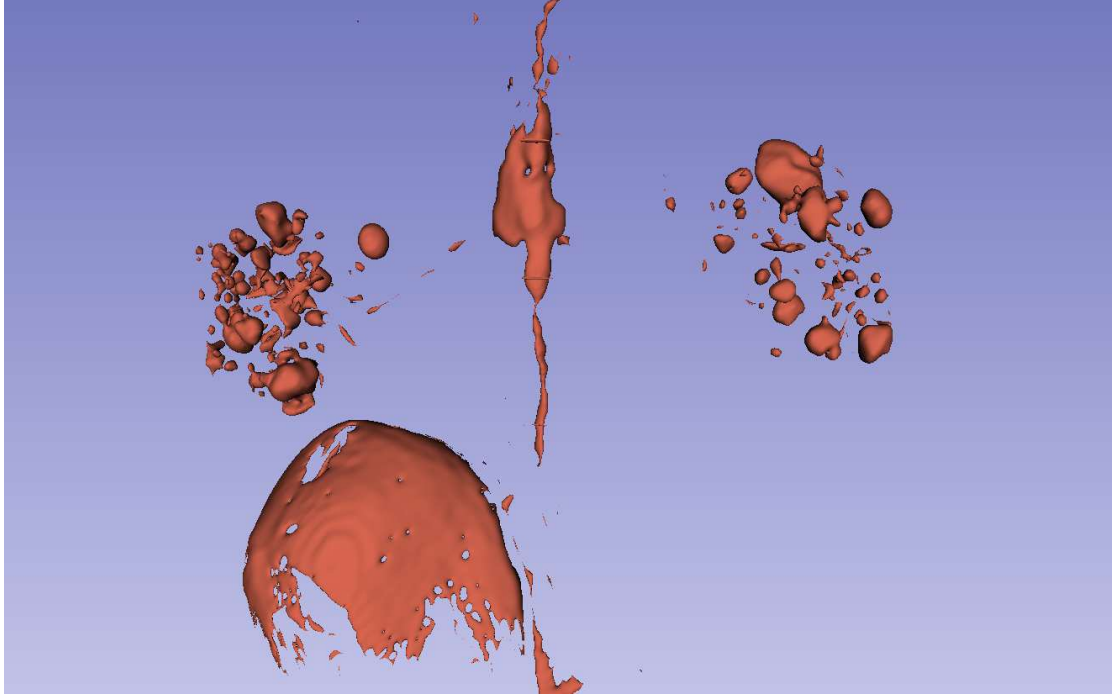


Figure 4: Cyst Segmentation Results acquired in November 2023 (TE = 100 ms). Cyst-level three-dimensional reconstruction was performed using the standardized segmentation workflow described in the Methods section. This visualization illustrates the application of MRI-based cyst segmentation for structural characterization of individual renal cysts.

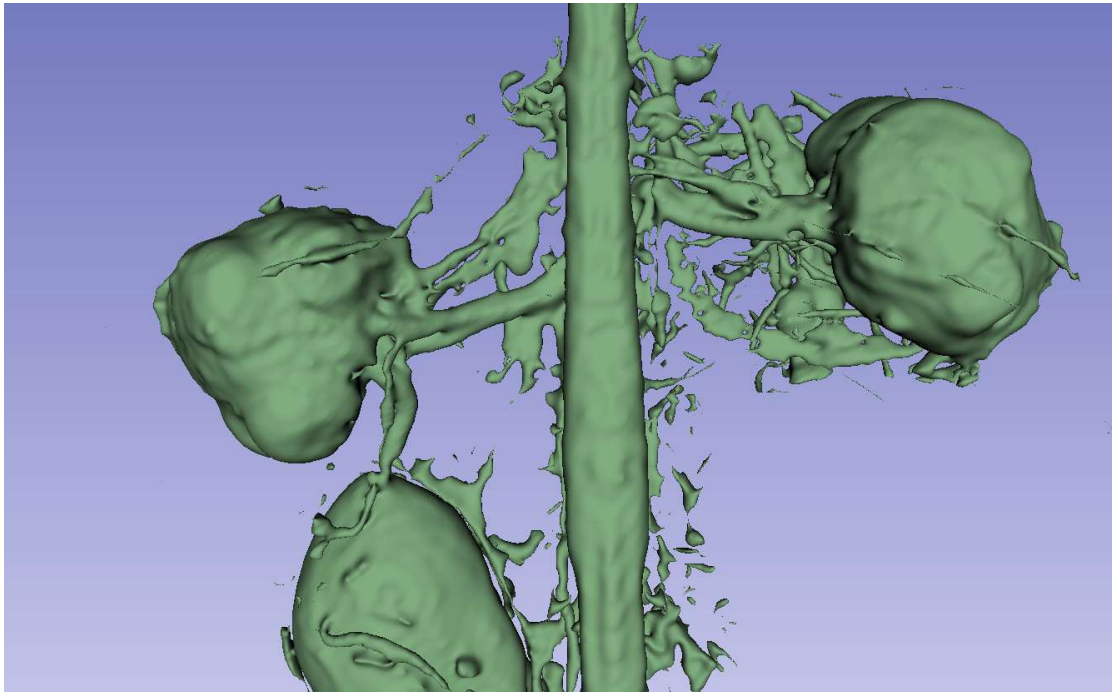


Figure 5: Renal Segmentation Results acquired in November 2024 (TE = 100 ms). Three-dimensional reconstruction of the renal structures was performed using the standardized segmentation workflow described in the Methods section. This visualization illustrates the application of the MRI-based segmentation workflow for structural assessment.

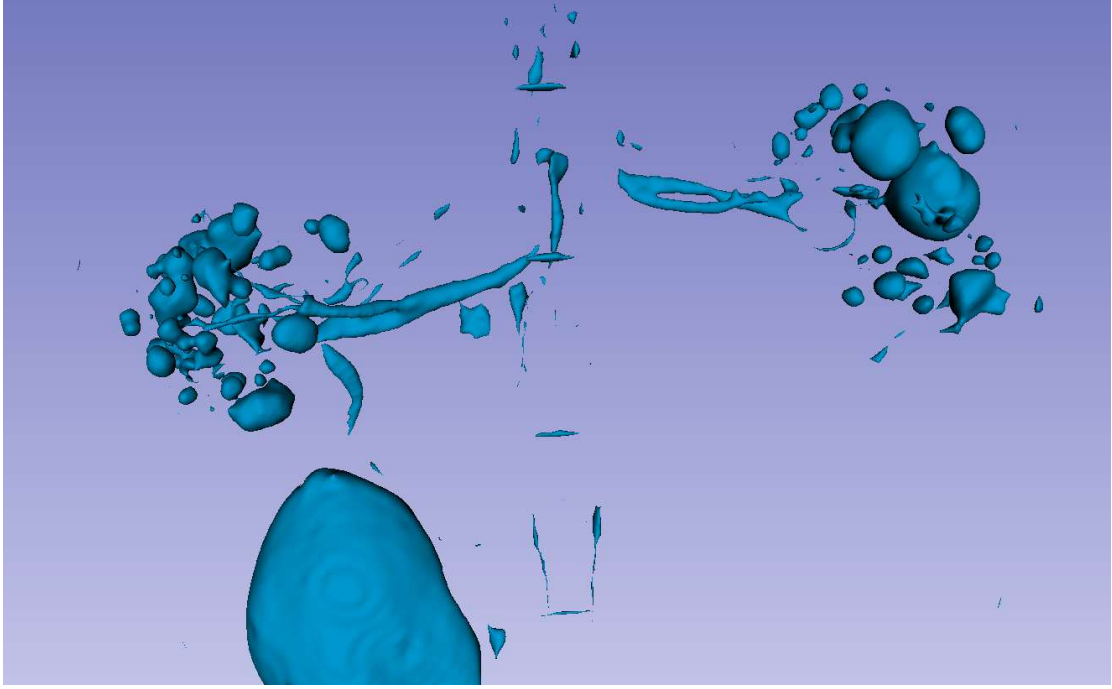


Figure 6: Cyst Segmentation Results acquired in November 2024 (TE = 100 ms). Cyst-level three-dimensional reconstruction was performed using the standardized segmentation workflow described in the Methods section. This visualization illustrates the application of MRI-based cyst segmentation for structural characterization of individual renal cysts.

Quantification of Renal Cyst Volumes. The three largest cysts in both the left and right kidneys were identified, and their individual volumes were measured (Tables 1–4).

Notable volume growth was observed in the cysts of the right kidney, whereas those in the left kidney remained relatively stable.

