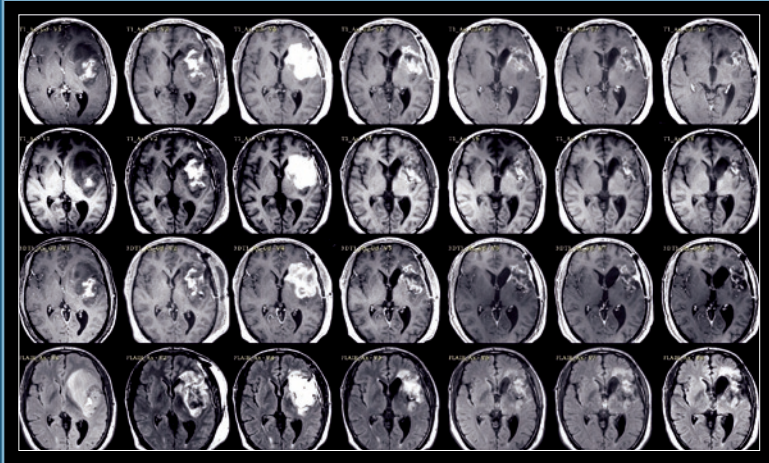


BioClinica's Image Processing Capabilities

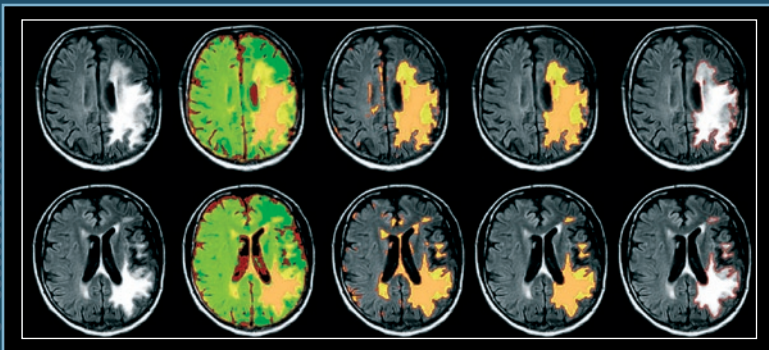
for Analyzing Quantitative Endpoints in Brain Tumor Studies

The use of quantitative MRI endpoints in brain tumor studies has become an important step for more reliable and valid tumor response assessment strategies. The use of volumetric, diffusion and perfusion-related MRI parameters may significantly improve the quality of clinical trials (quantitative follow-up and tumor characterization). This document provides a short overview of BioClinica's capabilities for enabling such endpoints in brain tumor studies.



3D Registration of MRI Sequences & Timepoints

From Left-Right: All timepoints in chronological order Pre-Surgery, Post-Surgery, Day 17, M3, M6, M9, M12 MRI visits. Top-Down: Post-Gd T1 (3mm thick), Pre-Gd T1 (3mm thick), Post-Gd 3DT1 (millimetric voxel) & FLAIR.



Pre-detection of brain tumors using 3D segmentation (2 slices)

From Left-Right: Native images, Segmented images (6 classes), Segmented images (2 "tumor" classes), Segmented images (keep tumor structure) & Final pre-detected tumor contours prior to central reads.

IMAGE REGISTRATION

A fully automated 3D mutual information-based registration algorithm is used to register all MRI sequences and timepoints with respect to a given reference MRI sequence at baseline. Subsequent image processing and assessment tasks will be of better quality, reliability and efficiency when registered image sets are used.

IMAGE SEGMENTATION FOR BRAIN TUMOR DETECTION

An unsupervised, 3D segmentation algorithm is used for the detection of brain tumors in FLAIR/T2 and gadolinium-enhancing T1-weighted sequences. The algorithm is based on Bayesian MRI signal intensity classification and Markov Random Field models. Segmentation consists of classifying image pixels in different anatomical classes (white matter, gray matter, cerebrospinal fluid and hyperintense [FLAIR] or enhancing [post-Gd 3DT1] tumors) based on MRI intensity-based image features and spatial information such as connectivity and regularity. The central readers will be able to edit and manually modify (draw/erase) the resulting contours/masks of brain tumors.

QUANTITATIVE FOLLOW-UP OF BRAIN TUMORS

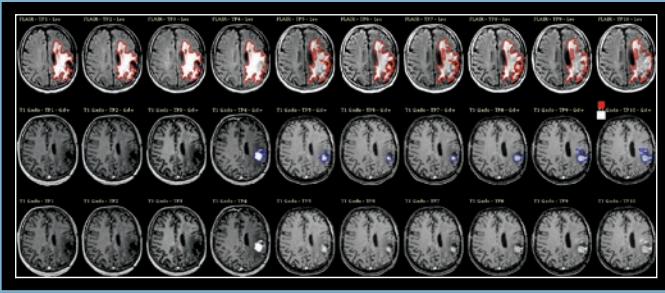
After validation of brain tumor masks by central readers, all detected tumors will be quantified as 4D objects (3D + Time) using a 4D-connectivity algorithm.

