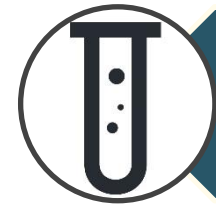


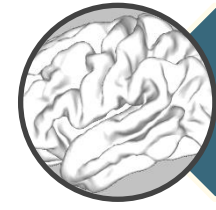
Connectome-derived Biomarkers

NICARA™ for clinical trials

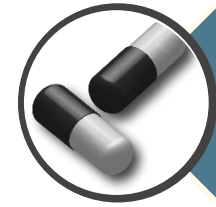
Biomarkers for Clinical Aging Studies - Requirements



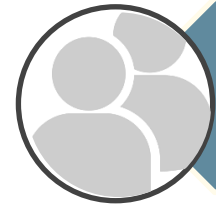
Biomarkers should be easy to obtain



Biomarkers should detect and quantify brain changes preceding gross atrophy



Biomarkers should respond to treatment



Biomarkers should serve as outcome marker in clinical trials



Biomarkers should be reproducible and reliable



Do your biomarkers fulfill all these requirements?

Quality Prediction of Biomarkers in Aging Studies – A Real Challenge

Volumetric Measurements

Widely used, but with
only moderate
prediction quality

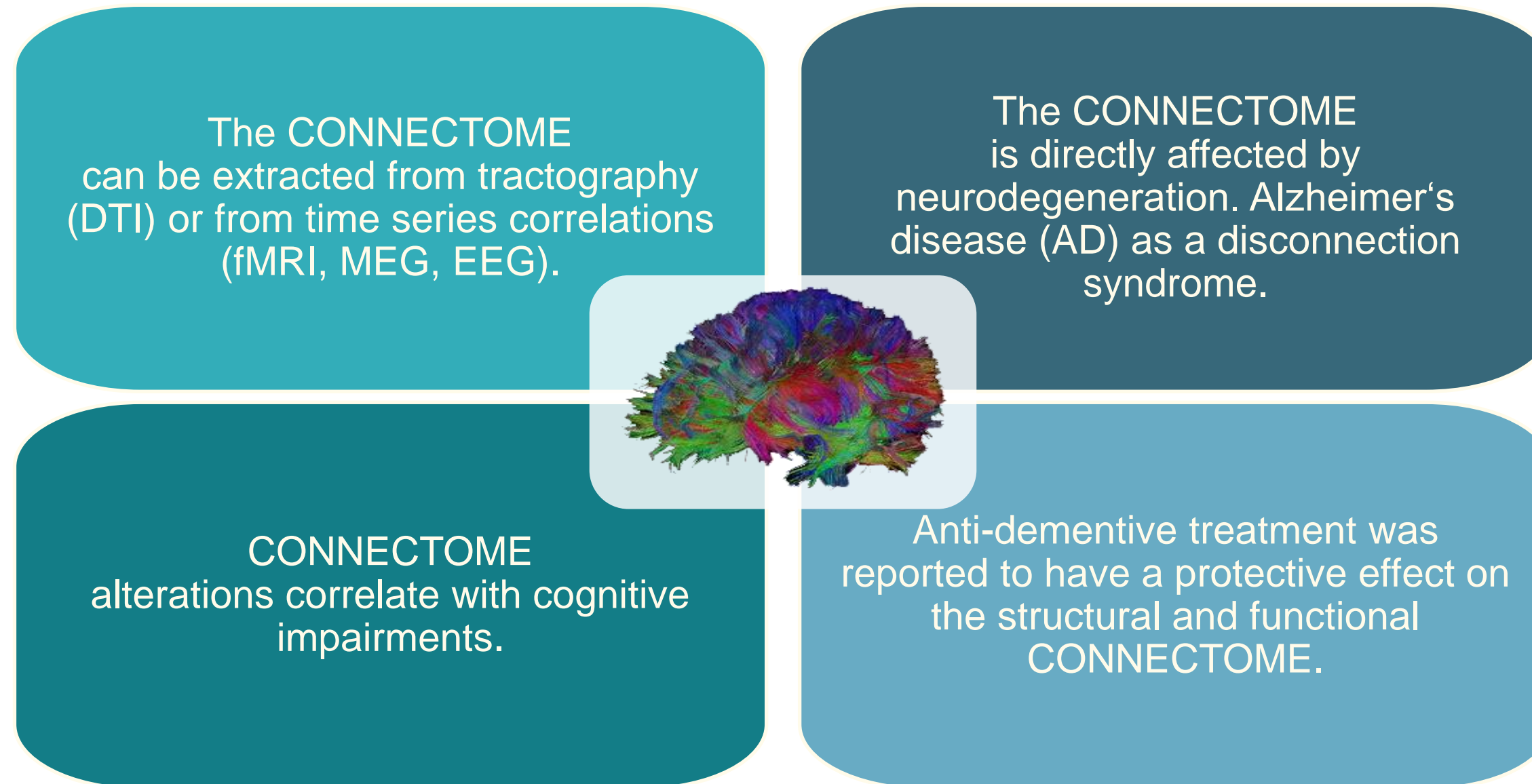
Cognitive Testing

Necessary,
but time consuming
and expensive

Sophisticated markers from PET-MRI, fMRI & DTI

Can greatly
enhance prediction
quality

Connectome-derived Biomarkers for Aging Studies?



However, extracting and analyzing the connectome requires expert knowledge in neuroimaging and expensive hardware.

Our Solution: NICARA™



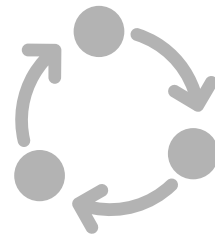
- > NICARA provides fully automated processing routines for structural and functional connectome extraction
- > NICARA allows fully integrated study management and catalog functions for connectome data
- > NICARA enables visualization, exploration and comparisons of multimodal connectome information and morphometry.

