7T VS 3T BRAIN MORPHOMETRICS WITH AGE

¹ Brain morphometrics correlations with age among

² 352 participants imaged with both 3T and 7T MRI:

³ 7T improves statistical power and reduces required ⁴ sample size

5

- 6 Cong Chu^{1#}, Tales Santini, PhD^{1#}, Jr-Jiun Liou, PhD¹, Ann D. Cohen PhD², Pauline M. Maki
- 7 PhD³, Anna L. Marsland, PhD⁴, Rebecca C. Thurston, PhD⁵, Peter J. Gianaros, PhD⁶, Tamer S.
- 8 Ibrahim, PhD^{7*}

- 10 ¹Department of Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, USA
- ²Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania, USA
- ³Departments of Psychiatry, Psychology and Obstetrics & Gynecology, University of Illinois
 Chicago, Chicago, Illinois, USA
- ⁴Department of Psychology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA
- ⁵Departments of Psychiatry, Clinical and Translational Science, Epidemiology and Psychology,
- 16 University of Pittsburgh, Pittsburgh, Pennsylvania, USA
- ⁶Departments of Psychology and Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania,
 USA
- ⁷Departments of Bioengineering, Psychiatry, and Radiology, University of Pittsburgh, Pittsburgh,
 Pennsylvania, USA
- 21
- 22 [#]Contributed equally and share the first authorship
- 23
- 24 ^{*}Correspondence:
- 25 Tamer S. Ibrahim, PhD
- 26 Professor of Bioengineering, Psychiatry, and Radiology

- 27 Director, 7 Tesla Bioengineering Research Program (7TBRP)
- 28 Swanson School of Engineering, and School of Medicine
- 29 University of Pittsburgh
- 30 3501 Fifth Avenue, Pittsburgh, PA 15213
- 31 tibrahim@pitt.edu
- 32
- **33** Word count: 4370

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

34 Abstract

35 Introduction

- 36 Magnetic resonance imaging (MRI) at 7 Telsa (7T) has superior signal-to-noise ratio to 3 Telsa
- 37 (3T) but also presents higher signal inhomogeneities and geometric distortions. A key knowledge
- 38 gap is to robustly investigate the sensitivity and accuracy of 3T and 7T MRI in assessing brain
- 39 morphometrics. This study aims to (a) aggregate a large number of paired 3T and 7T scans to
- 40 evaluate their differences in quantitative brain morphological assessment using a widely
- 41 available brain segmentation tool, FreeSurfer, as well as to (b) examine the impact of
- 42 normalization methods for subject variability and smaller sample sizes on data analysis.

43 Methods

- 44 A total of 452 healthy participants aged 29 to 68 were imaged at both 3T and 7T. Structural T1-
- 45 weighted magnetization-prepared rapid gradient-echo (MPRAGE) images were processed and
- 46 segmented using FreeSurfer. To account for head size variability, the brain volumes underwent
- 47 intracranial volume (ICV) correction using the Residual (regression model) and Proportional
- 48 (simple division to ICV) methods. The resulting volumes and thicknesses were correlated with
- 49 age using Pearson correlation and false discovery rate correction. The correlations were also
- 50 calculated in increasing sample size from 3 to the whole sample to estimate the sample size
- 51 required to detect aging-related brain variation.

52 *Results*

53 352 subjects (210 females) passed the image quality control with 100 subjects excluded due to 54 excessive motion artifacts on 3T, 7T, or both. 7T MRI showed an overall stronger correlation

- 55 between morphometrics and age and a larger number of significantly correlated brain volumes
- 56 and cortical thicknesses. While the ICV is consistent between both field strengths, the Residual
- 57 normalization method shows markedly higher correlation with age for 3T when compared with
- the Proportional normalization method. The 7T results are consistent regardless of the
- 59 normalization method used.

60 *Conclusion*

- 61 In a large cohort of healthy participants with paired 3T and 7T scans, we compared the statistical
- 62 performance in assessing age-related brain morphological changes. Our study reaffirmed the
- 63 inverse correlation between brain volumes and cortical thicknesses and age and highlighted
- 64 varying correlations in different brain regions and normalization methods at 3T and 7T. 7T
- 65 imaging significantly improves statistical power and thus reduces required sample size.

66 Keywords

67 Magnetic resonance imaging, 3T, 7T, brain morphometrics, aging

68 Key points

Compared to 3T, 7T has stronger inverse correlations of total grey matter, subcortical grey matter, and white matter volumes, and mean cortical thickness with age.