Table 1: Quantitative Analysis of the Three Largest Right Renal Cysts: Volume and Voxel Count acquired in November 2023 (TE = 600 ms)

Rank	Voxel Count	Volume (mm ³)
1	10610	359.7
2	2778	94.2
3	2020	68.5

The spatial locations and morphologies of the three largest renal cysts are shown in Figures 7 and 8.

Several cysts exhibited morphological changes suggestive of coalescence with adjacent cysts. Although their structural boundaries appeared less distinct, this observation reflects structural coalescence on MRI and does not provide evidence of, nor exclude the possibility of, luminal communication between cysts.

Table 2: Quantitative Analysis of the Three Largest left Renal Cysts: Volume and Voxel Count acquired in November 2023 (TE = 600 ms)

Rank	Voxel Count	Volume (mm ³)
1	6046	205.0
2	2704	91.7
3	1703	57.7

Table 3: Quantitative Analysis of the Three Largest Right Renal Cysts: Volume and Voxel Count acquired in November 2024 (TE = 600 ms)

Rank	Voxel Count	Volume (mm ³)
1	15772	534.7
2	8470	287.2
3	3634	123.2

Table 4: Quantitative Analysis of the Three Largest left Renal Cysts: Volume and Voxel Count acquired in November 2024 (TE = 600 ms)

Rank	Voxel Count	Volume (mm ³)
1	4180	141.7
2	2769	93.9
3	1686	57.2

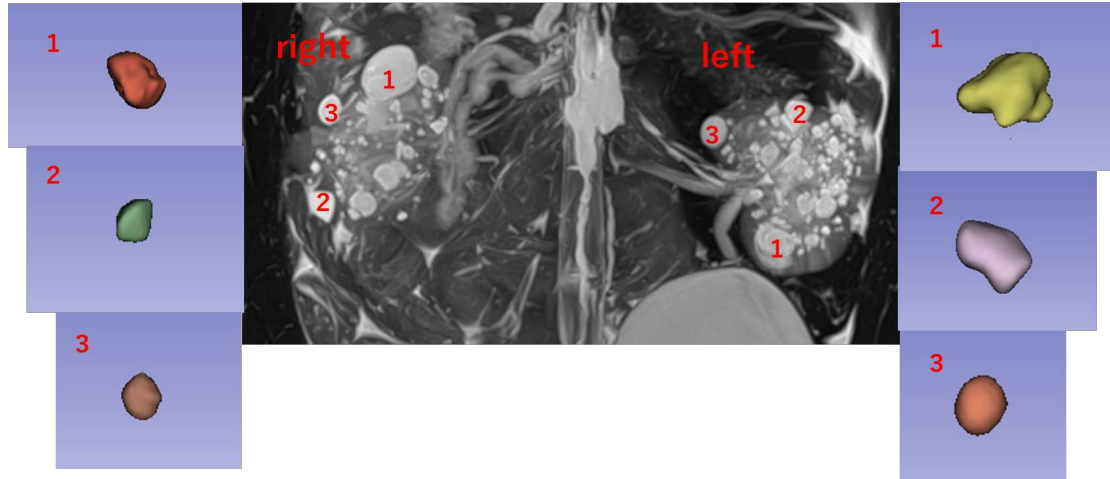


Figure 7: Spatial Location and Morphology of the Three Largest Renal Cysts (November 2023 MRI). The three largest cysts in each kidney were identified and segmented using the standardized workflow described in the Methods section. Their spatial distribution and three-dimensional morphology are shown relative to the corresponding renal anatomy.

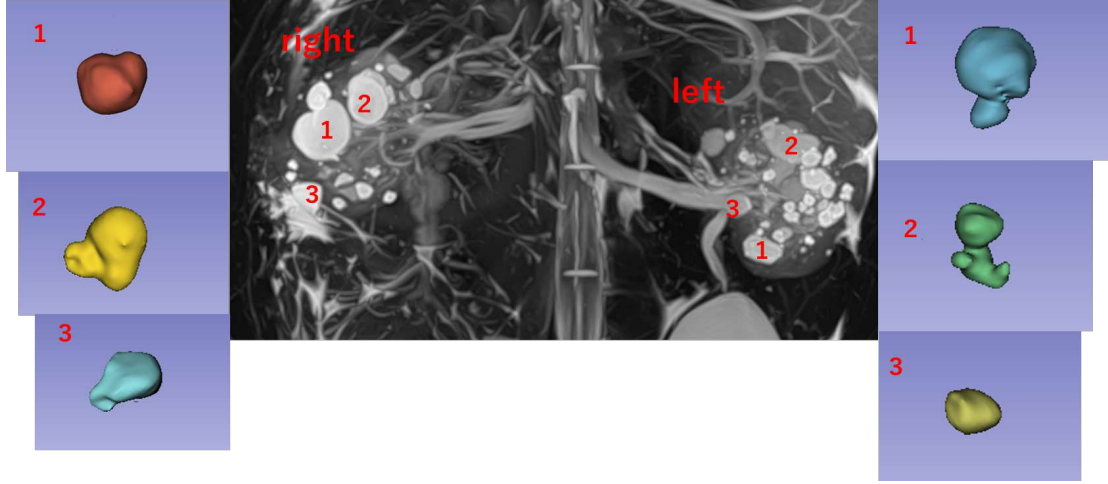


Figure 8: Spatial Location and Morphology of the Three Largest Renal Cysts (November 2024 MRI). The three largest cysts in each kidney were identified and segmented using the standardized workflow described in the Methods section. Their spatial distribution and three-dimensional morphology are shown relative to the corresponding renal anatomy.

Ultrasound-Based Cyst Progression. Ultrasound imaging for cyst monitoring was performed as follows.

Acquisition of 2D Ultrasound Images. Ultrasound examinations were performed in Aiko, a Persian cat diagnosed with polycystic kidney disease (PKD), over a two-year period to monitor renal cyst progression. Serial 2D ultrasound images were acquired at multiple timepoints during this period.

Quantification of Segmented Renal Cyst Areas. Segmentation of the polycystic kidneys was performed using 3D Slicer to visualize temporal changes in cyst area. The largest cyst in each of the left and right kidneys was identified and measured individually at each time point (Table 5 and 6).

Figure 9 presents a time-course analysis of renal cyst area in a Persian cat affected by PKD. Area growth appeared to be present in the cysts of the right kidney, while those in the left remained relatively stable.

Table 5: Quantitative Analysis of the Largest Cyst in the Right Kidney: Area and Pixel Count

Date	Pixel Count	spacing (mm)	Area (mm ²)
2023-03-15	6368	0.06944	30.7
2023-04-26	8187	0.06944	39.5
2023-11-15	6930	0.0868056	52.2
2024-06-01	23463	0.06944	113.1
2024-08-14	14254	0.0608	52.7
2025-02-23	14056	0.06944	67.8

Table 6: Quantitative Analysis of the Largest Cyst in the Left Kidney: Area and Pixel Count

Date	Pixel Count	spacing (mm)	Area (mm ²)
2023-03-15	2591	0.0868056	19.5
2023-04-26	2167	0.0868056	16.3
2023-11-15	1985	0.0868056	15.0
2024-06-01	2700	0.0868056	20.3
2025-02-23	2138	0.06944	10.3