NICARA Offers You Many Advantages



...precise patient stratification

...better monitoring of treatment outcome



... expert knowledge

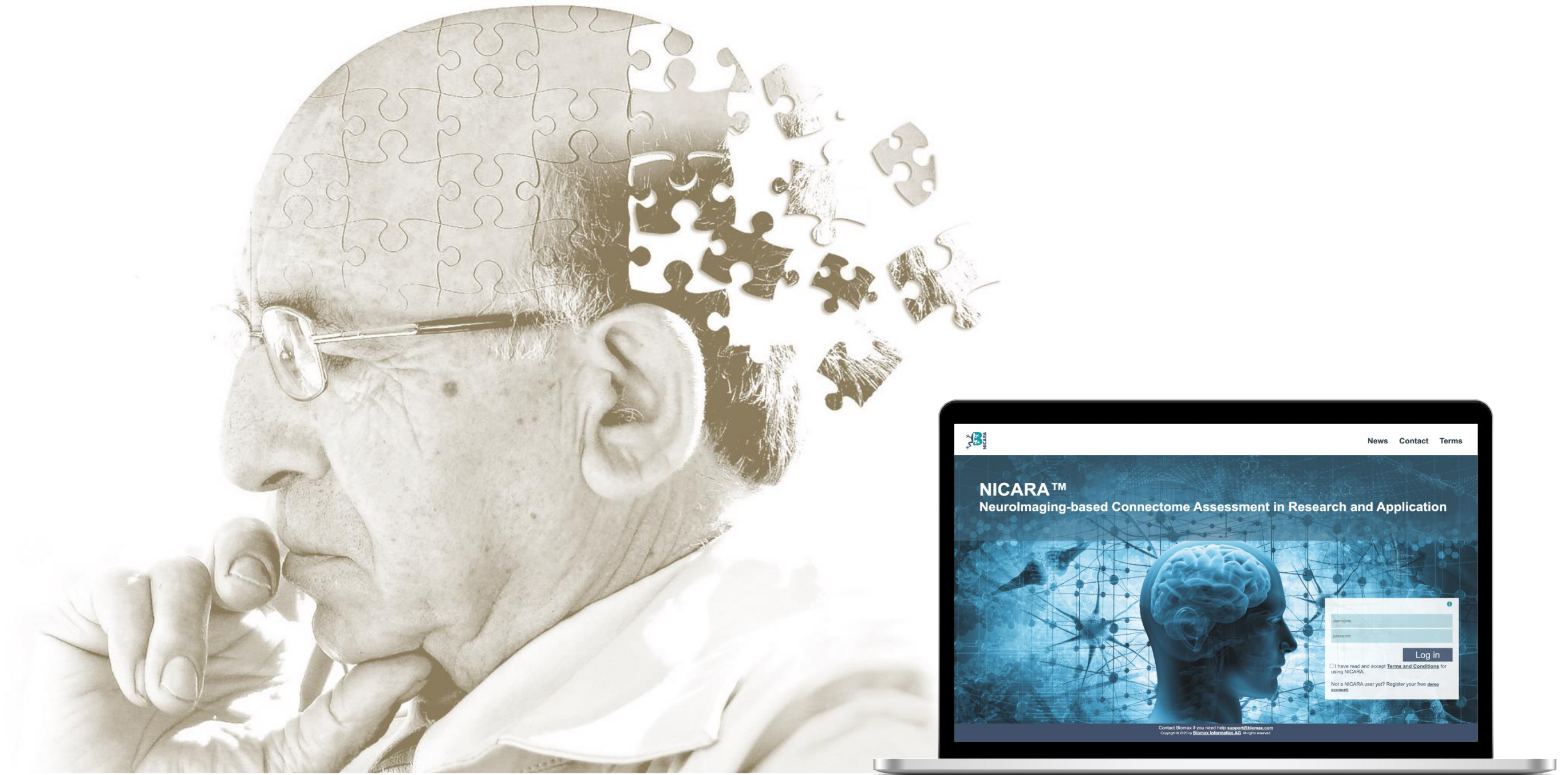
...hardware resources



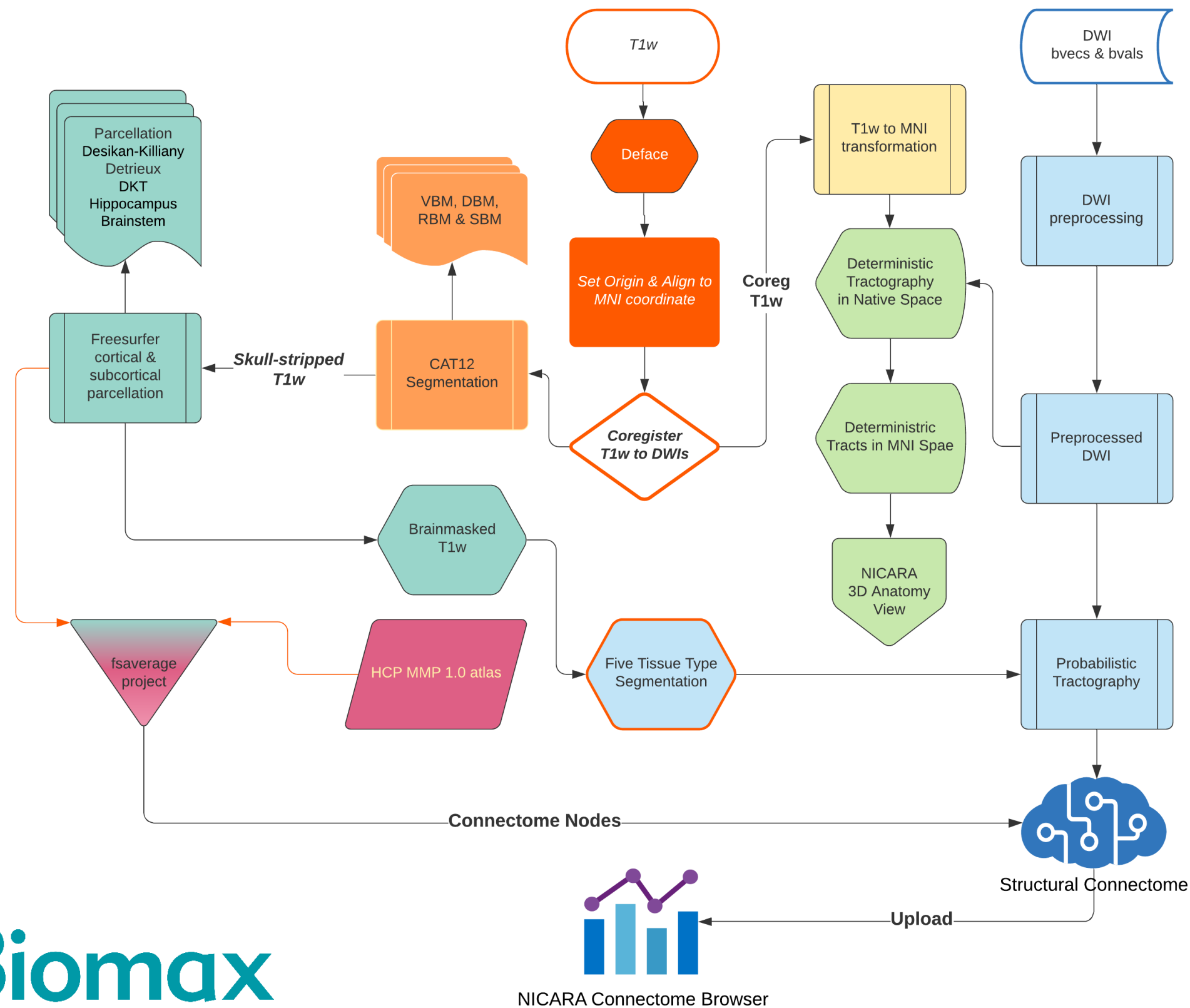
- > More precise **patient characterization** by earlier detection of, e.g., accelerated neurodegeneration
- > Better **monitoring of treatment outcome** by connectome assessments before and after treatment
- > Create **more predictive biomarkers** based on morphometry and connectome changes
- > No **neuroimaging knowledge** needed
- > **Hardware resources** provided by Biomax Informatics