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

- Compared to 3T, 7T shows a greater number of brain volumes and cortical thicknesses
 that have statistically significant correlations with age.
- For comparable statistical power at 3T, the required sample size for 7T is reduced for cortical and subcortical volumes, and substantially reduced for cortical thicknesses.

75 Introduction

Magnetic Resonance Imaging (MRI) provides optimal *in vivo* soft tissue contrast and is the method of choice to investigate many cerebral abnormalities such as tumors, atrophy, vascular diseases, demyelinating diseases, trauma, infection, and developmental anomalies (Barisano et al., 2019). The current state of the art clinical usage of MRI could shift from scanners with a static magnetic field of 3 Tesla (T) to the recently FDA-cleared 7T MRI (US FDA, 2024). However, this change is not merely a rescaling of the system but a major

82 engineering challenge.

The 7T MRI offers a higher signal-to-noise ratio (SNR) due to its inherently higher spin 83 84 signal, as well as improved tissue contrast due to longer T1 and shorter T2 and T2* relaxation times, which help to enhance image and angiography contrasts (Okada et al., 2022; Perera 85 86 Molligoda Arachchige & Garner, 2023). Moreover, its higher sensitivity to susceptibility 87 differences enhances BOLD contrast (Okada et al., 2022; Perera Molligoda Arachchige & 88 Garner, 2023), which is often used in functional imaging. However, the shorter wavelength of the 89 electromagnetic excitation at 7T increases image inhomogeneity (Ibrahim et al., 2007) and 90 average/local power deposition (Ibrahim & Tang, 2007) for neuroimaging. Both increased average and local power deposition limits the maximum allowed power to be used during the 91 92 scans (Fiedler et al., 2018). Moreover, the increased sensitivity to susceptibility can cause 93 distortions and artifacts in regions with thin air-brain interfaces, such as the sinus (Truong et al., 94 2006), depending on the subject's anatomy. Structural images can also be contaminated with 95 angiography signals, making it difficult for automated segmentation tools to determine brain 96 volumes in specific regions (Choi et al., 2020; Viviani et al., 2017)

97 Given these trade-offs, there is a need to investigate the sensitivity and specificity of using 3T and 7T MRI to brain morphometrics in a large data set where the same subjects 98 99 undergo scans at both field strengths. With no clear ground truth in whole brain morphometrics, 100 prior studies have shown that after the human brain reaches its maximum volume between the 101 ages of 25-30 (Fiell et al., 2014; Fiell, 2010), a subject-specific loss of cerebral volume is 102 expected over time. Therefore, MR studies have typically investigated the morphological 103 characteristics and atrophy of brain regions in relation to aging. Studies have found that total 104 grey matter volumes decrease consistently over age, while individual regions showed specificity 105 in their rate of decrease (Fjell et al., 2014; Fjell, 2010). Cortical thicknesses have also been 106 observed to negatively correlate with age (Fiell et al., 2014; Fiell, 2010). White matter volume, 107 on the other hand, differed from grey matter such that it shows modest changes until 40-50 years 108 before a rapid decrease in volume (Fjell et al., 2014; Fjell, 2010).

Compared to 3T, 7T MRI has been shown to provide improved spatial resolution for the
same acquisition times (Okada et al., 2022; Perera Molligoda Arachchige & Garner, 2023).
However, due to field inhomogeneities, 7T structural images provided restricted performance
improvement regarding clinical diagnosis (Springer et al., 2016) and morphometric assessment
(Lusebrink et al., 2013; Seiger et al., 2015). These studies, however, were limited by their small

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

- sample size of paired 3T and 7T images and by the hardware limitations such as commercial
- radiofrequency (RF) coils. Our study aims to analyze a large number of same-subject 3T and 7T
- scans (> 400) to investigate their performance difference in quantitative brain morphological
- assessment using a widely available brain segmentation tool, FreeSurfer, in addition to
- 118 homogeneous RF coils that largely eliminate field inhomogeneities and signal voids at 7T
- 119 (Andrea N Sajewski, 2023; Kim et al., 2016; Krishnamurthy et al., 2019; Santini et al., 2021;
- Santini et al., 2018). Specifically, we investigated how different statistical analysis and
- normalization methods may affect the resulting statistical power including correlation strength
- 122 and sample size. Finaly, provide regression models of the expected regional brain volumes and
- 123 cortical thicknesses by age.

