

MULTIPLE SCLEROSIS (MS) STUDIES

Medical Imaging Expertise



Magnetic Resonance Imaging (MRI) continues to play a major role in the evaluation of new therapeutic compounds for the treatment of MS. The objective evaluation of MS Lesion Burden and Activity by MRI has been accepted by regulatory agencies as a primary or secondary efficacy endpoint. Additional quantitative endpoints such as brain atrophy, Diffusion-Tensor Imaging (DTI) and Magnetization Transfer Imaging (MTI) serve as markers of neurodegeneration and have shown tremendous value for investigating the long term efficacy of new disease-modifying therapies.

Accelerated decision making for patient safety and monitoring

Expedited regulatory review based upon credible, reliable trial data and processes

Abbreviated timelines through efficient work flow processes and engaged KOL

Cost and time efficiencies through central review

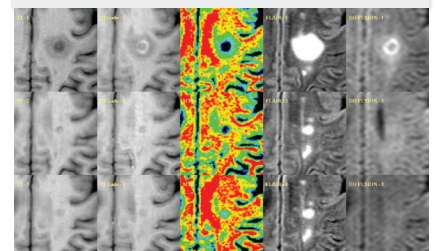
Expertise with Image Processing and Quantitative Analysis

- Semi-automated detection and quantification of MS lesions
 - Gadolinium-enhancing T1-weighted lesions
 - Hyperintense FLAIR/T2-weighted lesions
 - Hypointense T1-weighted lesions (“black holes”)
 - Fully automated 3D image registration
 - Facilitated detection of lesion changes using subtracted images
 - 4D Connectivity for automatic detection of new, enlarging and persisting lesions
 - Automatic detection of Combined Unique Lesions
- Automated brain volumetry using established methods (SIENAX, Freesurfer, multi-atlas segmentation)
 - Whole Brain and Ventricles
 - Hippocampus
 - Regional analysis (brain lobes, cerebellum, brainstem, corpus callosum, thalamus, etc.)
- Determination of atrophy using established methods
 - SIENA
 - Boundary Shift Integral (BSI)
 - Tensor Based Morphometry (TBM)
- Diffusion-Tensor Imaging (DTI)
- Magnetization Transfer Imaging (MTI)
- Functional MRI (fMRI)

3D image registration using Mutual Information

Rows: Baseline, M12 & M24 MRI scans of one MS patient

Columns: T1, Post-Gadolinium T1, MTR, FLAIR & DWI MRI sequences



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Independent Image Review By Expert Neuroradiologists

Board-certified Neuroradiologists highly specialized in MS and MR imaging independently evaluate native and processed MRI data for eligibility, safety and efficacy endpoints.

- Centralized image review significantly increases trial efficiency while minimizing trial costs.
- Image evaluations can be made available to the sponsor in real-time.

Lesion Quantification & Tracking

- MRI sequences and timepoints are spatially registered using an automated three-dimensional (3D) mutual information-based algorithm.
- Subtracted images (Moraal, Radiology 2009) are generated in order to increase sensitivity to change while validating lesion contours. Advanced editing tools are available to assist technicians.
- Gd-enhancing T1 lesions, hyperintense T2 lesions and hypointense T1 lesions (black-holes) can be assessed. Volume and number is evaluated by technicians and neuroradiologists. New or enlarging lesions and Cumulative Unique Active (CUA) lesions can be reported as needed, in agreement with study protocol.

Brain Volume Measurements and Atrophy Quantification

- Baseline brain volumes (whole brain and subregions) can be assessed using established techniques such as SIENAX, Freesurfer or multi-atlas segmentation.
- On follow-up visits, atrophy quantification can be carried out using SIENA, Tensor-Based Morphometry (TBM) or Boundary Shift Integral (BSI).

Exploratory Assessments

- Regional volume changes (white matter, grey matter, thalamus, cerebellum, etc.) and cortical thickness can be assessed using TBM.
- Spinal cord analysis can be carried out using the Spinal Cord Toolbox (SCT)
- MTR can be assessed globally, over specified brain regions, or at individual lesion level.
- Additional exploratory endpoints include Functional MRI, Myelin Water Fraction, etc.

Project Management Services

- Standardization of MRI protocol across vendors
- Development of imaging guidelines and charter
- Site qualification using test or phantom scans
- Image QC and interactions with sites for query resolution
- Data export in all standard formats (CSV, SAS, CDISC)
- Full regulatory compliance (FDA 21 CFR Part 11)