Use Case: NICARA for Alzheimer's Disease (AD)

(as an example for detecting brain changes in Aging, Neurodegeneration and Dementia)



A preferred DTI Pipeline for AD Connectomes



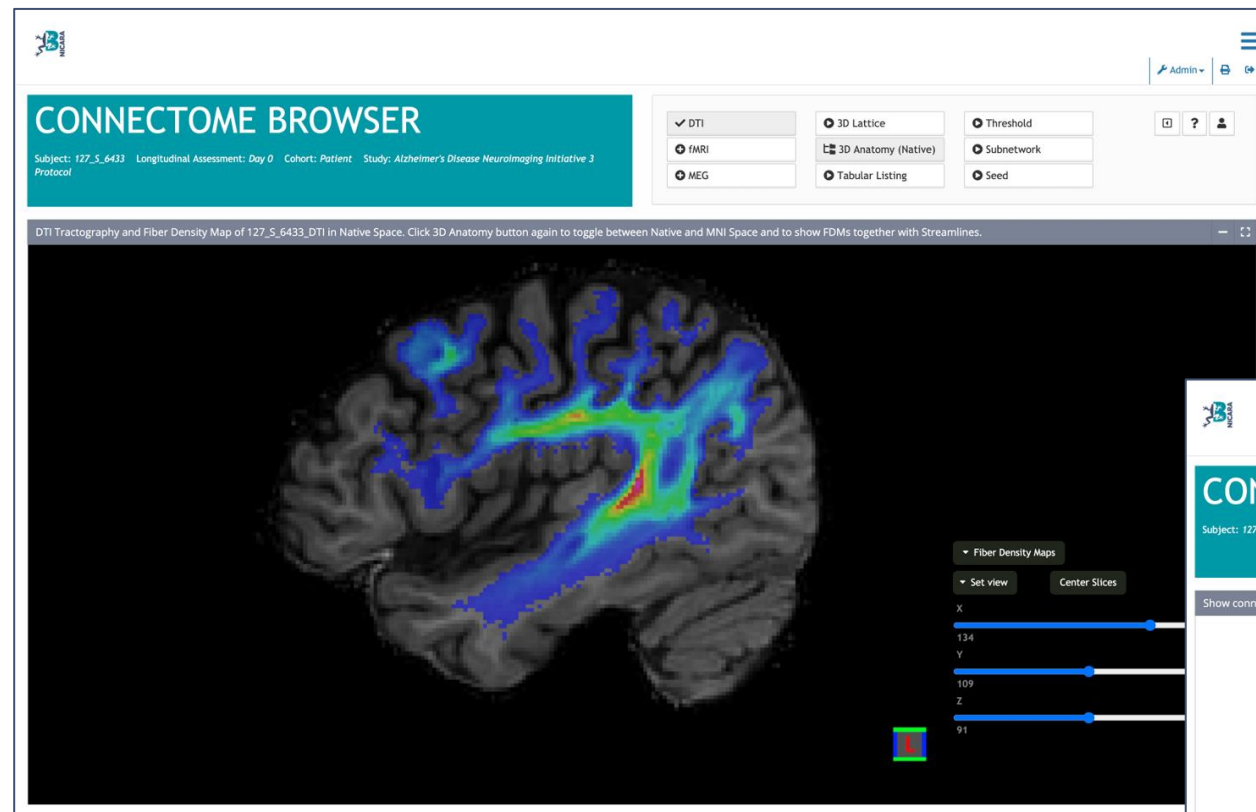
All pipeline tools executed by NICARA are...

- > open source
- > validated in hundreds of studies
- > suggested as preferred neuroimaging method for AD drug development*.

*in Falcon C, et al. Neuroimaging Methods for MRI Analysis in CSF Biomarkers Studies. Methods Mol Biol. In Biomarkers for Alzheimer's Disease Drug Development edited by Robert Perneczky (2018)

