



The Importance of Quantitative Volumetric Analysis for Brain MRI

10 Years of Clinical Practice

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Introduction

For over 20 years, volumetric MR imaging (vMRI) technology has been available in research and clinical environments. Initially, radiology centers developed and used their own imaging parameters and manually evaluated the resulting images. This made clinical application subjective, inconsistent from patient to patient and from scanner to scanner, and all but impractical. The introduction of large-scale multi-institutional research studies, such as ADNI (Alzheimer's Disease Neuroimaging Initiative) in 2004, initiated the streamlining and standardizing of acquisition protocols. In 2006, CorTechs Labs introduced NeuroQuant, the first FDA cleared automated segmentation software, which provided consistent, operator independent measurements of brain structure volumes. Together, these factors permitted clinical users to easily incorporate volumetric MRI technology into their clinical practice.

Since its introduction, a number of studies have evaluated the use of NeuroQuant automated quantification software in clinical practice, comparing it to other automatic or semi-automatic tools, as well as to manual brain segmentation. Consistently, the studies found that NeuroQuant produced segmentation results that were comparable in accuracy to and more precise than manual segmentations. Additionally, the studies found that NeuroQuant produced results in a faster and more reliable manner than manual segmentation methods.

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In addition to fast and consistent segmentation, NeuroQuant software automatically calculates brain structure volumes, which provide clinicians with additional neuroimaging information. The clinical *in vivo* quantitative MRI biomarkers provided vary for each clinical application from hippocampi, inferior lateral ventricles, and mesial temporal lobe, to changes in whole brain and total gray matter, to detailed evaluation of asymmetry between the left and right hippocampus.

Current clinical applications range from evaluation of mild cognitive impairment (MCI) to dementia, epilepsy, and multiple sclerosis, as well as traumatic brain injury (TBI) and other neurodegenerative disorders. NeuroQuant's quantitative volumetric analysis for brain MRI overcomes the initial time-consuming and subjective manual approach obstacles, providing an automated tool suitable for routine clinical use for patients 3 to 100 years of age.

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2 Advantages to CorTechs Labs Volumetric MRI Solutions

Automation and Standardization

A key factor in the success of quantitative volumetric brain segmentation lies in automation. Qualitative and high-level evaluations of MRI images are performed accurately and quickly in the daily clinical routine of a radiology department. However, quantification of brain volumes and quantification of changes in brain volumes are expensive because they are time consuming and often outsourced to 3D labs, if considered at all. In addition, manual segmentation shows a high degree of variability based on many factors [1].

Therefore, segmentation solutions that use automation to minimize user variability, reduce costs, and provide time savings.

CorTechs Labs product offerings, NeuroQuant and LesionQuant*, overcome these obstacles and concerns:

- By providing robustness against scanner variability such as field strength, and hardware differences on segmentation accuracy [2]
- By enabling robustness against minor variability of imaging protocols during acquisition on segmentation accuracy [3]
- Through high accuracy of segmentation [4]
- Through reliable reproducibility of segmentation [5]
- Through overall validation of accuracy of segmentation compared to the gold standard (expert manual segmentation) [6]
- Reducing costs and providing time savings over manual and semi-automatic methods [7]

* LesionQuant™ is part of the NeuroQuant® family of products.

Age Range

CorTechs Labs' patented Dynamic Atlas™ technology allows robust automatic segmentation and volume measurements for patients ranging from ages 3-100, without atlas discontinuity. Using proprietary algorithms, the patient's demographic data are used to predict atlas parameters for that individual at the time of processing. Image alignment, registration and segmentation are more accurate using this personalized approach than would be possible using a static atlas or atlases.

Normative Data

A key component of NeuroQuant is the normative database, providing the capability to compare an individual's brain structure volume measurements to a healthy population. Collected data from several thousand subjects from 3 to 100 years of age with an equivalence of gender are the building blocks of the normative database. NeuroQuant uses comparisons to a norms database to provide clinically relevant information to the user. The resulting information from NeuroQuant is normalized for intracranial brain volume (ICV), gender and age, then compared to healthy norms. This allows NeuroQuant to deliver a precise indication of where that individual's brain structure volume lies within an age- and gender- based reference chart, aiding physicians in their assessment of neurodegenerative conditions.

