MSMilan2023
ECTRIMS EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS
actrims AMERICAS COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS

P177

Interpretable Thalamic Volume Charts in Multiple Sclerosis

K. M. Leyden[1], D. Peterson[1] , L. Bajus[1], A. Alexander-Bloch[2]
[1]Octave Bioscience Inc., Menlo Park, CA, USA, [2]University of Pennsylvania, Philadelphia, PA, USA

Introduction

In people with multiple sclerosis (PwMS), the thalamus is among the earliest and most atrophied gray matter structures. FDA-cleared software systems for magnetic resonance imaging (MRI) estimate quantitative assessments of thalamic volume which can be provided for clinical interpretation.

However, interpreting these volumes & changes therein can be complicated by age-expected volume loss, natural subject-to-subject variability, and technical differences associated with image acquisition such as image quality & MRI hardware.

Objectives

To establish robust cross-sectional & longitudinal brain charts for thalamic volume based on MRI for PwMS.

Methods

- Data were acquired at 5 multiple sclerosis (MS) centers using 13 MRI scanner models (1.5T (n=262) and 3T (n=496)) employing protocols that included 3D T1 and T2 FLAIR imaging.
- 379 people (290 female and 89 male) living with MS aged 20 to 76 were imaged.
- Thalamic volumes were extracted using an FDA-cleared software tool (NeuroQuantMS v3.1, Cortechs.ai)
- Automated image quality assessment performed using MRIqc tool. [1]
- World Health Organization-recommended generalized additive modeling for location, scale, and shape (GAMLSS) was employed to chart expected quantiles of thalamic volume through the age span separately in biological males (m) & females (f). [2] [3]
- For longitudinal brain charts, conditional GAMLSS were fit for thalamic volume at follow-up timepoints based on scanner factors, contrast-to-noise measured from T1-weighted imaging (T1CNR), previously observed volume & time interval.
- Model fits were assessed by visual inspection of worm plots across scanner manufacturers & field strengths, age ranges, and image quality.