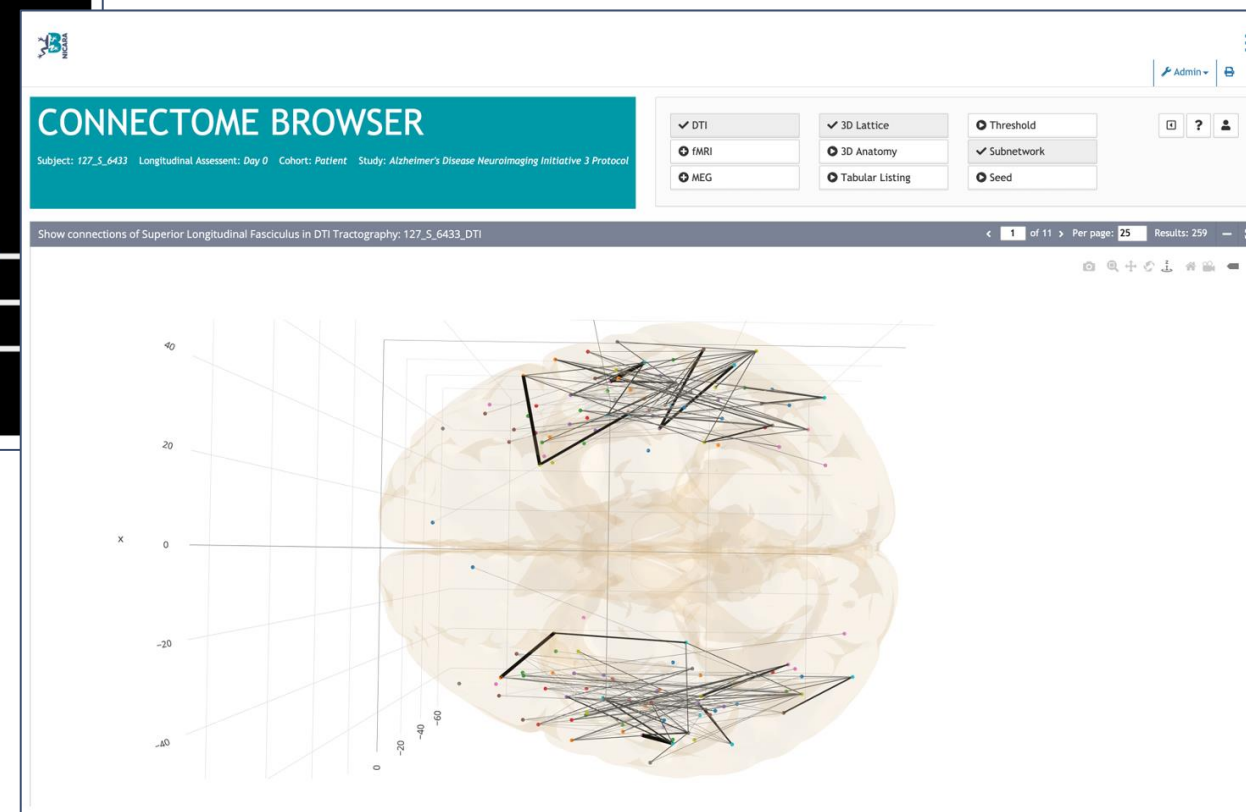
From Image to Feature Space: Exploring AD Connectomes

Fiber Density Maps (Image Space)



Reddish: high densities; Blueish: low densities of fibers of a major white matter tract in DTI tractography

3D Lattice Graph (Feature Space)

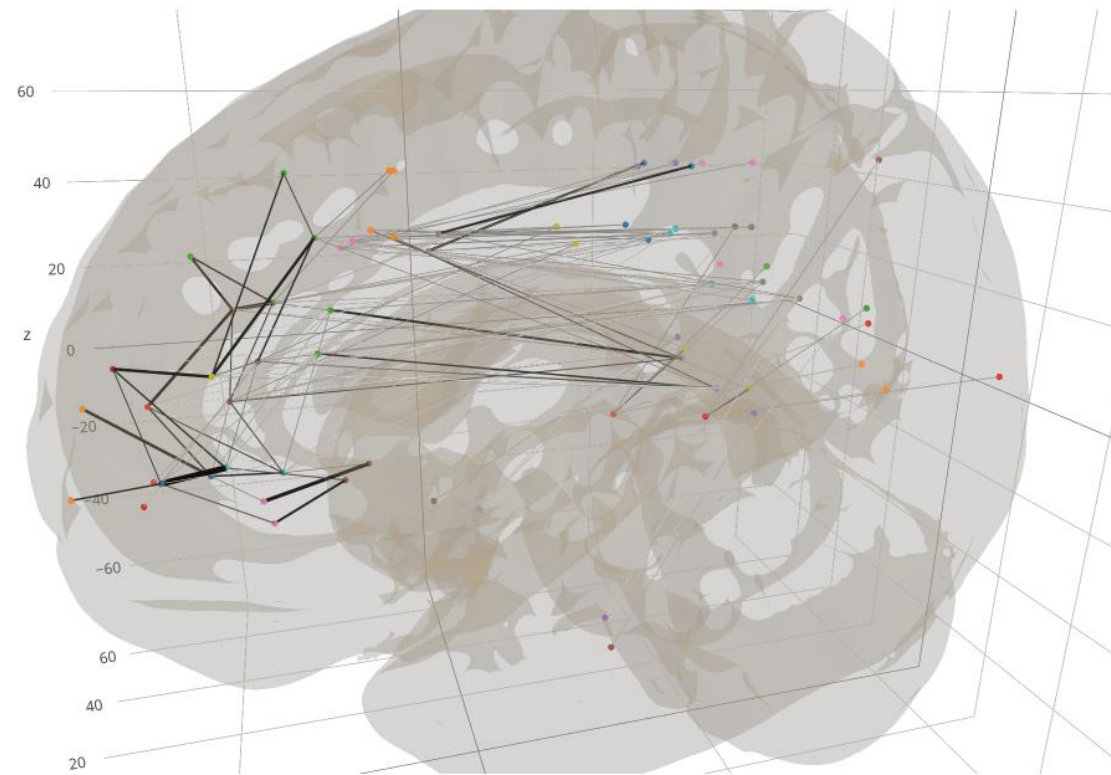


Bold lines: high fiber densities; Thin lines: low fiber densities (DTI tractography of a subnetwork)

- > **Image space** visualizations (e.g., fiber density maps) give a reliable overview of the patient's connectome.
- > The **feature space** representation allows for more precise quantification, multi-modal connectome integration and feasible inter-subject comparability.