124 Methods

125 Participants

126The dataset was pooled from multiple studies (NIH RF1AG053504, R01AG053504,

- P01HL040962, and R01DK110041) recruiting healthy participants under the Institutional
- 128 Review Board of The University of Pittsburgh, Pittsburgh, USA. Prior to their initial visit,
- participants underwent a comprehensive informed consent process, which included a detailed
- review of the study's objectives. Participants were eligible if they were between the ages of 18and 80 and had no contraindication to an MRI scan. Additionally, screening for pre-existing
- 132 dementia was conducted using both the Informant Questionnaire on Cognitive Decline in the
- 133 Elderly and the Clinical Dementia Rating scale for exclusions.
- 134 Data Collection

135 Before quality control, in total, 452 subjects had completed paired 3T and 7T MPRAGE sequence with an average (SD) interval of 4.96 (4.16) year. The 7T scans were acquired using a 136 137 7T Magnetom system in the sTx mode (single channel) with either the first (16 - combined into 138 one - transmit and 32 receive channels) or second (60 transmit - combined into one - transmit 139 and 32 receive channel) generation of in-house-designed Tic-Tac-Toe RF coil systems. These RF 140 coil systems are known for producing homogeneous images (Andrea N Sajewski, 2023; Kim et 141 al., 2016; Krishnamurthy et al., 2019; Santini et al., 2021; Santini et al., 2018). The 3T scans 142 were acquired with either a Trio or PRISMA systems and utilized an integrated whole-body RF 143 coil for excitation and a commercial 32-ch coil for reception. Description of the acquisition 144 parameters and type of sequences are provided in Table 1.

145 Image Processing

146 Both 3T and 7T scans were processed using the same pipeline. The images were 147 corrected for gradient distortion [https://github.com/Washington-University/gradunwarp] and 148 then underwent intensity bias correction using SPM12 (Statistical Parametric Mapping: The 149 Analysis of Functional Brain Images, 2006). Brain stripping was performed using SynthStrip 150 (Hoopes et al., 2022) followed by a 6 DOF rigid registration to MNI space with their respective 151 resolution using Greedy (https://github.com/pyushkevich/greedy). Finally, brain volumes and 152 cortical thicknesses were extracted using FreeSurfer version 7.1.1 (Fischl, 2012) and using the 153 "highres" flag. Intracranial volumes were calculated from the brain mask output of SynthStrip.

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

154 The quality control process of the FreeSurfer segmentation output began with classifying 155 the scans into three grades: 1) pass, 2) re-run, and 3) fail. For grade 2 scans, control points were placed on white matter regions that failed to be identified by FreeSurfer. After the re-run with 156 157 control points, scans were reclassified into either pass of fail. If a subject had either 3T or 7T 158 segmentation classified as failed, both 3T and 7T scans were excluded from the analysis. We also 159 identified and excluded regions that are not consistently segmented due to the presence of dura, 160 or due to the presence of arteries on the 7T images but not on the 3T images. Both issues impact 161 the accuracy as well as the consistency of the FreeSurfer segmentation of the excluded cortical 162 regions on both the 3T and 7T images.

163 Statistical Analysis

164 The volume of the brain regions underwent intracranial volume (ICV) correction using 165 two methods (Wang et al., 2024): In the Residual method, the regions along with ICV and sex 166 were entered into a multiple regression. We extracted the residuals which represented the 167 morphometric information without the effect of ICV and sex. In the Proportional method: the 168 volume regions were divided by their respective ICV and then corrected for sex using regression. 169 Cortical thicknesses were only corrected by sex.

Each region was then correlated with age using Pearson correlations in MATLAB 170 171 (version R2022a) (MathWorks, Natick MA). Multiple comparison corrections using Benjamini-172 Hochberg method for False Discovery Rate (FDR) (Benjamini & Hochberg, 1995) were then 173 performed on the p-values within groups separated by cortical volumes, cortical thicknesses, and 174 subcortical volumes. Regions with FDR corrected p-values lower than 10% FDR threshold were 175 considered significantly correlated with age. Linear regression was used to calculate the slope of 176 the correlation. The regions were also fitted with a second order polynomial to estimate the effect 177 of aging on the rate of volume or thickness change. When comparing the correlation coefficient 178 between 3T and 7T data, z-test was performed on the R values undergoing Fisher's z 179 transformation. The correlation coefficient was statistically stronger than one another when the

180 resulting one-tailed p value was less than 0.05.

181 To evaluate the effects of the sample size in the number of regions significantly 182 correlated with age, the correlations were calculated in increasing sample size (n = 3 to full 183 sample) for 3T and 7T scans. Each subsample was randomly selected 1000 times without 184 repeating to estimate the error range.