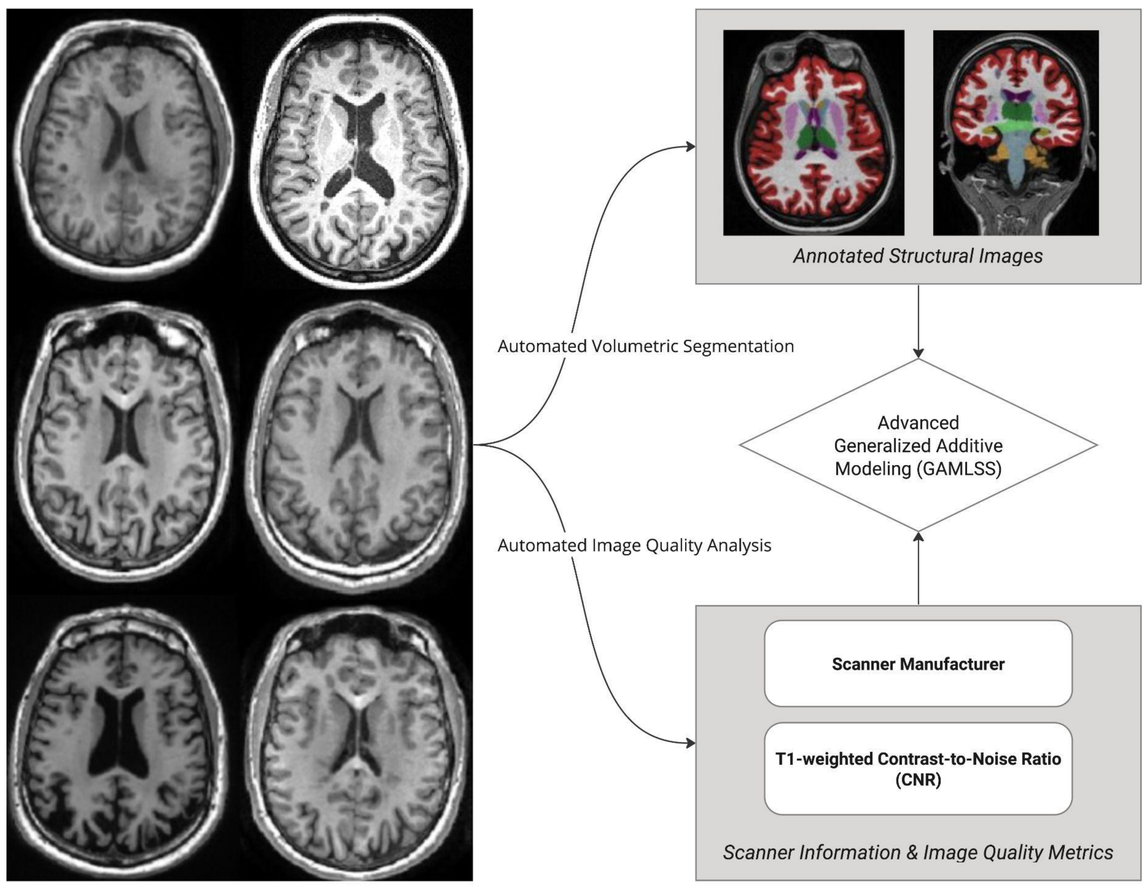

Figure 1. Brain chart modeling strategy integrating structural image analysis to extract thalamic lesion segmentation and quantitative image quality metrics with auxiliary scanner information.

Results

- Cross sectional average thalamic volume estimates evolved through the age span in MS (finding in f, $p<0.001$) & differed across scanner field strengths (m, $p<0.01$).
- Longitudinal thalamic growth chart modeling found associations between average follow-up thalamic volume measurements and:
  - baseline thalamic volume (m and f, $p<2^{-16}$)
  - time interval (f, $p<0.05$)
  - scanner field strength (m, $p<0.03$)
  - T1CNR (m, $p<0.03$)
- Differences across scanner manufacturers in follow-up thalamic volume variance (m and f, $p<0.001$) and kurtosis (m, $p<0.001$) were also demonstrated.
- Model diagnostics indicated good fit of the models across technical factors and age ranges.

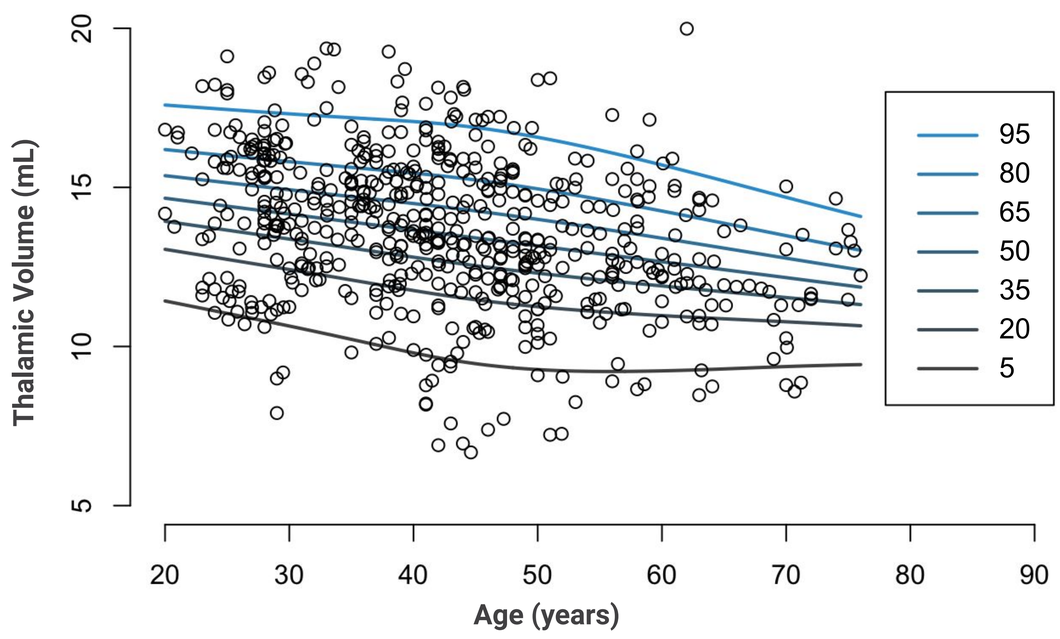

Figure 2: Percentile curves for thalamic volume across the age range in the sample, as determined by GAMLSS.