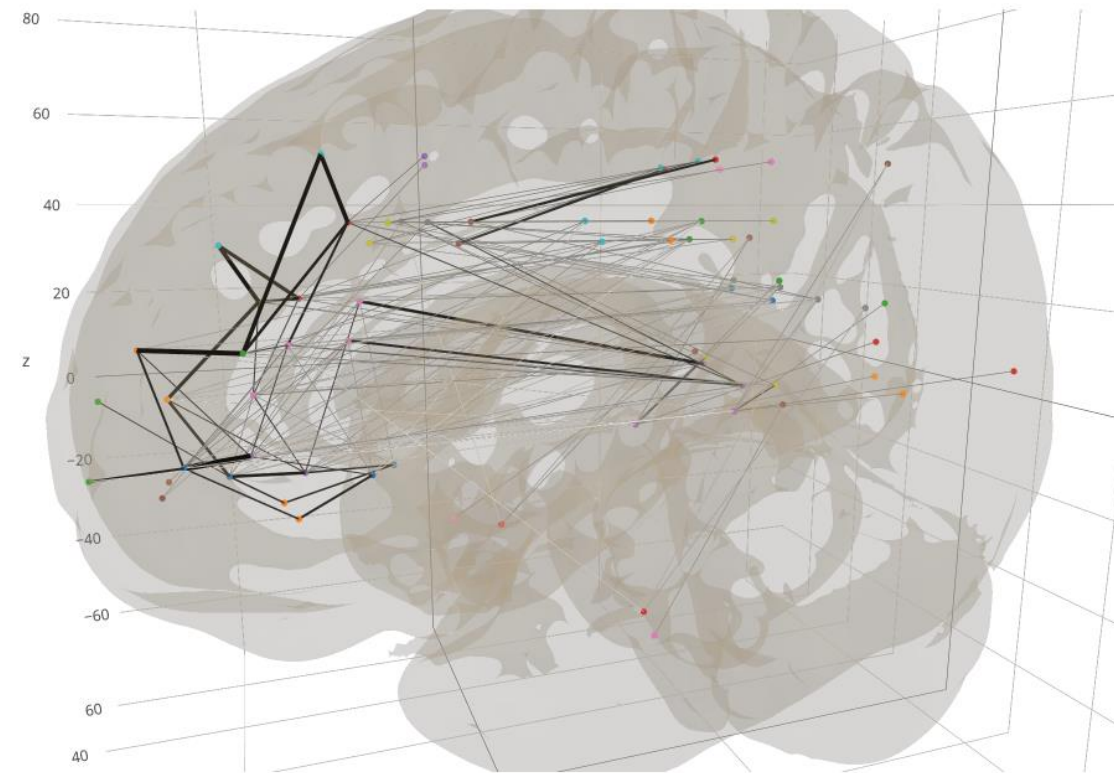
Characterization of AD Patients with Brain Network Comparison

AD Patient



AD patient: reduced densities

Matched Control

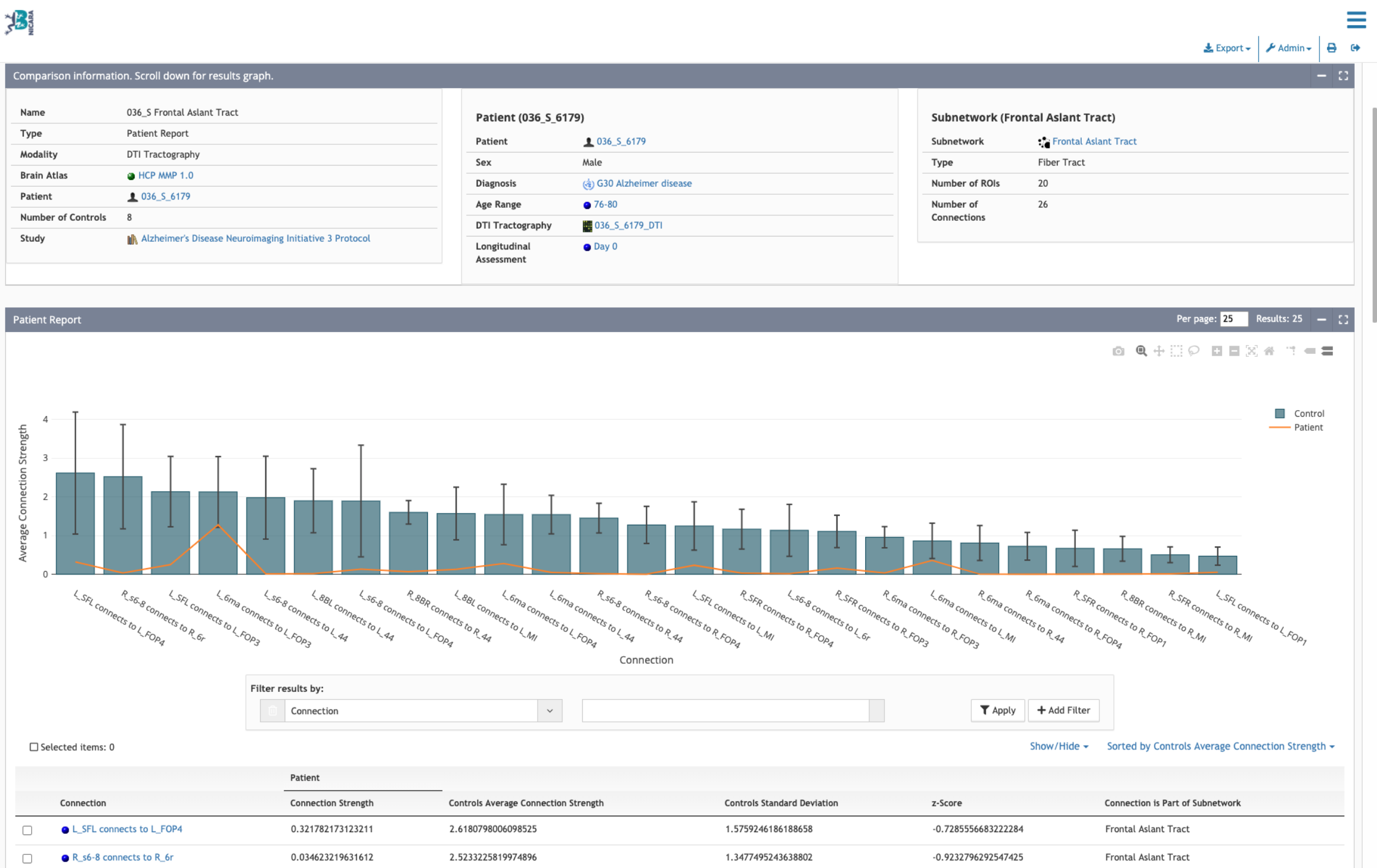


Healthy matched control: stronger and more connections

- > NICARA detects differences in the connectome of AD patients and healthy matched controls of any fiber tract* or functional brain network.