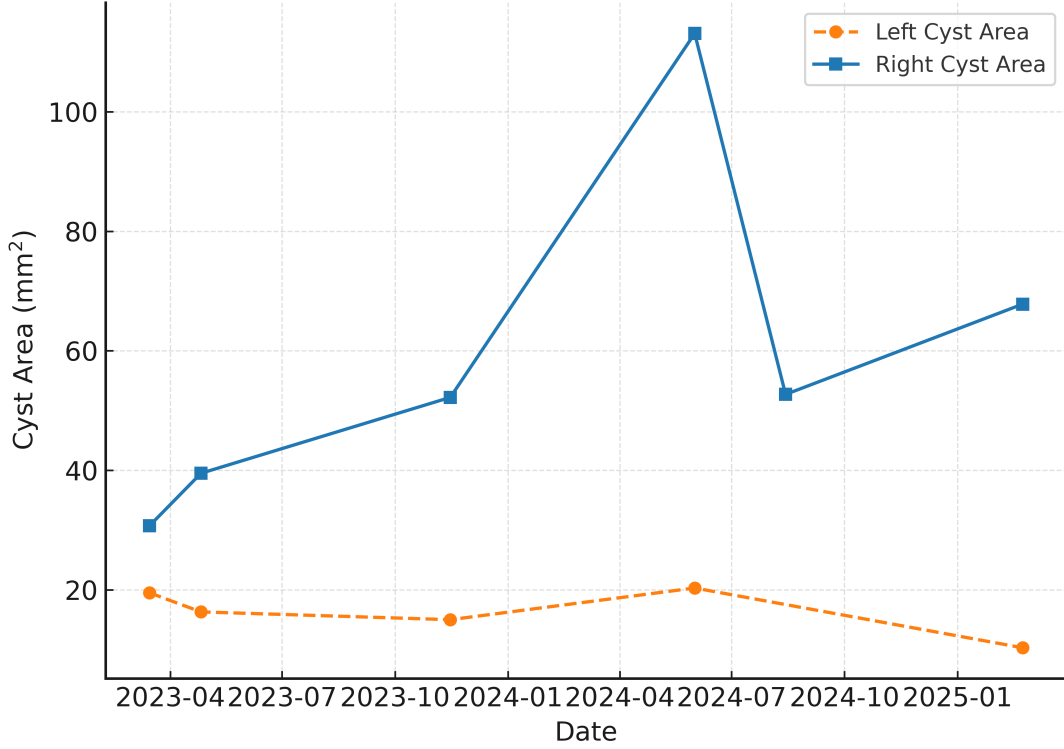


Figure 9: Time-course analysis of renal cyst area in a Persian cat affected by polycystic kidney disease (PKD). Serial two-dimensional ultrasound measurements showed an overall increasing trend in right renal cyst area, whereas left renal cyst area remained relatively stable or decreased over the observation period. Given the measurement variability of 2D ultrasound, these values are interpreted as directional trends rather than precise quantitative estimates, and short-term fluctuations should be interpreted with caution.

Together, these MRI and ultrasound results demonstrate complementary spatial and temporal perspectives on cyst dynamics. While MRI provides high-resolution volumetric precision to detect structural remodeling, ultrasound offers high-frequency temporal monitoring that captures short-term fluctuations. Integrating these complementary modalities allows the framework to identify not only asymmetric volumetric progression but also morphological transitions such as cyst coalescence, setting the stage for structural coalescence analysis in the following section.

In addition to quantitative area trends, a representative ultrasound frame acquired on February 23, 2025, showed a heart-shaped cyst configuration with loss of the intervening wall between

two adjacent right renal cysts (Figure 10). This morphology is consistent with structural coalescence—that is, the persistent loss of visible boundaries between adjacent cysts, as defined by MRI and not implying luminal communication—and is shown for illustrative purposes to visually support the MRI-defined findings described below.

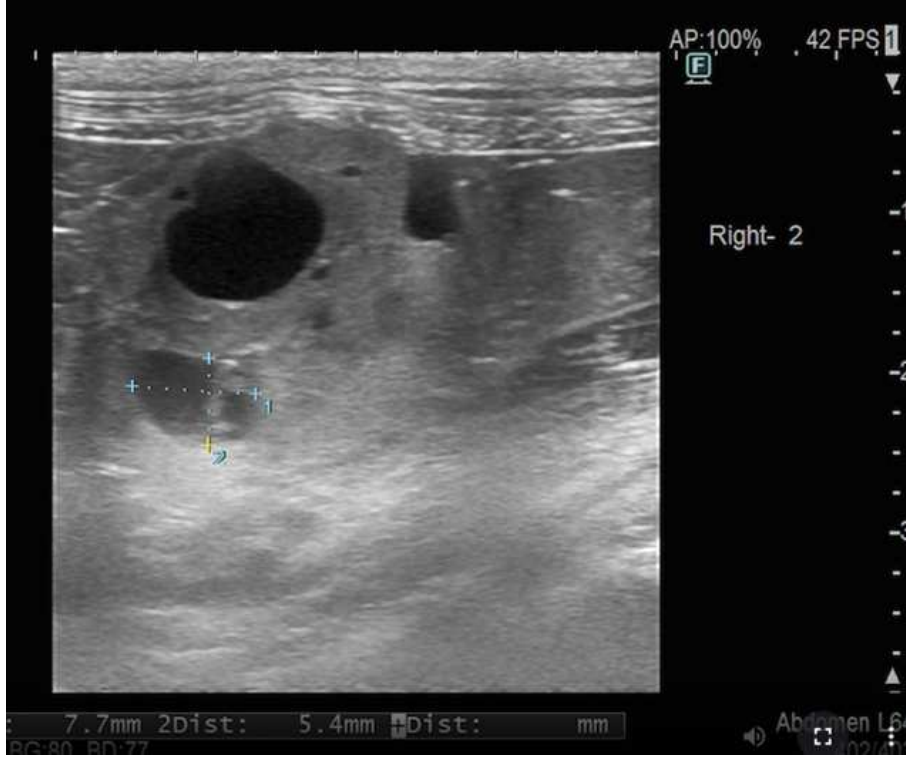


Figure 10: Illustrative ultrasound image showing a heart-shaped cyst configuration consistent with structural coalescence. Ultrasound frame (February 23, 2025) from the right kidney showing loss of the intervening echogenic wall between two adjacent cysts and a characteristic heart-shaped contour. This image is shown for illustrative purposes to provide visual support for MRI-defined structural coalescence and was not used as a diagnostic criterion. In this study, structural coalescence is defined on MRI as the persistent loss of visible boundaries between adjacent cysts and does not imply luminal communication. Image acquired at Grace Animal Hospital (Tokyo, Japan) under standardized linear-probe conditions.

Notably, the representative ultrasound frame (Figure 10) provides intuitive visual support for MRI-defined structural coalescence, highlighting the complementary strength of dual-modality integration and enhancing interpretability for future validation studies.

MRI-Observed Structural Coalescence Events. MRI observations revealed the loss of visible boundaries between adjacent cysts, consistent with MRI-defined structural coalescence (Figures 7 and 8). These findings were exclusively defined by MRI as the reference modality for structural assessment. Ultrasound, acquired at a higher temporal frequency, showed short-term fluctuations in cyst area during the same period; however, due to the inherent measurement

variability of 2D ultrasound, these fluctuations were not used to define structural coalescence. Instead, ultrasound served only to provide supportive temporal context, while MRI remained the sole determinant for structural coalescence identification.

Together, these results demonstrate that the integrated MRI–ultrasound framework can capture both volumetric progression and structural remodeling of renal cysts at the individual level. The significant enlargement of right-sided cysts, the relative stability of the left kidney, and the MRI-based identification of structural coalescence collectively reveal that cyst dynamics in feline PKD are heterogeneous across both kidneys and over time. By combining high-resolution MRI with high-frequency ultrasound, this longitudinal approach provides complementary spatial and temporal insights, enabling earlier detection of unilateral acceleration that might otherwise remain undetected. These findings provide a methodological foundation for future multi-center validation and serve as a bridge to the subsequent discussion on clinical and translational implications.

Discussion

Integrated MRI–US Analysis, Key Benefits and Broader Insights. In this study, MRI-defined structural coalescence between adjacent cysts is not proposed as a validated endpoint, but rather as a candidate imaging feature that warrants further evaluation in larger and multi-center cohorts.

Within this context, the value of MRI-defined coalescence emerges from the complementary integration of MRI and ultrasound, which provides both structural specificity and temporal context for interpreting cyst-level changes.

The present study demonstrates that integrating volumetric MRI with serial ultrasound enables a more sensitive and interpretable assessment of asymmetric cyst progression than volumetric MRI alone, by combining high-resolution structural precision with high-frequency temporal monitoring. While MRI remains the gold standard for volumetric quantification and morphological assessment, its limited sampling frequency restricts the ability to contextualize short-term fluctuations. In contrast, ultrasound provides frequent temporal information that complements MRI-based findings and enhances longitudinal interpretability when interpreted as directional trends rather than absolute measurements.

Previous human studies have established MRI-derived total kidney volume (TKV) as a validated surrogate endpoint for disease progression in autosomal dominant polycystic kidney disease

(ADPKD) [1–4,27]. Comparative studies further indicate that ultrasound-based measurements can approximate MRI-derived kidney volumes with acceptable accuracy under standardized conditions [19,20]. In parallel, advances in automated and deep learning-based segmentation have confirmed the reproducibility and clinical feasibility of MRI-based volumetric analysis in ADPKD [30–32]. Notably, the successful clinical deployment of AI-assisted MRI-derived TKV measurement in real-world radiology practice further supports the robustness and translational readiness of such volumetric frameworks [33].

