CASE STUDY · GASTROENTEROLOGY & METABOLIC

ADPKD Trial With Total Kidney Volume MRI

50 sites · Non-contrast T2-weighted MRI · Height-adjusted total kidney volume and Mayo imaging class

Challenge

Intrinsic Imaging supported this study’s imaging activities, addressing the scientific and operational considerations that inform the work of an imaging CRO and imaging core lab. Autosomal dominant polycystic kidney disease progresses slowly, and kidney function can remain normal for years while the kidneys enlarge. Total kidney volume has been qualified by regulators as a prognostic enrichment biomarker precisely because it identifies the patients most likely to decline during a trial. In this Phase III program, height-adjusted total kidney volume on MRI served two purposes: to classify each candidate at screening into the Mayo imaging class that determined eligibility, and to measure the rate of kidney growth over 24 months as a key secondary endpoint.

Both purposes demand precise, reproducible kidney segmentation. The annual growth rate in the eligible population is a few percent, so measurement error of similar magnitude would obscure the treatment effect. Contrast agents were to be avoided because of the participants' renal function, which placed the full burden on non-contrast T2-weighted sequences whose quality varied across the 50 sites' scanners. Screening decisions also had to be returned quickly so that sites could complete eligibility within the protocol window. The sponsor therefore required a segmentation method whose reproducibility was established before enrollment and monitored throughout.

Intrinsic Imaging’s Solution

Intrinsic Imaging issued a non-contrast MRI protocol specifying coronal and axial T2-weighted sequences with fixed slice thickness, no gap and full renal coverage, with vendor-specific parameter sheets for the scanners in use. Site qualification required a volunteer or phantom acquisition reviewed for coverage, motion and contrast before activation, and every incoming screening examination was quality-checked within one business day so that a non-conforming scan could be repeated in time.

Kidney segmentation was performed centrally using a standardized semi-automated method with analyst correction and physician review, with each participant's follow-up examinations segmented by the same analyst against baseline to minimize longitudinal variability. Height-adjusted total kidney volume and the resulting Mayo imaging class were calculated from the segmentation and age and returned to the site as an eligibility determination. Reproducibility was established before enrollment with repeat segmentation of a test set and monitored throughout the study by periodic blinded re-segmentation.

Exophytic cysts, liver cysts abutting the kidney and partial-volume effects at the renal poles were addressed with explicit segmentation rules in the analysis manual, since these are the places where analysts most often diverge. Growth-rate calculations were reviewed by a nephrology-experienced physician for biological plausibility before release, and any change exceeding the expected range triggered re-segmentation of both timepoints, so that the longitudinal dataset reflected disease rather than analyst variation.

Intrinsic Imaging’s Results

- 2.1% coefficient of variation for intra-analyst kidney segmentation reproducibility, established on a test set before enrollment, documented in the charter and maintained throughout the study
- 9% of screened candidates excluded on central Mayo imaging class determination, enriching the randomized population for progression exactly as the protocol's enrichment strategy intended
- Two business days median turnaround for screening eligibility results, supported by quality control of every screening examination within one business day of receipt
- 24-month height-adjusted total kidney volume dataset delivered complete for the secondary endpoint analysis, with every growth rate reviewed for biological plausibility

Read the full study online: https://intrinsicimaging.com/case-studies/nephrology-adpkd

About Intrinsic Imaging, LLC

Intrinsic Imaging is an ISO certified medical imaging CRO and imaging core lab providing comprehensive services in support of Phase I-IV clinical trials and Class I, II, III medical device trials. Intrinsic Imaging is also a world leader in conducting Artificial Intelligence studies. With its team of more than 50 board-certified and fellowship-trained physicians, Intrinsic Imaging’s team has sub-specialization in all therapeutic areas, including Cardiovascular, Central Nervous System,Gastroenterology, Musculoskeletal, Oncology and Ophthalmology. Certified by the British Standards Institution (BSI), Intrinsic Imaging is the only company in the world to hold five ISO certifications specifically for providing imaging core lab services on clinical trials. For more information, please visit www.IntrinsicImaging.com.

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