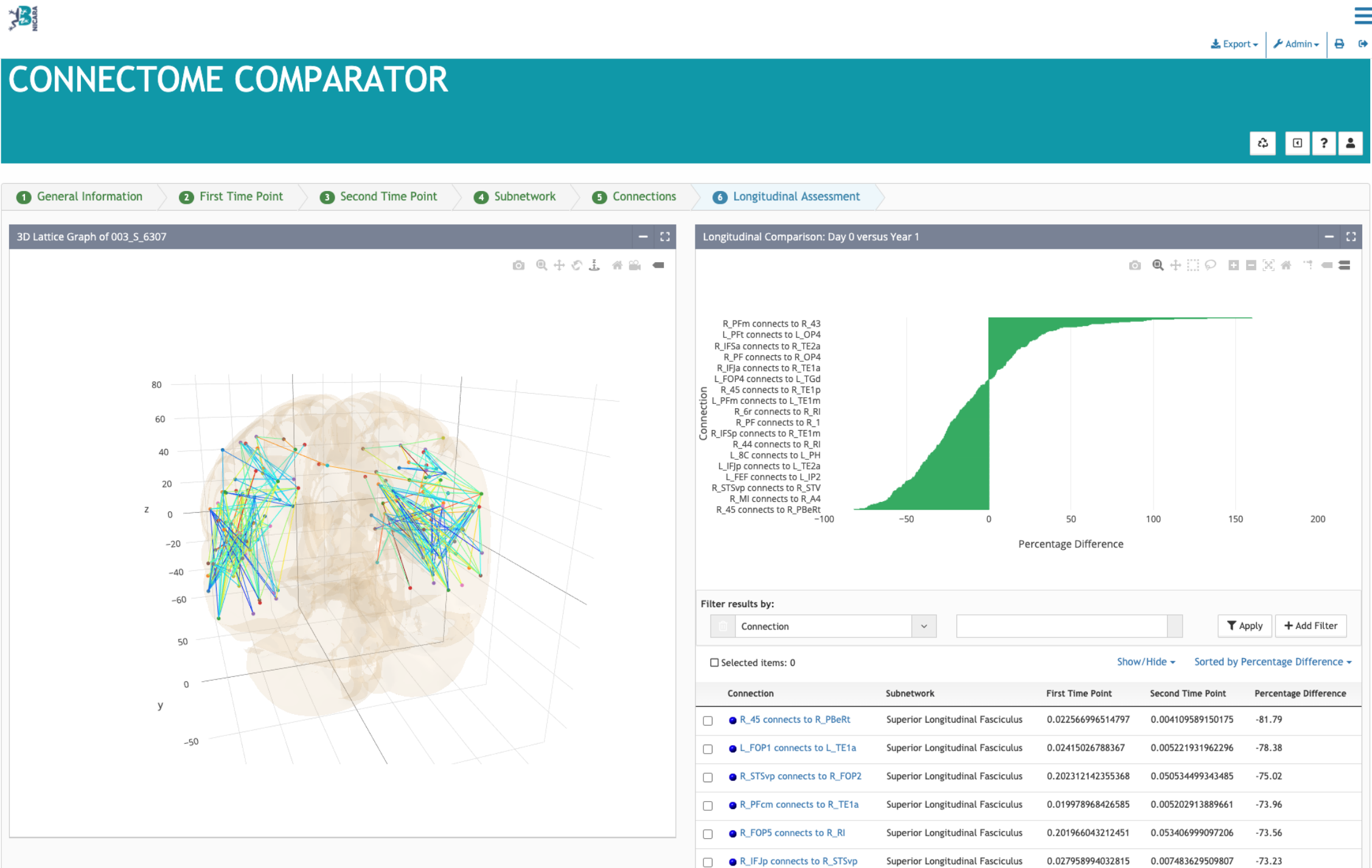
* here: Cingulum fiber tract

Easy to Interpret Patient Report



> NICARA delivers an overview of the patient's brain connectivity in comparison to averaged connectivity of matched controls and standard distribution.

Effects of Treatment with Longitudinal Assessments

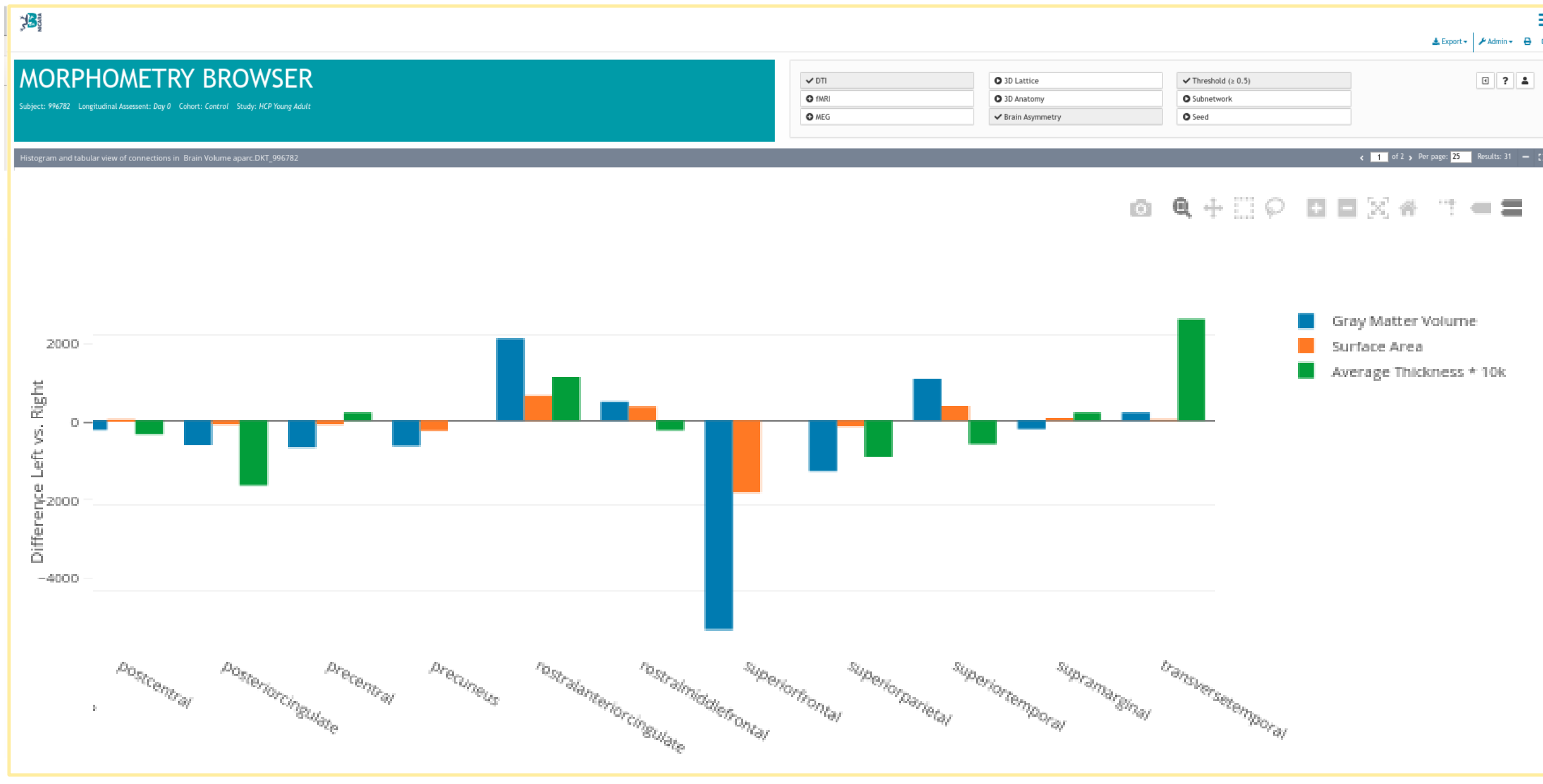


Changes in brain connectivity from cold to warm colors

Percentage changes (x-axis) of connections (y-axis)
(sorted from strongest increase to strongest decrease)