Beyond kidney-level volumetrics, recent methodological advances have enabled cyst-level segmentation and quantification in human ADPKD using semantic segmentation approaches [25], establishing a precedent for extending cyst-centered analyses across species. Within this context, the present feline PKD case demonstrates that cyst-level dynamics—including growth heterogeneity, laterality, and structural remodeling—can be captured through a standardized MRI-US integration pipeline. Importantly, the focus of this study is not algorithmic innovation itself, but the methodological integration of modalities in a longitudinal framework that preserves interpretability and methodological consistency.

For ultrasound imaging, prior work has shown that fully automated boundary regression and classification networks can achieve robust renal segmentation performance in clinical datasets [14], supporting the feasibility of incorporating advanced ultrasound analytics into longitudinal PKD monitoring. Moreover, emerging techniques such as ultrasound localization microscopy (ULM) have demonstrated the ability to visualize renal microvasculature and perfusion with super-resolution precision in experimental and clinical settings [15,34–36]. Although these techniques were not applied in the present study, their reported performance highlights the potential for future expansion of multimodal PKD imaging frameworks beyond structural volumetry, complementing cyst-level morphological analysis with vascular and perfusion-related biomarkers. In addition, advanced diagnostic imaging approaches, including PET/CT for detecting cyst-related complications such as infection, have been reported as clinically actionable endpoints in ADPKD [37], further underscoring the evolving role of multimodal imaging in cystic kidney diseases.

Within veterinary medicine, prior feline PKD studies have established the genetic basis of the disease and demonstrated the feasibility of longitudinal imaging using MRI or ultrasound independently [17,18]. Importantly, our feline case aligns with these genetic and imaging foundations, while extending them by integrating longitudinal MRI and ultrasound at the cyst level.

However, systematic longitudinal integration of these modalities and kidney-specific asymmetry in cyst progression have not been previously documented in cats. The present study provides longitudinal evidence of marked right–left asymmetry in cyst progression, with sustained enlargement and structural remodeling observed predominantly in the right kidney, while the left kidney remained stable or showed regression in cyst burden.

Morphological changes suggestive of cyst coalescence were identified exclusively on MRI, defined as the persistent loss of visible boundaries between adjacent cysts. Ultrasound was intentionally not used to define structural coalescence events due to its lower spatial resolution and higher measurement variability, and instead served as a supplementary modality to provide temporal context. This conservative definition minimizes overinterpretation and ensures that structural coalescence is treated as a structural imaging phenomenon rather than a physiological assessment of cyst communication.

Methodologically, the integrated MRI–US framework addresses the inherent trade-offs of each modality: MRI offers anatomical precision and reproducibility but is costly and infrequently acquired, whereas ultrasound allows frequent monitoring but lacks volumetric accuracy. By combining these complementary strengths, the present workflow enables high-frequency, high-precision longitudinal monitoring without increasing procedural burden. Importantly, the novelty of this approach lies in its cyst-centered perspective, establishing individual cyst growth, asymmetry, and structural remodeling as candidate imaging features that extend beyond traditional kidney-level volumetrics.

From a translational perspective, this framework provides a conceptual and methodological bridge to human ADPKD research. Although systematic longitudinal MRI–US integration has not yet been fully established in human cohorts, the present feline proof-of-concept demonstrates feasibility and interpretability of this multimodal approach, while future studies are required to evaluate its reproducibility and broader applicability. In veterinary practice, early identification of unilateral acceleration may prompt targeted monitoring or intervention strategies. In human ADPKD, where disease-modifying therapies such as vasopressin V2 receptor antagonists are employed, kidney-specific and cyst-level imaging endpoints may support more personalized monitoring and trial design, in alignment with the imaging biomarker framework advocated by recent KDIGO guidelines [11].

Asymmetric Cyst Progression in Feline PKD. Previous studies in feline polycystic kidney disease (PKD) have established the genetic basis (PKD1 mutations) and demonstrated the progressive enlargement of renal cysts detectable by MRI or ultrasound at single time points. However, few investigations have integrated both imaging modalities in a longitudinal framework, and kidney-specific asymmetry in cyst progression has not been extensively characterized in cats.

In this study, longitudinal observations of asymmetric cyst progression in feline PKD are presented, characterized by marked enlargement in the right kidney while the left kidney remained stable or decreased in cyst burden. Furthermore, our analysis revealed morphological changes suggestive of cyst coalescence, highlighting a potential mechanism of accelerated expansion.

These findings underscore the novelty of combining volumetric MRI with serial ultrasound to capture both long-term progression and short-term fluctuations, providing a methodological framework for future studies of unilateral disease acceleration.

Comparative Perspective: Structural Coalescence and Imaging Biomarkers in Human ADPKD. While structural coalescence of cysts has not been systematically characterized in human ADPKD, imaging-based predictors of disease progression—including cyst morphology and connectivity—have been recognized as important candidate biomarkers [38]. Longitudinal MRI studies have quantitatively documented continuous cyst and kidney enlargement and their association with functional decline in human ADPKD [4]. These findings collectively suggest that structural remodeling processes accompanying cyst expansion may contribute to accelerated disease progression. By capturing analogous morphological transformations in a standardized MRI-US framework, our study provides empirical support for the concept that cyst coalescence can be considered a measurable imaging phenomenon relevant to progression dynamics. Importantly, ultrasound served as a complementary modality providing higher temporal sampling for alignment with MRI findings, but structural coalescence events in this study were strictly defined by MRI as the reference modality for structural assessment. Imaging-defined coalescence should be interpreted as a morphological surrogate marker and does not constitute a physiological assessment of cyst-to-cyst communication.

Interpretation of MRI Findings. This longitudinal MRI analysis revealed a clear asymmetry in cyst progression between the right and left kidneys, with the right kidney exhibiting a sustained volumetric increase in its largest cysts, while the left kidney remained comparatively

stable. Morphological changes suggestive of cyst coalescence were observed, with some cyst walls appearing less distinct over time. Such fusion-like events result in structural changes to the cysts, potentially affecting the renal parenchyma. The ability to visualize and quantify these morphological transformations over time highlights the value of high-resolution, volumetric MRI in characterizing disease dynamics.

Interpretation of Ultrasound Findings. Ultrasound imaging supported the MRI observations, revealing marked progression in the cyst area of the right kidney, while the left kidney remained relatively stable. While 2D US cannot provide reliable volumetric measurements due to its limited spatial resolution and greater variability, its higher temporal frequency offered supportive information on short-term fluctuations that complemented MRI-based findings. Thus, US should be regarded as a supplementary tool for monitoring trends rather than a primary determinant of structural coalescence or progression.

Measurement Variability in 2D Ultrasound. Ultrasound-based measurements of cyst area occasionally showed short-term spikes, such as the June 2024 value (113.1 mm²). Due to the high measurement variability of 2D ultrasound, these fluctuations cannot be considered evidence of biological change or structural coalescence. In this study, US data were therefore interpreted only as indicators of overall directional trends and not as determinative endpoints. MRI volumetry, with its superior precision and established reproducibility in volumetric assessment, was retained as the reference approach for defining structural coalescence events.

Clinical and Translational Implications. In veterinary medicine, early identification of unilateral acceleration in cyst growth could prompt targeted interventions to prevent bilateral deterioration. In human PKD, where vasopressin V2 receptor antagonists and other disease-modifying strategies are used, the framework proposed in this study could help personalize monitoring and interventions by identifying kidney-specific progression patterns. Thus, beyond its application in veterinary medicine, this framework also provides a theoretical foundation to guide the design of future imaging-based clinical trials in PKD, aligning with the recommendations outlined in the most recent KDIGO 2025 ADPKD guidelines [11].

Scope of Laterality Discussion. This study provides empirical evidence of asymmetry between the left and right kidneys, underscoring the significance of renal laterality in PKD progression. However, the full physiological interpretation of this asymmetry, including the underlying

mechanisms and its clinical implications, will need to be addressed in future research. Specifically, future work will focus on providing a theoretical framework for understanding kidney-specific asymmetry, with an emphasis on exploring how these mechanisms contribute to disease progression, leading to the development of more targeted therapeutic strategies.

Limitations. This study has several limitations that must be acknowledged. First, the analysis is based on a single case of feline PKD ($n=1$), which inherently limits the generalizability of the findings. However, this does not diminish the core contribution of the work, which was to present a methodological framework integrating MRI and ultrasound for longitudinal cyst analysis, rather than establishing epidemiological prevalence.

Despite the single-case design, methodological consistency was supported through standardized acquisition, segmentation, cross-modality alignment, and open-source pipelines, ensuring the findings are methodological rather than anecdotal. This proof-of-concept established a transferable platform for broader validation and identified MRI-defined structural coalescence between adjacent cysts as a candidate imaging feature associated with accelerated progression, highlighting its potential relevance for evaluating unilateral acceleration in PKD, which requires further validation.

