

Major Kidney Clinical Research Studies and Projects Inventory*

Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP)

1. Administrative Data

(a) Name of study/research project and acronym:

Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease
(CRISP)

(b) Type of study/research project (randomized clinical trial, epidemiological study, database, etc.):

Cohort for technology development

(c) Funding status (currently funded, study/project completed):

Funded

(d) Recruitment status (recruitment completed, currently recruiting):

Recruitment completed

(e) For studies/projects currently recruiting, indicate total sample size/ number currently enrolled, anticipated period of recruitment:

N/A

(f) Data Coordinating Center Principal Investigator contact information (mailing address, phone, fax, e-mail address):

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(g) Number of recruiting sites, list of principal investigators at recruiting sites, and contact information as in (f) above:

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(h) List of principal investigators at central laboratories/facilities (identify type of central facility) and contact information as in (f) and (g) above:

Coordinating Center is both an Image Analysis Center and Coordinating Center, Dr. Bae is in charge of the Image Analysis Facility.

Bae, Kyongtae T., M.D., Ph.D.
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GFR by non-radiolabeled Iothalamate Clearance Test is analyzed centrally by Dr. Torres.

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(i) Roster of Data and Safety Monitoring Board/Scientific Advisory Committee or other oversight committee(s):

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(j.) Private-sector support (type of support, e.g., financial, donation of drugs/placebo, etc.):

None

2. Study Design (For completed studies, a copy of the primary publication can substitute for information below.)

(a) Objective:

- To determine if MR, including gadolinium enhancement, detects small changes in renal volume, cystic volume, and non-cystic renal parenchymal volume over a short period of time (e.g., 1-2 years) in ADPKD individuals.
- To determine if ultrasound measurement of cross-sectional cyst area based on representative cross-sectional images is similar to percent cyst volume based on total renal volume and cyst volume measurements obtained by MR.
- To determine if changes in renal volume, cystic volume, and non-cystic renal parenchymal volume will correlate with changes in renal function in ADPKD individuals.
- To determine which factors predict disease progression defined as an increase in total renal volume, cyst volume, and percent cyst volume over time.
- To determine if changes in renal volume, cystic volume, and non-cystic volume and decline in glomerular filtration rate will be greater in ADPKD individuals categorized as high risk in comparison to ADPKD individuals categorized as low risk for progression to renal failure.
- To determine if correlation between changes in renal volume, cystic volume, non-cystic renal parenchymal volume exists with the occurrence of signs, symptoms, and complication of ADPKD, including but not limited to, the development of hypertension, frequency and severity of pain, and frequency and duration of hematuria.

(b) Study design:

Prospective measurements at baseline and annual examination at 12, 24, and 36 months

(c) Major inclusion criteria:

- ADPKD diagnosis

- Age 15-45
- GFR from Cockcroft-Gault or 24-hour creatinine clearance > 70 ml/min

(d) Major exclusion criteria:

- Serum creatinine > 1.4 mg/dl for women or > 1.6 in men
- Absence of one or both kidneys
- Prior renal cyst reduction surgery
- Renal vascular disease
- 24-hour urinary protein > 2 grams
- Contraindications to MR studies
- Presence of significant CVD, CHD, diabetes, systemic illness with renal involvement
- Pregnancy

(e) Description of the intervention(s):

None

(f) Baseline/eligibility visit schedule (number of visits, major assessments):

Single screening visit with necessary labs for exclusion. Can be combined with baseline exam.

(g) Follow-up contact schedule (frequency, type of visit-phone, in-clinic, major assessments):

Annual in person visits with MR and US imaging, GFR and other labs.
Telephone contacts every 3 months

(h) Primary outcome, secondary outcomes:

- Renal volume, cyst volume, % non-cystic renal volume by MR
- Change in renal volume, % non-cystic renal volume over time by MR

- % cross-sectional cyst volume by US
- Change in % cross-sectional cyst volume by US over time
- Relationships between changes in volumetric measures and changes in renal function by GFR
- Renal blood flow by MR

(i) Brief summary of power estimates used to justify sample size/duration, including critical assumptions (i.e., effect-size estimates, estimated event rates, or rate of change in outcome measure):

In considering the sample size, we have chosen to focus on the hypothesis that the rate of progression in the high-risk cohort is greater than that in the lower risk cohort. By using prior experience of CRISP investigators with CT images over long follow-up periods, we estimated that the average rate of growth in kidney volume for PKD patients is 48 ml/yr, with a standard deviation of 44.5. From the analysis of the standardization study, which included repeat scans at each site as well as the variability due to inter- and intra-observer variance in estimating total kidney size, we can estimate the residual error as 175. The error term was obtained from this confounded standard deviation because this represents the actual measurement process during the study.