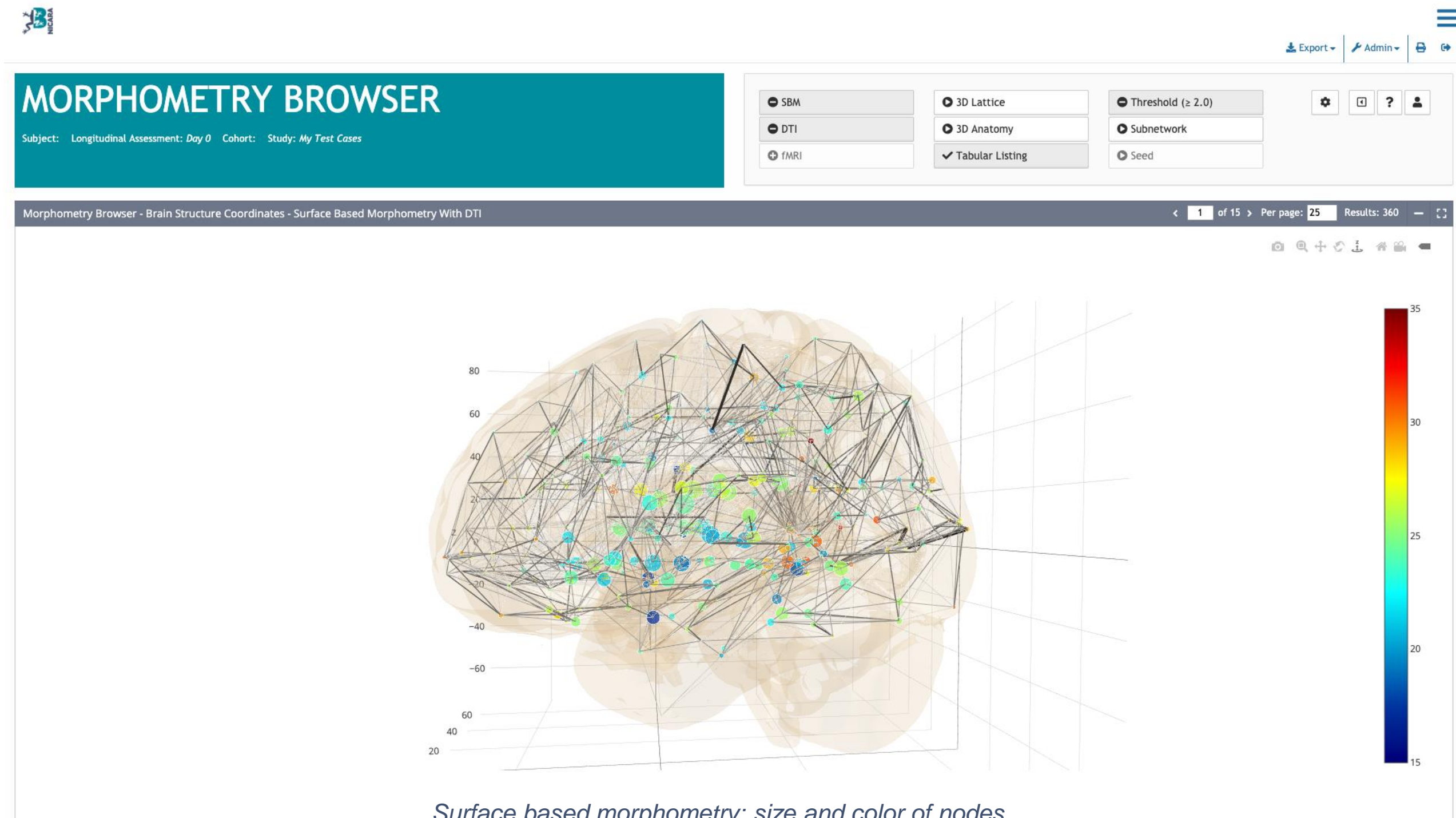
> NICARA helps assess longitudinal changes in brain connectivity before and after treatment.

Morphometry Reports with NICARA



> NICARA delivers manifold reports on the quantification of morphometry of the patient's brain regions.