- For cortical grey matter volume regions, we also calculated the annual rate of change.
 The linear regression equation was used to calculate the volume at the median age of the
 negative and the abange of volume in one voer
- 187 population and the change of volume in one year.

188 Results

189 Demographics and quality control outcomes

352 subjects out of 452 (female = 210) ranged between 29 and 68 years passed the
quality control and were included in the analysis. 100 subjects were excluded due to motion
artifacts. Demographics, including sex, race, and years of education, as well as the medical
history of the dataset included in the analysis are shown in Table 2. Of the participants imaged,

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

194 59.7% are female, 87.5% are white, and received 17.3 years of education (16 = college graduate;

195 18 = master's degree). Less than 5% of them have high blood pressure, heart murmur, and

anxiety disorders. Participants completed their 3T scan at a mean age of 45.7 years,

approximately five years prior to the 7T scan (50.9 years).

198 The quality control process also identified 6 cortical regions (entorhinal, 199 parahippocampal, rostral anterior cingulate, caudal anterior cingulate, insula, and transverse 200 temporal) where FreeSurfer was not able to generate accurate and consistent segmentations due 201 to the presence of blood vessels and dura. Examples can be found in **Supplementary Figure S1**. 202 We therefore removed these regions when comparing the correlation results between 3T and 7T. 203 Statistics of the removed regions are still included in Supplementary Table S1. The correlation 204 results therefore included 50 cortical volumes and 50 cortical thicknesses, and 38 subcortical 205 volumes.

206 Correlations of brain volumes and cortical thicknesses with age

207 Correlation between regional brain morphometrics and age from 352 pairs of 3T and 7T 208 scans were calculated. Figure 1 provides an overview of the results by categorizing the regions 209 into total cortical grey matter volumes, total subcortical grey matter volumes, cerebral white 210 matter volumes, and mean cortical thickness. For cortical and subcortical grey matter volumes, 211 we saw both types of ICV corrections improved the correlation coefficient with age at 7T while 212 weakening it at 3T. Pearson's R values at 7T were significantly higher than at 3T using both the 213 Residual and Proportional methods for both the cortical (pResidual < 1e-4, pProportional < 1e-7) and 214 subcortical (p_{Residual} < 1e-5, p_{Proportional} < 1e-3) grey matter volumes. While not notably changing 215 the outcomes at 7T, the Residual method showed better R values at 3T when compared to the 216 Proportional method. These results were independent of the ICV estimations, since they were 217 almost identical at 3T and 7T (R=0.98, Figure 4). White matter volume showed weaker 218 correlation with age than grey matter and had failed to show significance at 3T with both ICV 219 correction methods. Mean cortical thickness which included sex only correction also failed to 220 show significance at 3T while showing strong significance (p < 1e-10) and R value (-0.34) at 7T.

221 Pearson's R values mapped into individual cortical regions are illustrated in Figure 2. The regions in the frontal and occipital lobe showed a generally stronger correlation than the 222 temporal and parietal lobe. Regions with a strong correlation such as the superior frontal gyrus 223 224 can be found significant at both 3T and 7T. Supplementary Table S1 lists the correlation results 225 of all regional brain volumes and cortical thicknesses after FDR correction (using the residual 226 methods for ICV correction), as well as the respective linear regression slope and second-degree 227 coefficient of the polynomial fit. When using the Residual method, 48 (50) out of 54 cortical 228 volumes, 12 (40) out of 54 cortical thicknesses, and 25 (27) out of 38 sub-cortical volumes were 229 found significantly correlated with age at 3T (7T). When using the Proportional method, 32 (53) 230 out of 54 cortical volumes, 12 (40) out of 54 cortical thicknesses, and 21 (24) out of 38 sub-231 cortical volumes were found significant at 3T (7T).