We compute the power using the method of Lefante (Lefante JJ. The power to detect differences in average rates of change in longitudinal studies. *Stat Med* 9:437-46, 1990) to determine the necessary sample size to detect a 50% difference in the average slope (e.g., the average rate of change in the high risk cohort is 48 ml/yr, with the average rate in the low-risk cohort of 24 ml/yr. For a power of .90, and with twice as many high risk participants as low risk, we will need a total of 165 participants for the entire 3-year period of the protocol. If we assume that 20% of those recruited will not complete the entire protocol with acceptable images, then we would need to recruit a total of 206 participants. Since the data from those subjects who do not provide all 4 images is still informative, this gives an added assurance that the study will have adequate power.

(j) Web site:

<http://www.pkd.wustl.edu/crisp/>

3. Data and Biological Sample Resources

(a) Biological samples collected in ongoing studies/research projects (specify the type of sample, e.g., blood, urine, etc., the amount, and the point in the study when samples were

collected, e.g., baseline visit #1, baseline visit #2, follow-up visit #1; specify months after randomization/study entry):

The primary biological sample is MR-and US-based images of the kidneys according to a standardized protocol. These are collected at baseline and with respect to DNA, cell lines have been generated from 100% of the CRISP participants at Emory University and from approximately 60% of the participants recruited at the other sites. These cell lines provide an inexhaustible source of DNA. The DNA obtained from the remaining participants is sufficient for the PKD genotyping and many additional studies, but it is not inexhaustible. If deemed advisable by the EAC, cell lines can be generated from these participants at the time of a follow-up visit.

At least 10 ml of blood and aliquots of 24-hour urine has been saved on each participant at baseline and at each annual visit.

(b) Biological samples currently in storage from completed trials (grid showing sample collection time, type of sample, amount and number of study participants sample was collected from, and physical location of where the samples are stored):

Study is ongoing. Samples are now stored from baseline and first annual visit on all participants. Images are stored centrally at the Image Analysis facility.

(c) Brief summary of typical informed consent provisions (template informed consent form acceptable), including major variables in participant consents, if applicable (e.g., “use for other studies or not”, “allow genetic studies or not.”). Does consent include use of samples in other studies that are not part of the main study?

Consents allow genetic analysis. They do not consistently deal with use of samples in other studies.

(d) Data collected (grid of data collection by time/clinic visit with specificity on the type of information collected, e.g., quality of life with SF-MOS 36, measurement of kidney function by GFR, serum creatinine measurement, etc.):

Primary data collection is for MR and US images of kidneys, GFR via cold iothalomite to be collected at baseline and annually thereafter. Locally obtained standard blood and 24-hour urine panels. All data collected at baseline and at annual visits.

(e) Any provisions for distributing resources outside of the study? What is the sharing plan?

Images collected will be made available at the conclusion of the study.

4. Ancillary Studies

(a) Process and contact person (name, address, phone, fax, and e-mail address) for application to perform ancillary studies:

Proposals need to be approved by the Steering Committee and the Ancillary Studies Committee. Inquiries should be sent to the Chair of the Steering Committee:

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(b) List of ancillary studies approved, completed, and ongoing (including source of funding and amount):

None

5. List of Publications and Presentations (full citations, also note manuscripts in progress)

Bae KT, Commean PK, Lee JR. Volumetric Measurement of Renal Cysts and Parenchyma using MRI: Phantoms and Patients with Polycystic Kidney Disease. *Journal of Computer Assisted Tomography* 2000; 24:614-619.