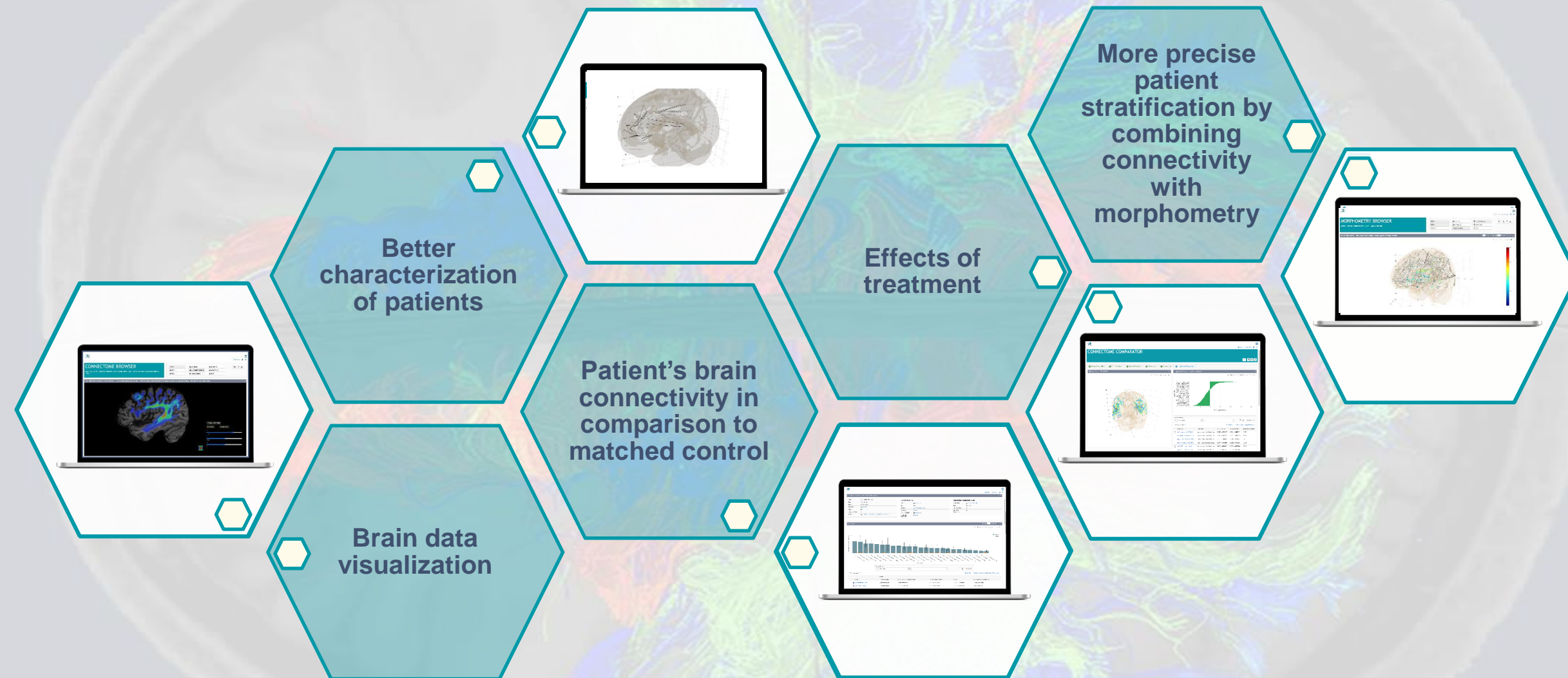
Connectivity Combined with Surface Based Morphometry



Surface based morphometry: size and color of nodes
Surface based full brain DTI tractography: links between nodes

> Direct comparisons between surface based morphometry of brain regions and surface based full brain DTI tractography for a more precise patient characterization in clinical trials.

NICARA for Clinical Trials at a Glance

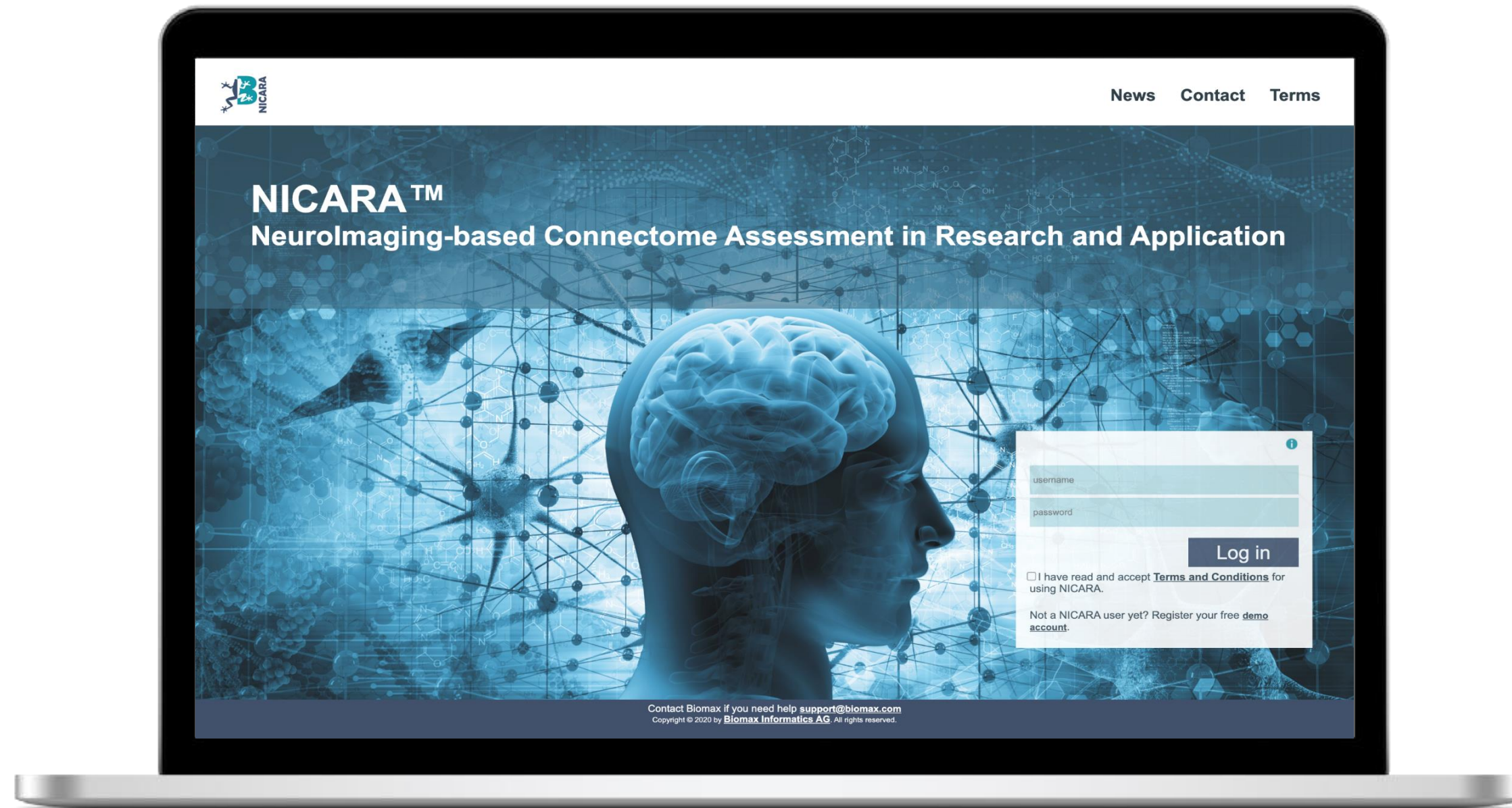


Choose Biomax Informatics as your Preferred Partner

- > We have more than 20 years of experience in knowledge management for the life sciences
- > We have a validated technology through multi-year contracts with reference customers and thousands of users worldwide
- > We have a multidisciplinary team of life science and software experts
- > We have a flexible technology to adapt to your individual needs fast and effectively
- > We are fully GDPR compliant and certified according to ISO 9001 and ISO 27001



Interested in a DEMO of NICARA?



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or contact nicara@biomax.com for a free consultation!