Longitudinal Evaluation

NeuroQuant's longitudinal reporting feature is a major component in the personalized care path that follows an initial evaluation. It provides physicians with more objective data to help with clinical assessments and when outlining possible clinical courses. When multiple time point measurements of the same patient are available, the longitudinal or multi time point result are displayed on a single volumetric output report, allowing physicians to see a clear progression of any changes to the patient's relevant brain structures.

Workflow Integration

Volumetric MRI can easily be integrated into clinical workflows. NeuroQuant only requires ordering a 3D T1 sequence as part of the brain MRI protocol (as well as a 2D or 3D FLAIR when doing LesionQuant), and does not need any additional non-standard imaging data. NeuroQuant processing can be requested either at the MRI console through DICOM destinations (AETitles), or directly from the PACS system. The entire NeuroQuant output, including spatially corrected and anatomically labeled MR series and volumetric reports, are sent back to the PACS system in 5-7 minutes (up to 20 minutes for LesionQuant) and filed along with other scans from that exam where the radiologist can review them along with the original MRI scans.

3 Volumetric MRI in Clinical Practice

Clinical Use of Quantitative Volumetric Brain Structure Information

For many neurological diseases, disease progression is accompanied by regional or generalized atrophy that can be detected in brain structures measured noninvasively through structural MRI, then quantified using automated volumetric MRI tools, such as NeuroQuant [7].

Dementia/Alzheimer's Disease (AD)

A growing aging population has caused dementia to become one of the largest health concerns in the western world. The advances in neuroimaging using MRI enable the clinical user to closely monitor the progression of neurodegenerative conditions, specifically in the mesial temporal lobe, a key region affected in dementia and a source of cognitive decline.

In addition, studies have shown that certain brain structure volume measurements compared to a healthy norm can help in differential diagnosis between AD and other types of dementia from non-dementia-related causes of cognitive impairment [9][10][11]. Quantitative MR imaging and volume measurements act as *in vivo* biomarkers that may aid in the evaluation of a disease as well as monitor disease modifying effects of potential treatments [8][12] in patients exhibiting symptoms of memory loss.

The NeuroQuant Age Related Atrophy Report includes the volume, percentage of intracranial volume, and normative percentiles for the hippocampi, lateral ventricles, and inferior lateral ventricles, as well as the Hippocampal Occupancy Score (HOC), a calculated factor that is used to quantify mesial temporal lobe atrophy.

Epilepsy

Of the various forms of epilepsy, Temporal Lobe Epilepsy (TLE) is the most common form – presenting in about 65% of all cases. In about 25-30% of cases, TLE does not respond to medication and surgery becomes an option. Before surgery, confirmation of the diagnosis using invasive video electroencephalographic (EEG) recordings is one option, however considering the patient's age, non-invasive volumetric MRI (vMRI) is an alternative path. In general, atrophy in epilepsy patients is not limited to one specific brain structure, however, the volumetric evaluation and asymmetry quantification of the hippocampus is a strong biomarker when evaluating patients that suffer from TLE-related seizures [13].

A recent study found that accurate classification of TLE was improved from 76% using visual inspection of clinical MR imaging studies to 85% using visual inspection of volumetric MR imaging. 94% classification accuracy was achieved using hippocampal asymmetry as the linear classifier [14].

The NeuroQuant Hippocampal Asymmetry Report includes the volume, percentage of intracranial volume, and normative percentiles for the left and right hippocampus, as well as the asymmetry between them.

Multiple Sclerosis (MS)

MS is a complex neurodegenerative disorder that targets both the white and gray matter of the central nervous system. T2 FLAIR white matter lesion quantification such as lesion burden, total volume, lesion count as well as T1 hypointensity information are considered successful biomarkers for the evaluation of disease progression in RRMS. In addition to lesion information, quantification of brain structure volumes such as whole brain, hippocampi, thalami and cerebral gray matter provide the clinical user with new biomarkers for the evaluation of cognitive impairment which significantly affects the patient's quality of life, occupational, and social functioning and can be a predictor of disability [15][16].

MR imaging is the most sensitive and commonly used tool to monitor inflammatory disease activity in MS. It can be used to evaluate disease progression and disease activity during a disease-modifying therapy. Any worsening can be used in the evaluation whether a change in therapy management is to be considered [17].