Furthermore, although ultrasound provided high-frequency temporal information, its measurements were only interpreted as indicators of directional trends due to inherent variability. Structural coalescence events were strictly defined by MRI, which served as the reference modality for structural assessment. This conservative approach minimizes overinterpretation but underscores the need for further advances in US-based quantitative accuracy.

Future Directions. The following steps outline key areas of focus for advancing this research.

Reproducibility, Generalizability, and Sample Size Expansion. Future research will evaluate the applicability of this workflow across different cohorts, including veterinary and human ADPKD subjects, and will also test the generalizability of the workflow and evaluate its potential as a reliable imaging biomarker for disease progression. Although based on a single case ($n=1$), this study provides a foundation for future methodological validation. Expanding the sample size in future studies will validate and broaden the approach’s applicability.

Acknowledging Limitations and Advancing Methodology. Recognizing the limitations of the study will ensure transparency while emphasizing the methodological strengths of the frame-

work. This clarity will guide future investigations, supporting the expansion of the framework into multi-center and cross-species research.

Integration with Biomarker-Driven Stratification and Coalescence as a Biomarker for Early Intervention. Integrating the imaging approach with biomarker-driven stratification (e.g., vasopressin dynamics, plasma copeptin) will facilitate the development of a platform for early intervention strategies, improving clinical trial designs and enabling personalized PKD treatments. Future studies will also focus on validating coalescence as a reliable biomarker for disease progression and exploring its potential as a surrogate endpoint in clinical trials. This combined approach will enhance PKD treatment outcomes through more precise and timely interventions.

Conclusion. This study demonstrates the feasibility of integrating MRI and ultrasound for longitudinal cyst analysis in feline PKD. Despite being based on a single case ($n=1$), the standardized acquisition, segmentation, and temporal alignment procedures supported methodological consistency, highlighting the methodological nature of the findings.

This framework provides a proof-of-concept approach to capture and quantify MRI-defined structural coalescence between adjacent cysts as a candidate imaging feature associated with cyst expansion that requires validation in larger cohorts. Recent clinical evidence has shown that cyst fraction outperforms TKV in predicting functional decline in human ADPKD patients [39], strengthening the translational bridge between feline PKD and human ADPKD. Advances in imaging biomarker research, including MRI radiomic studies, further validate our methodology, demonstrating high reproducibility of noncystic tissue characteristics in ADPKD patients [40]. Ultrasound-based kidney volume measurements correlate strongly with MRI-derived values (Spearman $r \approx 0.94$) [20], supporting ultrasound as a reliable, accessible method when MRI is not feasible. Reviews highlight ultrasonography’s emerging role in ADPKD diagnostics and monitoring, emphasizing both its practical utility and limitations [41]. These findings enhance confidence in our dual-modality approach and its translational relevance across both veterinary and human ADPKD research.

The standardized framework provides a foundation for future multi-center validation, supporting its potential applicability to human ADPKD research and monitoring. Structural coalescence events are defined by MRI, with ultrasound used for monitoring trends, highlighting the need for broader validation. This framework also may inform future PKD clinical trials by supporting the development of standardized endpoints and advancing translational nephrology, with

an ethical data-sharing plan that promotes reproducibility, transparency, and animal welfare considerations.

Note on intellectual property. Portions of the methodological framework described in this study are the subject of separate patent applications [42–46]. These citations are provided solely to disclose the existence of related intellectual property and do not constitute evidence of scientific novelty or validation. The present manuscript is limited to scientific evaluation and methodological assessment, while determinations of novelty and scope of protection are addressed independently through the patent system.

Methods

Study Design and Experimental Workflow. The study design consists of four main stages: (1) characterization of the study subject, a Persian cat diagnosed with PKD; (2) continuous subcutaneous fluid therapy under veterinary supervision; (3) longitudinal imaging using volumetric MRI at annual intervals and serial ultrasound examinations at multiple time points; and (4) integration of MRI and ultrasound datasets for temporal alignment and quantitative analysis.

An overview of the experimental workflow is provided in Figure 11. This flowchart summarizes the sequential steps of the methodology, from clinical management and data acquisition to multimodal analysis of cyst progression.

Study Subject. The study subject (Aiko) was a female Persian cat weighing approximately 3.2 kg and 4 years old as of 2025, diagnosed with autosomal dominant polycystic kidney disease (PKD), genetically confirmed at the Veterinary Medical Center of the University of Tokyo through testing for PKD1 mutations in 2022. It was a privately owned Persian cat maintained as a household companion animal and was not obtained from a research colony or breeding facility.

As part of the longitudinal follow-up, continuous subcutaneous fluid therapy was administered under veterinary supervision at home starting in 2022. Longitudinal imaging and clinical assessments were conducted throughout the observation period to document changes in cyst morphology and overall health status.

In February 2023, a ureteral anastomosis was performed on the left kidney following the detection of ureterolithiasis. Postoperative monitoring and imaging findings were recorded, but

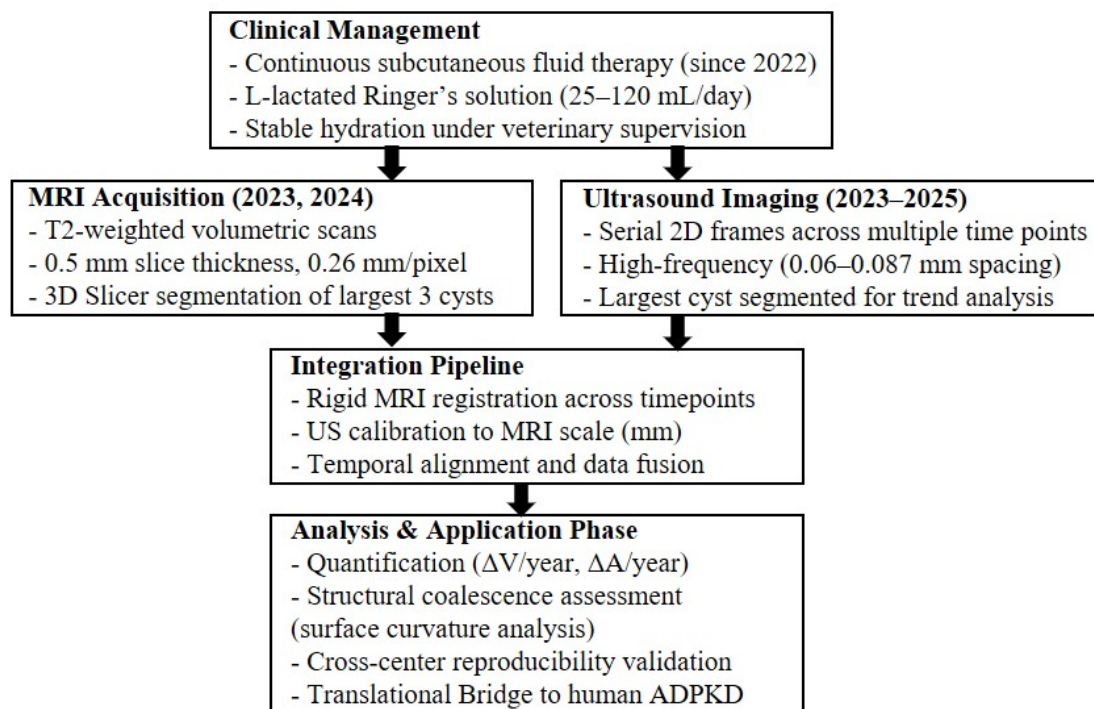


Figure 11: Overview of the experimental workflow integrating fluid therapy, MRI, and ultrasound into a standardized analytical pipeline. This standardized framework can serve as a basis for future multi-center validation, and its translational potential lies in adapting the workflow to human ADPKD trials and other renal diseases showing asymmetric progression.

detailed results are not included in this study.

In July 2023, an ovariohysterectomy was conducted after ovarian follicular cysts were identified by ultrasonographic and clinical evaluation.

Through ongoing management for PKD, the subject continued receiving subcutaneous fluid therapy, with regular imaging and clinical assessments to track the disease's progression.

Fluid Therapy. Subcutaneous fluid therapy was continuously administered under veterinary supervision from 2022 onward, using L-lactated Ringer's solution (Lactec Inj., Otsuka Pharmaceutical Factory, Japan). The daily infusion volume ranged from 25 to 120 mL and was adjusted according to the clinical condition (Table 7). Throughout the observation period from 2022 to 2025, the therapy was performed once or twice daily at home by the owner under veterinary supervision, and all administration records—including frequency and volume—were documented in detail.