Bae KT, Brummer M, Kenney PJ, King BF, Wetzel LH. MR Imaging to Assess the Progression of Polycystic Kidney Disease. Radiological Society of North America, 2001.

Bae KT, Commean PK, Lee JR, Suh JD, Brunnsden BS. Development of Image Analysis Methodology for Volumetric Measurement of Renal Cysts and Parenchyma using MRI. Radiological Society of North America, 2001.

Bae K, Chapman A, Grantham J, et al. Progression of Polycystic Kidney Disease (PKD) Evaluated by MR Imaging. American Society of Nephrology, 2002.

Bae K, Suh JD, Baumgarten D, et al. MR Imaging to Assess the Progression of Polycystic Kidney Disease: Baseline and On-going Follow-up Study. Radiological Society of North America, 2002.

Chapman A, Guay-Woodford L, Grantham J, et al. Magnetic Resonance Imaging (MRI) in Early Autosomal Dominant Polycystic Kidney Disease (ADPKD): Baseline characteristics of the Consortium for Radiographic Imaging Studies of Polycystic Kidney Disease (CRISP) Cohort. American Society of Nephrology, 2002.

Chapman AB, Guay-Woodford LM, Grantham JJ, Torres VE, Base KT, Baumgarten DA, Kenney PJ, King BF, Glockner JF, Wetzel LH, Brummer ME, O'Neill WC, Robbin ML, Bennett WM, Klahr S, Hirschman GH, Kimmel PL, Thompson PA, Miller JP. Renal Structure in Early Autosomal Dominant Polycystic Kidney Disease (ADPKD): The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) Cohort. *Submitted*.

Davila J, King B, Glockner J. Cine Phase Contrast Measurement of Renal Blood Flow as a Marker of Disease Progression in Autosomal Dominant Polycystic Kidney Disease (CRISP). European Uroradiology/American Genitourinary Radiology, 2002.

Glockner J, King BF, Torres V. Cine Phase Contrast Measurement of Renal Blood Flow as a Marker of Disease Progression in Autosomal Dominant Polycystic Kidney Disease. International Society of Magnetic Resonance in Medicine, 2002.

King BF, Torres V, Glockner J, Chapman A, Bae KT, CRISP. Magnetic Resonance Measurements of Renal Blood Flow as a Marker of Disease Progression in Autosomal Dominant Polycystic Kidney Disease. American Society of Nephrology, 2001.

King BF, Torres V, Brummer M, Chapman A, Glockner J, Bae KT. Magnetic Resonance Measurements of Renal Blood Flow as a Marker of Disease Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD), baseline characteristics. American Society of Nephrology, 2002.

King BF, Torres VE, Brummer ME, Chapman AB, Bae KT, Glockner JF, Arya K, Felmlee JP, Grantham JJ, Guay-Woodford LM, Bennett WM, Klahr S, Hirschman GH, Kimmel PL, Thompson PA, Miller JP, and the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP). Magnetic Resonance Measurements of Renal Blood Flow as a Marker of Disease Progression in Autosomal Dominant Polycystic Kidney Disease, *submitted*.

Moore S, Maffitt D, Blaine G, Bae KT. A Workstation Acquisition Node for Multi-center Imaging Studies, Medical Imaging 2001: PACS and Integrated Medical Information Systems: Design and Evaluation, San Diego, California USA, February 17-22, 2001. Vol. 4323. SPIE - The International Society for Optical Engineering.

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O'Neill WC, Robbin M, Bae KT. Comparison of Ultrasound and Magnetic Resonance Imaging for Measurements of Size and Cyst Involvement in Autosomal Dominant Polycystic Kidney Disease. American Society of Nephrology, 2002.

Thompson PA, Littlewood S, Adelman AJ, Miller JP. The Web Data Entry System: Methods for Web Development and SAS Data Management. Proceedings of the 27th Annual SAS Users Group International Conference, 2002.

Wetzel LH, King BF, Kenney PJ, Bae KT, Baumgarten D, Grantham J. Magnetic Resonance Antiography Findings in Autosomal Dominant Polycystic Kidney Disease. American Society of Nephrology, 2001.

***Cooperative Agreement, Contract, and Selected Investigator-Initiated NIDDK-Supported Studies**