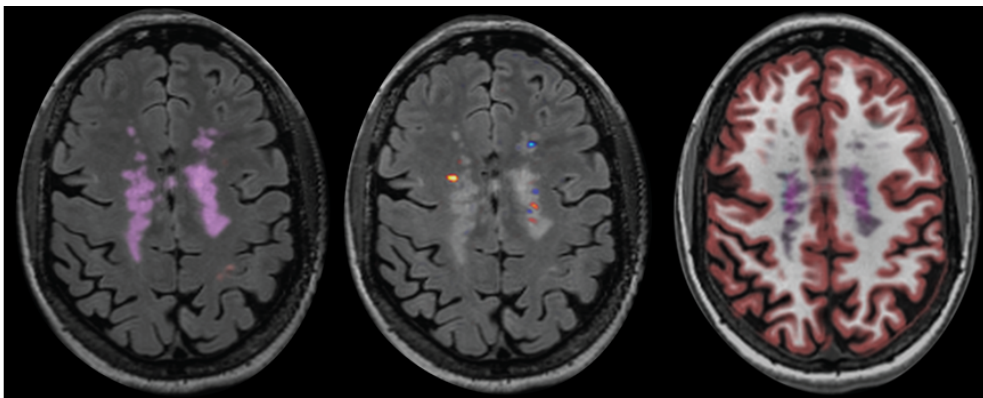
The NeuroQuant Multi Structure Atrophy Report includes the volume, percentage of intracranial volume, and normative percentiles for the for nine brain structures, including the whole brain, white and gray matter, lateral ventricles, inferior lateral ventricles, thalami, 3rd ventricle and hippocampi, as well as, T1-weighted white matter hypointensities.

The LesionQuant FLAIR Lesion Reports include lesion visualization, total number and volume of lesions, lesion burden calculation, new and enlarging lesion identification and quantification, and anatomical lesion distribution, as well as percentage of intracranial volume, and normative percentiles for eight brain structures, including the whole brain, cerebral white and cerebral gray matter, lateral ventricles, inferior lateral ventricles, thalami, 3rd ventricle and hippocampi.

Brain Trauma

Brain trauma or traumatic brain injury (TBI) is one of the most common neurological disorders, contributing to about one-third of all injury-related deaths in the United States. Brain trauma events are a recognized risk factor for cognitive decline and dementia long after surviving a brain injury [18], such as brain trauma sustained by professional athletes who have a history of repetitive brain trauma (concussions and sub-concussions), military personnel who have experienced sudden and violent head movement, for example, from a blast wave, as well as adults and children, in the general population, who have experienced brain injuries from motor vehicle accidents severe brain trauma from falls or blows to the head. The timeline of atrophy development in specific brain structures, as a consequence of brain trauma, is still being researched. However, quantification of the atrophy in very specific brain structures is becoming a key factor in the prognosis of trauma related to long term effects [19][20].

The NeuroQuant Triage Brain Atrophy report is designed to quickly highlight brain structures that may have been affected by trauma and provides quantitative measurements to aid in clinical assessments of brain anatomy after injury. The report includes the normative percentile for 39 brain structures for both the right and left hemisphere and is sorted by lobe and region and it highlights in color the areas that are above or below normative values.



“In addition to fast and consistent segmentation, NeuroQuant software automatically calculates brain structure volumes, which provide clinicians with additional neuroimaging information.”

4 Summary and Conclusions

Automatic and consistent volumetric brain imaging is a powerful tool in the evaluation of many neurodegenerative conditions. The clinical applications range from MCI, dementia (AD), MS, epilepsy, to TBI, and the list grows longer every day. Improvements in volumetric imaging technologies, such as NeuroQuant and LesionQuant, allow for the associated biomarkers to be easily implemented in clinical practice.

NeuroQuant solves following problems:

Problem	Solution
<i>Non-standardized imaging protocol</i>	3D T1 sequence parameters use the established ADNI protocol as a base
<i>Spatial distortions on MR data</i>	Spatial distortions corrected using advanced imaging tools
<i>Labor intensive MRI methods are susceptible to inter-operator variability</i>	Automation of segmentation reduces labor (one-click solution) and removes operator variability
<i>Lack of normative ranges for volume measurements</i>	Normative data for ages 3-100 years

Automated MR image quantification tools, such as NeuroQuant and LesionQuant, have been deemed reliable and suitable for clinical use by several regulatory bodies worldwide. This, along with the ease of workflow incorporation, and a variety of reports providing quantitative measurements from MRI brain studies that can be used in conjunction with other clinical findings as part of physicians' clinical assessments, make incorporating quantitative volumetric analysis into routine clinical practice an obvious and necessary choice.

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