- New and enlarging tumors will be detected by comparing consecutive timepoints using a 4D connectivity algorithm
- Each tumor detected on FLAIR will be associated with the corresponding gadolinium-enhancing T1-weighted lesions (if any)

BIOCLINICA[™]
Global clinical trial solutions. Real-world results.

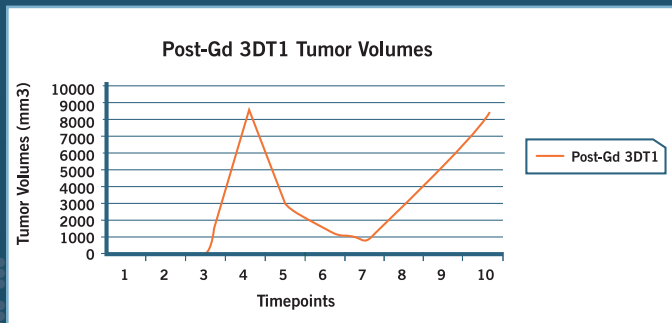
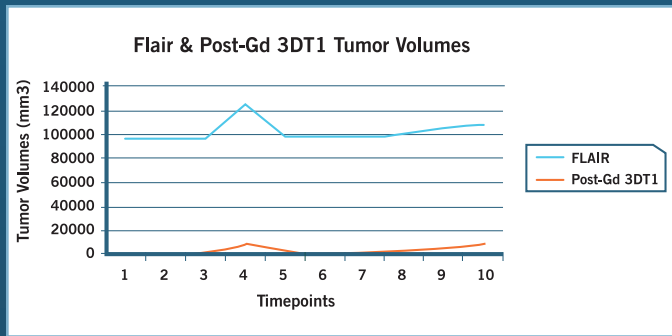
BioClinica's Image Processing Capabilities

for Analyzing Quantitative Endpoints in Brain Tumor Studies

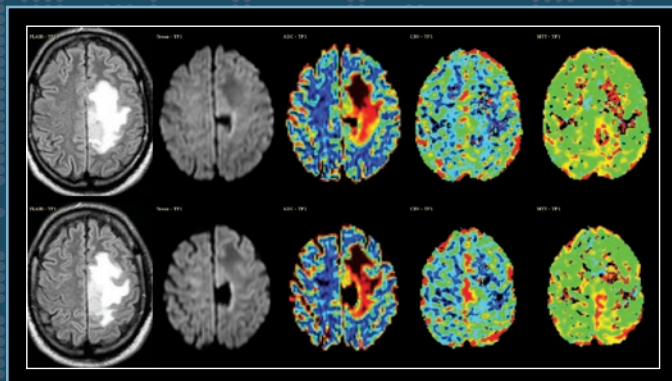


FLAIR & Post-Gd 3DT1 Tumor Segmentation

Top-Down: FLAIR (+ tumor contours), Post-Gd 3DT1(+ tumor contours) & Post-Gd 3DT1 (native). Left-Right: 10 timepoints displayed in chronological order.



Quantitative Follow-up of Tumor Volumes in Longitudinal Datasets
FLAIR & Post-Gd 3DT1.



FLAIR, DWI-MD, DWI-ADC, PWI-CBV & PWI-MTT
2 slices, same patient.

DIFFUSION AND DIFFUSION TENSOR IMAGING

DWI & DTI sequences can be used for a better characterization of brain tumors.

The following DWI maps can be computed:

- Mean Diffusivity (DWI_MD)
- Apparent Diffusion Coefficient (DWI_ADC)

The following DTI maps can be computed (The DTI sequence will use a 6-directions acquisition technique or more. The same number of directions will be applied to all sites):

- Mean Diffusivity (DTI_MD)
- Apparent Diffusion Coefficient (DTI_ADC)
- Fractional Anisotropy (DTI_FA)

The DWI/DTI maps, which may be provided by the sites, will not be used for the final quantitative analysis because their generation will be manufacturer-dependent and use different software modules and methodologies. BioClinica will use native DWI and DTI scans provided by the sites to centrally generate all DWI and DTI maps using the same algorithm and quantification methodology for all sites, patients and timepoints.

ROI-based histogram data analysis can be performed. ROIs may correspond to different tumors or healthy parts of the brain: Mean, Height, Peak and SD values will be computed for all histograms.

PERFUSION IMAGING

Perfusion-weighted sequences can be used for a better characterization of brain tumors.

The following parametric maps can be computed:

- Cerebral Blood Flow
- Cerebral Blood Volume
- Mean Transit Time
- Time To Peak

For any technical questions or software demonstration,
please contact us at +1.267.757.3000 or info@bioclinica.com.

BIOCLINICATM
Global clinical trial solutions. Real-world results.