The L-lactated Ringer's solution contained Na^+ 130 mEq/L, K^+ 4 mEq/L, Ca^{2+} 3 mEq/L, Cl^- 109 mEq/L, and L-lactate 28 mEq/L. This solution is isotonic or slightly hypotonic relative to plasma and is therefore not expected to significantly affect plasma osmolality. The recorded

hydration data were retained as part of the longitudinal clinical and imaging records.

Table 7: Chronological Record of Subcutaneous Fluid Therapy

Each row represents the initiation of a new fluid therapy protocol. Values were maintained until the next change.

Year-Month	Freq./Day	Vol./Session (mL)	Total/Day (mL)
2022-8	1	25	25
2023-3	1	50	50
2023-11	1	80	80
2024-5	2	60	120

MRI Acquisition and 3D Volume Analysis. MRI-based volumetric measurements were performed in accordance with existing imaging protocols for autosomal dominant polycystic kidney disease (ADPKD) [47]. Recent multi-center quality control studies have standardized the MRI-based total kidney volume (TKV) measurement protocol in ADPKD, emphasizing reproducibility across centers [48]. All image segmentation and volumetric quantification were consistent with the established quantitative imaging pipeline [49]. Furthermore, deep learning-based automated segmentation techniques have demonstrated the feasibility of automation in PKD imaging [50], and their clinical deployment has been confirmed [33].

MRI Acquisition. To evaluate the progression of polycystic kidney disease (PKD) in this case, two MRI examinations were conducted at a one-year interval at the Veterinary Medical Center of the University of Tokyo (Tokyo, Japan). Data acquisition was performed at this center, while data analysis was conducted by the author. T2-weighted MRI images were acquired in November 2023 and November 2024, with echo times (TE) of 100 ms and 600 ms. Each MRI volume consisted of 100 axial slices with a matrix size of 576×576 pixels, an in-plane resolution of 0.2604 mm/pixel, and a slice thickness of 0.5 mm.

MRI-based Volume Segmentation and Quantification. Renal cyst segmentation and volumetric quantification were performed using MRI datasets in 3D Slicer (version 5.8.1; www.slicer.org). Renal cysts were identified on T2-weighted images based on their high fluid signal intensity and anatomical location. The three largest cysts in each kidney were independently selected at each MRI time point and segmented using the Segment Editor module with intensity-based thresholding followed by manual refinement using paint and erase tools when necessary.

Cyst volumes and voxel counts were calculated using the Segment Statistics module. The same segmentation workflow and selection criteria were applied to both MRI datasets acquired in November 2023 and November 2024.

The quantified volumes were tabulated and compared over time between the left and right kidneys. In addition, spatial distribution and morphological changes in the cysts were visually presented using figures and tables.

Note that the three largest cysts were selected independently at each MRI time point; therefore, the analysis represents representative dominant cyst structures rather than longitudinal tracking of identical cysts.

Ultrasound Imaging and Cyst Segmentation. Between 2023 and 2025, two-dimensional (2D) ultrasound examinations were performed multiple times per year at Grace Animal Hospital (Tokyo, Japan) to monitor the progression of polycystic kidney disease (PKD). Each image had a matrix size of 1024×768 pixels, with in-plane pixel spacing ranging from 0.0608 mm to 0.0868 mm (Table 5 and 6). Data acquisition took place at Grace Animal Hospital, while the processing and analysis of the ultrasound data were performed by the author.

Ultrasound images were processed using 3D Slicer (v5.8.1; www.slicer.org), an open-source medical image analysis platform. Manual and semi-automated segmentation techniques were applied to delineate renal cysts. For consistency, only the largest cyst in each kidney was identified and quantified at each timepoint using the same selection criteria. Segmentation parameters, including thresholding and smoothing settings, were kept consistent across all sessions to enhance intra-study reproducibility, in accordance with recent methodological recommendations for PKD imaging reproducibility [12, 48, 49].

Note that the “largest cyst” refers to the cyst showing the greatest cross-sectional area at each timepoint, which may differ across scans. Thus, the same cyst was not necessarily tracked longitudinally, and the ultrasound data represent kidney-level directional trends rather than single-cyst trajectories.

MRI and Ultrasound Image Integration and Temporal Analysis. To achieve high-precision longitudinal analysis, an image integration framework was implemented.

Preprocessing of Multimodal Data. MRI and ultrasound (US) datasets were obtained as described above. All MRI datasets were imported into 3D Slicer version 5.8.1 (www.slicer.org) and aligned to a unified anatomical coordinate system through rigid registration across sequential scans. US images were also imported and calibrated using fiducial-based scaling, which converts pixel spacing into real-world dimensions (mm) and matches the physical scale of MRI

voxels. In this study, device calibration was assumed as a prerequisite of routine clinical use, and no additional system-level calibration was performed.

This calibration enabled MRI and US images to be analyzed within the same physical coordinate system for direct cross-modality comparison.

Segmentation and Cyst Identification. Cyst segmentation was performed independently for MRI and US modalities. For MRI, semi-automated thresholding followed by manual refinement was applied to delineate cyst volumes. For US, the largest cyst in each kidney was manually annotated at each timepoint, followed by contour smoothing. Segmentation settings (threshold range, smoothing kernel, and morphological filters) were kept constant across all timepoints to ensure reproducibility.

Temporal Alignment and Asymmetry Analysis. A three-step alignment process was implemented: (1) rigid registration between sequential MRI scans using vertebral landmarks; (2) scaling and translation correction for US images to match MRI anatomical coordinates; and (3) temporal mapping of cyst volumes and areas to a unified timeline. Differences in progression rates between the left and right kidneys were quantified as $\Delta V/\text{year}$ (MRI) and $\Delta A/\text{year}$ (US). Morphological coalescence tendencies were assessed through surface curvature analysis.

MRI-US Integration and Temporal Evaluation. MRI and US datasets were co-registered to a common anatomical reference frame. Scaling corrections were applied so that the US pixel spacing matched the MRI voxel size in millimeter units. This approach allowed volumetric ($\Delta V/\text{year}$) and planar ($\Delta A/\text{year}$) changes to be compared on the same physical scale. Coalescence-like morphological events were evaluated by analyzing curvature-based surface shape changes, consistent with previous longitudinal PKD imaging frameworks [50].

Coalescence Analysis. In this study, MRI-defined structural coalescence events were defined as findings where the boundaries between adjacent cysts are lost or blurred, based on a qualitative imaging-based assessment of cyst surface morphology. MRI was used as the reference modality for identifying these events, while ultrasound (US) provided supplementary time-series data for temporal alignment due to its lower spatial resolution and higher measurement variability.

In this context, structural coalescence refers to the persistent loss of visible boundaries between adjacent cysts on MRI without suggesting luminal communication or fluid continuity between the cysts.

Beyond structural coalescence identification, the integration of MRI and ultrasound enhances the tracking of disease progression by combining MRI’s structural precision with ultrasound’s temporal resolution. This multimodal approach improves sensitivity to early unilateral PKD progression and establishes a methodological foundation for longitudinal and cross-species PKD imaging studies.

Ethics statement. All procedures were conducted in accordance with institutional and national guidelines for animal care, and complied with the ARRIVE guidelines for reporting animal research [51]. The study subject was a privately owned cat (Aiko). Written informed consent was obtained from the owner (who is also an author) not only for diagnostic imaging and clinical care, but also for subsequent research use, data analysis, and publication of anonymized data. All procedures were performed as part of routine veterinary care, and clinical decisions were made independently of the research objectives. No experimental interventions beyond standard veterinary care were performed.

Ethical approval was not required because all procedures were part of routine veterinary care. This determination was made in accordance with generally accepted clinical practice standards applied at veterinary institutions, under which routine diagnostic imaging and clinical management are not considered research activities requiring prior ethical approval.

Data availability

The datasets generated and/or analysed during the current study are not publicly available due to animal privacy considerations but are available from the corresponding author on reasonable request. Anonymized MRI and ultrasound imaging data, along with segmentation parameter files from 3D Slicer, can be shared for academic and non-commercial research purposes with the owner’s approval, in accordance with the informed consent obtained.

In addition, while the datasets are not publicly available at present due to privacy considerations, anonymized datasets will be considered for controlled sharing in future international multi-center validation studies, in order to ensure reproducibility and broader validation of the findings.

