CASE STUDY · MUSCULOSKELETAL

Pivotal Phase II Biologic Trial in a Rare Degenerative Neuromuscular Disorder

22 sites in 6 countries · Quantitative muscle MRI, DXA · Fat fraction and lean mass endpoints

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. A pivotal Phase II trial of a novel biologic for a rare degenerative neuromuscular disorder relied on imaging biomarkers of muscle composition as key efficacy measures. Quantitative muscle MRI fat fraction and DXA lean mass are sensitive to scanner vendor, sequence implementation and positioning, and in a rare disease with small per-site enrollment, every patient's longitudinal data carried disproportionate weight.

The sponsor required measurement precision sufficient to detect slow changes over the treatment period, consistent muscle segmentation across readers and visits, and a protocol that patients with limited mobility could tolerate. Because the trial was pivotal, the imaging methodology also had to be documented to a standard suitable for regulatory review. Muscle fat fraction and lean mass characterize composition rather than directly measuring strength or daily function. Their relevance as efficacy measures therefore depends on a clear distinction between reproducible tissue assessment and demonstrated clinical benefit. In a small longitudinal dataset, an isolated technical deviation can also complicate interpretation of an individual trajectory.

Intrinsic Imaging’s Solution

Intrinsic Imaging's musculoskeletal team designed the imaging charter around a quantitative MRI protocol, including Dixon-based fat-fraction sequences and defined anatomical coverage, with positioning aids and scan-time limits appropriate for patients with impaired mobility. Each of the 22 sites was qualified with phantom and volunteer scans, and DXA systems were cross-calibrated using a travelling phantom before enrollment. Defined anatomical coverage anchors serial comparisons to the intended muscle regions, while positioning aids address practical limitations imposed by impaired mobility. Phantom qualification and DXA cross-calibration address technical comparability, but these controls do not make the modalities interchangeable or eliminate the need to interpret their measurements separately.

Fellowship-trained musculoskeletal radiologists performed segmentation and fat-fraction analysis under a standardized reading charter, with the same reader following each patient longitudinally where possible and a second reader on a defined sample for reproducibility assessment. Qualitative review captured edema, atrophy and other structural change alongside the quantitative measures. Consistent segmentation limits changes in tissue boundaries as an alternative explanation for an apparent fat-fraction shift. Longitudinal reader assignment and sampled reproducibility assessment address complementary sources of analytical variability. Qualitative observations provide structural context, although they do not independently establish the biological mechanism underlying a quantitative change.

Project management maintained a per-patient imaging schedule across the trial, and quality control at receipt caught positioning and sequence deviations early enough for re-acquisition within protocol windows, protecting the small dataset from avoidable losses. Visit-level tracking is particularly relevant when missing observations can substantially reduce the information available for an individual patient. Early technical review supports usable follow-up, while comprehensive documentation makes methodological choices traceable without implying that imaging precision alone establishes therapeutic efficacy.

Intrinsic Imaging’s Results

- Quantitative MRI and DXA data acquired at 22 sites in 6 countries with vendor-neutral protocols and cross-calibrated DXA systems
- Fewer than 4% of imaging visits lost to unevaluable examinations in a rare-disease population where each visit was material to the analysis
- Intra- and inter-reader reproducibility of fat-fraction measurement documented on a prespecified sample, supporting the pivotal designation
- Complete regulatory-ready documentation of protocol, calibration, reader training and analysis methodology delivered with the final dataset

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Read the full study online: https://intrinsicimaging.com/case-studies/musculoskeletal-neuromuscular-biologic

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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