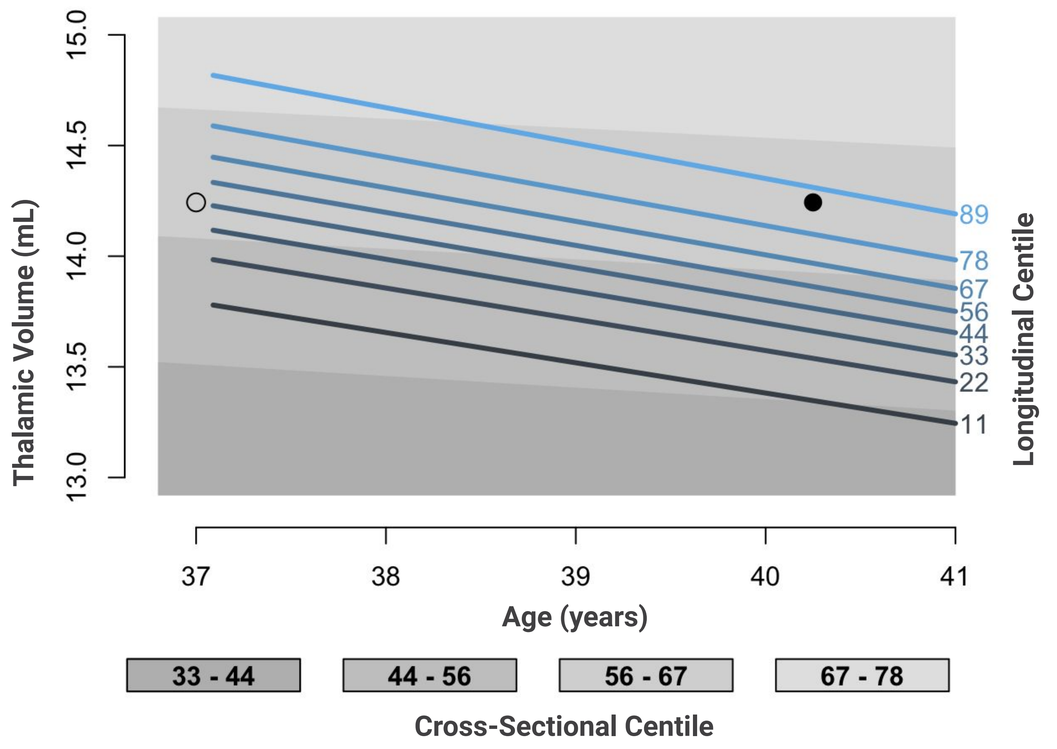

Figure 3: Centiles in a representative patient across two timepoints. In this patient, stable thalamic volume over a three year period may be interpreted as a modest increase in the cross-sectional centile, and a large increase in the longitudinal centile. This indicates stable thalamic volume **relative to other PwMS** who would be expected to have decreased volume over time.

Conclusions

Brain charts for thalamic volume promise to transform difficult-to-interpret quantitative measurements into clinically actionable information for single MRI studies and in the setting of longitudinal monitoring of PwMS.

Disclosure: KML, DP, and LB are employees of Octave Bioscience, Inc. AFA-B receives consulting income from Octave Bioscience, holds equity in Centile Bioscience, and serves on the board of Centile Bioscience.

References: [1] O. Esteban, et al, "MRIQC: Advancing the automatic prediction of image quality in MRI from unseen sites," PLOS ONE, vol. 12, no. 9, p. e0184661, Sep. 2017, doi: 10.1371/journal.pone.0184661.
[2] E. Borghi et al., "Construction of the World Health Organization child growth standards: selection of methods for attained growth curves," Stat. Med., vol. 25, no. 2, pp. 247–265, Jan. 2006, doi: 10.1002/sim.2227.
[3] D. M. Stasinopoulos and R. A. Rigby, "Generalized Additive Models for Location Scale and Shape (GAMLSS) in R," J. Stat. Softw., vol. 23, no. 7, 2007, doi: 10.18637/jss.v023.i07.