References

- [1] Irazabal, M. V., Rangel, L. J., Bergstralh, E. J., Osborn, S. L., Harmon, A. J., Sundsbak, J. L. *et al.* Imaging classification of autosomal dominant polycystic kidney disease: a simple

- model for selecting patients for clinical trials. *J. Am. Soc. Nephrol.* **26**, 160–172 (2015). <https://doi.org/10.1681/ASN.2013101138>.
- [2] Bae, K. T., Shi, T., Tao, C., Yu, A. S. L., Torres, V. E., Perrone, R. D. *et al.* Expanded imaging classification of autosomal dominant polycystic kidney disease. *J. Am. Soc. Nephrol.* **31**, 1640–1651 (2020). <https://doi.org/10.1681/ASN.2019101121>.
- [3] Yu, A. S. L., Shen, C., Landsittel, D. P., Harris, P. C., Torres, V. E., Mrug, M. *et al.* Baseline total kidney volume and the rate of kidney growth are associated with chronic kidney disease progression in autosomal dominant polycystic kidney disease. *Kidney Int.* **93**, 691–699 (2018). <https://doi.org/10.1016/j.kint.2017.09.027>.
- [4] Grantham, J. J., Torres, V. E., Chapman, A. B., Guay-Woodford, L. M., Bae, K. T., King, B. F. *et al.* Volume progression in polycystic kidney disease. *N. Engl. J. Med.* **354**, 2122–2130 (2006). <https://doi.org/10.1056/NEJMoa054341>.
- [5] Li Cavoli, G., Finazzo, F., Mongiovi, R., Bono, L., Ferrantelli, A., Azzolina, V. *et al.* The imaging of total kidney volume in ADPKD. *Braz. J. Nephrol.* **42**, 384–385 (2020). <https://doi.org/10.1590/2175-8239-JBN-2019-0218>.
- [6] Caroli, A. & Kline, T. L. Abdominal imaging in ADPKD: beyond total kidney volume. *J. Clin. Med.* **12**, 5133 (2023). <https://doi.org/10.3390/jcm12155133>.
- [7] Ghanem, A., Borghol, A. H., Debeh, F. G. M., Paul, S., AlKhatib, B., Harris, P. C. *et al.* Biomarkers of kidney disease progression in ADPKD. *Kidney Int. Rep.* **9**, 2860–2882 (2024). <https://doi.org/10.1016/j.ekir.2024.07.012>.
- [8] Wigerinck, S., Gregory, A. V., Smith, B. H., Iliuta, I.-A., Hanna, C., Chedid, M. *et al.* Evaluation of advanced imaging biomarkers at kidney failure in patients with ADPKD: a pilot study. *Clin. Kidney J.* **16**, 1691–1700 (2023). <https://doi.org/10.1093/ckj/sfad114>.
- [9] Yilmaz, K., Saygili, S., Canpolat, N., Akgun-Dogan, O., Yuruk Yildirim, Z. N., Cicek-Oksuz, R. Y. *et al.* Magnetic resonance imaging based kidney volume assessment for risk stratification in pediatric autosomal dominant polycystic kidney disease. *Front. Pediatr.* **12**, 1357365 (2024). <https://doi.org/10.3389/fped.2024.1357365>.
- [10] Prince, M. R., Weiss, E. & Blumenfeld, J. D. Size matters: how to characterize

- ADPKD severity by measuring total kidney volume. *J. Clin. Med.* **12**, 6068 (2023). <https://doi.org/10.3390/jcm12186068>.
- [11] Kidney Disease: Improving Global Outcomes (KDIGO) ADPKD Work Group. KDIGO 2025 Clinical Practice Guideline for the Evaluation, Management, and Treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD). *Kidney Int.* **107**(Suppl. 2S), S1–S239 (2025). <https://doi.org/10.1016/j.kint.2024.07.009>.
- [12] Fedorov, A., Beichel, R., Kalpathy-Cramer, J., Finet, J., Fillion-Robin, J.-C., Pujol, S. *et al.* 3D Slicer as an image computing platform for the Quantitative Imaging Network. *Magn. Reson. Imaging* **30**, 1323–1341 (2012). <https://doi.org/10.1016/j.mri.2012.05.001>.
- [13] Fedorov, A., Clunie, D., Ulrich, E., Bauer, C., Wahle, A., Brown, B. *et al.* DICOM for quantitative imaging biomarker development: a standards-based approach to sharing clinical data and structured PET/CT analysis results in head and neck cancer research. *PeerJ* **4**, e2057 (2016). <https://doi.org/10.7717/peerj.2057>.
- [14] Yin, S., Peng, Q., Li, H., Zhang, Z., You, X., Fischer, K. *et al.* Automatic kidney segmentation in ultrasound images using subsequent boundary distance regression and pixelwise classification networks. *Med. Image Anal.* **60**, 101602 (2020). <https://doi.org/10.1016/j.media.2019.101602>.
- [15] Qiu, L., Zhang, J., Yang, Y., Zhang, H., Lee, F.-F. & He, Q. *et al.* In vivo assessment of hypertensive nephrosclerosis using ultrasound localization microscopy. *Med. Phys.* **49**, 2295–2308 (2022). <https://doi.org/10.1002/mp.15583>
- [16] Schirrer, L., Marín-García, P. J. & Llobat, L. Feline polycystic kidney disease: an update. *Vet. Sci.* **8**, 269 (2021). <https://doi.org/10.3390/vetsci8110269>
- [17] Shitamori, F., Nonogaki, A., Motegi, T., Matsumoto, Y., Sakamoto, M., Tanizawa, Y. *et al.* Large-scale epidemiological study on feline autosomal dominant polycystic kidney disease and identification of novel *PKD1* gene variants. *J. Feline Med. Surg.* **25**, 1098612X231185393 (2023). <https://doi.org/10.1177/1098612X231185393>
- [18] Yu, Y., Shumway, K. L., Matheson, J. S., Edwards, M. E., Kline, T. L. & Lyons, L. A. Kidney and cystic volume imaging for disease presentation and progression in the cat

- autosomal dominant polycystic kidney disease large animal model. *BMC Nephrol.* **20**, 259 (2019). <https://doi.org/10.1186/s12882-019-1448-1>
- [19] Akbari, P., Nasri, F., Deng, S. X., Khowaja, S., Lee, S. H., Warnica, W. *et al.* Total kidney volume measurements in ADPKD by 3D and ellipsoid ultrasound in comparison with magnetic resonance imaging. *Clin. J. Am. Soc. Nephrol.* **17**, 827–834 (2022). <https://doi.org/10.2215/CJN.14931121>
- [20] Fernandez, J. M., Hernández-Socorro, C. R., Robador, L. O., Rodríguez-Esparragón, F., Medina-García, D., Quevedo-Reina, J. C. *et al.* Ultrasound versus magnetic resonance imaging for calculating total kidney volume in patients with ADPKD: a real-world data analysis. *Ultrasound J.* **17**, 13 (2025). <https://doi.org/10.1186/s13089-025-00400-0>
- [21] Chookhachizadeh Moghadam, M., Aspal, M., He, X., Romano, D. J., Sharbat-daran, A., Hu, Z. *et al.* Deep learning-based liver cyst segmentation in MRI for autosomal dominant polycystic kidney disease. *Radiol. Adv.* **1**, umae014 (2024). <https://doi.org/10.1093/radadv/umae014>
- [22] Kim, Y., Bae, S. K., Cheng, T., Tao, C., Ge, Y., Chapman, A. B. *et al.* Automated segmentation of liver and liver cysts from bounded abdominal MR images in patients with autosomal dominant polycystic kidney disease. *Phys. Med. Biol.* **61**, 7864–7880 (2016). <https://doi.org/10.1088/0031-9155/61/22/7864>
- [23] Zhu, C., He, X., Blumenfeld, J. D., Hu, Z., Dev, H. Sattar, U. *et al.* A primer for utilizing deep learning and abdominal MRI imaging features to monitor autosomal dominant polycystic kidney disease progression. *Biomedicines* **12**, 1133 (2024). <https://doi.org/10.3390/biomedicines12051133>
- [24] Keshwani, D., Kitamura, Y. & Li, Y. Computation of total kidney volume from CT images in autosomal dominant polycystic kidney disease using multi-task 3D convolutional neural networks. Preprint at <https://doi.org/10.48550/arXiv.1809.02268> (2018).
- [25] Kline, T. L., Edwards, M. E., Fetzer, J., Gregory, A. V., Anaam, D., Metzger, A. J. *et al.* Automatic semantic segmentation of kidney cysts in MR images of patients affected by autosomal-dominant polycystic kidney disease. *Abdom. Radiol. (NY)* **46**, 1053–1061 (2021). <https://doi.org/10.1007/s00261-020-02748-4>

- [26] Torres, V. E. & Harris, P. C. Autosomal dominant polycystic kidney disease: the last 3 years. *Kidney Int.* **76**, 149–168 (2009). <https://doi.org/10.1038/ki.2009.128>
- [27] Kistler, A. D., Poster, D., Krauer, F., Weishaupt, D., Raina, S., Senn, O. *et al.* Increases in kidney volume in autosomal dominant polycystic kidney disease can be detected within 6 months. *Kidney Int.* **75**, 235–241 (2009). <https://doi.org/10.1038/ki.2008.558>
- [28] Edwards, M. E., Blais, J. D., Czerwiec, F. S., Erickson, B. J., Torres, V. E. & Kline, T. L. Standardizing total kidney volume measurements for clinical trials of autosomal dominant polycystic kidney disease. *Clin. Kidney J.* **12**, 71–77 (2019). <https://doi.org/10.1093/ckj/sfy078>
- [29] Zhu, C., Dev, H., Sharbatdaran, A., He, X., Shimonov, D., Chevalier, J. M. *et al.* Clinical quality control of MRI total kidney volume measurements in autosomal dominant polycystic kidney disease. *Tomography* **9**, 1341–1355 (2023). <https://doi.org/10.3390/tomography9040107>
- [30] Kline, T. L., Korfiatis, P., Edwards, M. E., Blais, J. D., Czerwiec, F. S., Harris, P. C. *et al.* Performance of an artificial multi-observer deep neural network for fully automated segmentation of polycystic kidneys. *J. Digit. Imaging* **30**, 442–448 (2017). <https://doi.org/10.1007/s10278-017-9978-1>
- [31] van Gastel, M. D. A., Edwards, M. E., Torres, V. E., Erickson, B. J., Gansevoort, R. T. & Kline, T. L. Automatic measurement of kidney and liver volumes from MR images of patients affected by autosomal dominant polycystic kidney disease. *J. Am. Soc. Nephrol.* **30**, 1514–1522 (2019). <https://doi.org/10.1681/ASN.2018090902>
- [32] Goel, A., Shih, G., Riyahi, S., Jeph, S., Dev, H., Hu, R. *et al.* Deployed deep learning kidney segmentation for polycystic kidney disease MRI. *Radiol. Artif. Intell.* **4**, e210205 (2022). <https://doi.org/10.1148/ryai.210205>
- [33] Potretzke, T. A., Korfiatis, P., Blezek, D. J., Edwards, M. E., Klug, J. R., Cook, C. J. *et al.* Clinical implementation of an artificial intelligence algorithm for magnetic resonance-derived measurement of total kidney volume. *Mayo Clin. Proc.* **98**, 689–700 (2023). <https://doi.org/10.1016/j.mayocp.2022.12.019>

- [34] Gao, J.-y. & Hou, C. Progresses and clinical application of super-resolution ultrasound imaging: a narrative review. *Ultrasound J.* **17**, 29 (2025). <https://doi.org/10.1186/s13089-025-00432-6>
- [35] McDermott, A., Panduro, N. S., Taghavi, I., Kjer, H. M., Sogaard, S. B., Nielsen, M. B. *et al.* Analysing the renal vasculature using super-resolution ultrasound imaging: considerations for clinical and research applications. *Diagnostics (Basel)* **15**, 1515 (2025). <https://doi.org/10.3390/diagnostics15121515>
- [36] Chen, Q., George, M. W., McMahon, B., Rosenthal, J. A., Kim, K. & Tan, R. J. Super-resolution ultrasound to assess kidney vascular changes in humans with kidney disease. *Am. J. Kidney Dis.* **85**, 393–395 (2025). <https://doi.org/10.1053/j.ajkd.2024.06.021>
- [37] Treglia, G., Albano, D., Rizzo, A., Bellasi, A., Glaudemans, A. W. J. M. & Gheysens, O. Performance of [^{18}F]FDG PET/CT in diagnosing cyst infections in patients with autosomal dominant polycystic kidney disease: a systematic review and a bivariate meta-analysis. *Diagnostics (Basel)* **14**, 1603 (2024). <https://doi.org/10.3390/diagnostics14151603>
- [38] Benz, E. G. & Hartung, E. A. Predictors of progression in autosomal dominant and autosomal recessive polycystic kidney disease. *Pediatr. Nephrol.* **36**, 2639–2658 (2021). <https://doi.org/10.1007/s00467-020-04869-w>
- [39] Karner, L. A., Arjune, S., Todorova, P., Maintz, D., Grundmann, F., Persigehl, T. *et al.* Cyst fraction as a biomarker in autosomal dominant polycystic kidney disease. *J. Clin. Med.* **12**, 326 (2023). <https://doi.org/10.3390/jcm12010326>
- [40] Lussana, F., Lanzarone, E., Villa, G., Mastropietro, A., Caroli, A. & Scalco, E. Reliability of radiomic analysis on multiparametric MRI for patients affected by autosomal dominant polycystic kidney disease. *Sci. Rep.* **15**, 16526 (2025). <https://doi.org/10.1038/s41598-025-99982-x>
- [41] Lee, W.-C., Cheng, B.-C., Lee, C.-T. & Liao, S.-C. Update on the application of ultrasonography in understanding autosomal dominant polycystic kidney disease. *J. Med. Ultrasound* **32**, 110–115 (2024). https://doi.org/10.4103/jmu.jmu.77_23
- [42] Nakanishi, N. Japanese Patent Application, No. 2025-139272 (2025).
- [43] Nakanishi, N. Japanese Patent Application, No. 2025-139269 (2025).

- [44] Nakanishi, N. Japanese Patent Application, No. 2025-139270 (2025).
- [45] Nakanishi, N. Japanese Patent Application, No. 2025-139271 (2025).
- [46] Nakanishi, N. Japanese Patent Application, No. 2025-139273 (2025).
- [47] Bae, K. T., Zhu, F., Chapman, A. B., Torres, V. E., Grantham, J. J., Guay-Woodford, L. M. et al. Magnetic resonance imaging evaluation of hepatic cysts in early autosomal dominant polycystic kidney disease: the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease cohort. *Clin. J. Am. Soc. Nephrol.* **1**, 64–69 (2006). <https://doi.org/10.2215/CJN.00080605>
- [48] Sore, R., Cathier, P., Vlachomitrou, A. S., Bailleux, J., Arnaud, K. & Juillard, L. et al. Deep learning-based segmentation of kidneys and renal cysts on T2-weighted MRI from patients with autosomal dominant polycystic kidney disease. *Eur. Radiol. Exp.* **8**, 122 (2024). <https://doi.org/10.1186/s41747-024-00520-7>
- [49] Kim, Y., Bu, S., Tao, C. & Bae, K. T. Deep learning-based automated imaging classification of ADPKD. *Kidney Int. Rep.* **9**, 1802–1809 (2024). <https://doi.org/10.1016/j.ekir.2024.04.002>
- [50] Hsu, J.-L., Singaravelan, A., Lai, C.-Y., Li, Z.-L., Lin, C.-N., Wu, W.-S. et al. Applying a deep learning model for total kidney volume measurement in autosomal dominant polycystic kidney disease. *Bioengineering* **11**, 963 (2024). <https://doi.org/10.3390/bioengineering11100963>
- [51] Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, et al. The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. *BMC Vet Res.* **16**, 242 (2020). <https://doi.org/10.1186/s12917-020-02451-y>.

Acknowledgments

The author gratefully acknowledges the veterinary team at the University of Tokyo Veterinary Medical Center (Tokyo, Japan) for their assistance with MRI scheduling and clinical coordination, and the veterinary staff at Grace Animal Hospital (Tokyo, Japan) for their support with ultrasound imaging. Their procedural and logistical support facilitated smooth data acquisition.

Author contributions

Naruhiko Nakanishi (Takeru Lab, Tokyo, Japan) conceived and designed the study, acquired and analyzed the data, performed image segmentation and quantitative analysis, developed the methodological framework, and wrote the manuscript. All aspects of the study, including conceptualization, methodology, data interpretation, and preparation of figures and tables, were independently conducted by the author.

Funding

This study received no external funding.

Competing interests

The author (Naruhiko Nakanishi, PhD; Takeru Lab) is the owner of the study subject (Aiko) and is the inventor on multiple patent applications filed with the Japan Patent Office (August 6, 2025). These interests did not influence the study design, data analysis, interpretation of results, or the conclusions presented. The author declares no other competing interests.

Supplementary Information

Supplementary Information provides additional materials, including the Graphical Abstract, Figure S1, Figure S2, Figure S3, Table S1, and Supplementary Methods. Please refer to these materials for further details.

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