The relationship between number of significant regions and sample size (N from 3 to 352) at 3T and 7T considering the different methods of ICV corrections is shown in **Figure 3**. For all brain volumes and cortical thicknesses combined, 32% (n = 111) of the 7T sample size were required to reach 85 significant regions found from the full 3T sample size (n = 352), corrected for ICV using the Residual method which achieves better correlation than the

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

- 237 Proportional method most especially at 3T. When considering only cortical volumes
- (thicknesses), 73% (12%) of the 7T sample size were required to reach the same number of
- significant regions when compared with the full sample of 3T. For all 74 regions that were
- significant at both 3T and 7T, we compared the correlation coefficients and found that 20 (1,
- 241 Optic Chiasm) regions had statistically stronger R value at 7T (3T) than the other field strength.
- 242 Supplementary Table S1 lists the p value for comparison between all regions.
- Figure 4 first affirmed the consistent ICV calculation between 3T and 7T, with a Pearson's R=0.98. It then displayed the effect of ICV correction by showing the linear regression between corrected total cortical grey matter volume and ICV. Despite the fact that the Residual method proved to be effective at both 3T and 7T, interestingly we saw that the 7T images are less sensitive to the method of ICV correction.
- We also mapped the cortical volume annual rate of change onto a brain atlas in **Figure 5**. The mean rate of change among regions with significant correlation with age was 0.32% for both 3T and 7T. We saw the frontal and occipital lobe, along with part of the temporal lobe volume decrease faster in general. The Residual method was used for this analysis.

252 Discussion

253 In this study, we analyzed a large dataset of paired 3T and 7T MR images acquired on 254 normal aging adults from 29 to 68 years of age, which allowed us to characterize the difference in their statistical performance when assessing cross-sectionally the brain morphometrics 255 256 correlations as we age. We showed a heterogenous negative correlation between brain volume and age while providing an overview of how correlation of individual brain regions may be 257 258 observed differently at either 3T or 7T. When subjected to a feasible scan time, less subjects 259 would be necessary by scanning at 7T, providing studies with more flexibility to acquire 260 additional sequences and/or save costs. When considering cortical thicknesses, which is required 261 for AD cortical signature detection (Dickerson et al., 2009), only 7T provides sufficient brain 262 coverage and sensitivity to aging effects.

The innovative radiofrequency coil developments (Andrea N Sajewski, 2023; Kim et al., 264 2016; Krishnamurthy et al., 2019; Santini et al., 2021; Santini et al., 2018) mitigated the 265 excitation inhomogeneity traditionally observed at 7T MRI, potentially allowing more brain 266 regions to be reliably quantified. Tailored preprocessing steps along with manual quality 267 assurance and correction could further refine the automatic cortex parcellation by FreeSurfer.

268 The method of ICV correction greatly affects the results of correlation analysis, most 269 notably in the 3T dataset. Previous studies (Wang et al., 2024) had investigated such effect on the correlation between brain volumetric measurements and cognitive performance at 3T, in which 270 271 they showed that the regression based method was preferable in relation to the proportional 272 method, which generated results that were biologically implausible. In our analysis, limited to 273 morphometric variables alone, both correction methods were able to deliver plausible results, 274 i.e., negative correlation between age and brain regional volumes. However, we noted that after 275 correction using the Proportional method, the 3T dataset maintained a strong correlation between 276 brain volumes and ICV, which could be interacting with the effect of age and thus reducing 277 Pearson's R values. The 7T dataset, on the other hand, showed little sensitivity as to which

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

correction method was used. The Residual method seems to be the preferable one, since it givesits universal applicability.

Previous longitudinal studies (Fjell et al., 2013; Otsuka et al., 2022) on the relationship between grey matter volume and age reported an annual rate of change around 0.4% across brain regions. In our cross-sectional linear regression analysis, we derived a mean annual rate of change of 0.32% at both 3T and 7T at the study median age. The demographics as well as the image acquisition methods varied between our dataset and those of the published data. The Fjell study was using 1.5T MRI while the cohort lacked control for cognitive performance. The crosssectional nature of our dataset may also play a role in the difference.

287 The white matter volume showed stability over aging at 3T and a small effect size, but significant, at 7T after adjusting for ICV. Studies have shown that white matter volume 288 289 progresses differently with age compared to grey matter volume. Previous studies also showed 290 modest changes in white matter volume until 40-50 years old before an accelerated decline (Fiell 291 et al., 2014; Fjell, 2010). Hence a simple linear regression may not be enough to fully 292 characterize the change of white matter volume with age. Further efforts shall be made to model 293 the white matter volume by separating the age range while controlling other factors affecting 294 white matter such as white matter hyperintensities and perivascular spaces (Fiell et al., 2014; 295 Fjell, 2010).

296 As we gathered this large dataset of same-subject 3T and 7T scans, there was an average 297 scan interval of 5.2 ± 4.5 years (after quality control). While the lack of field strength specific 298 harmonization methods limited our ability to perform longitudinal analysis, the distance between 299 the 3T and 7T scan resulted in different age distribution between groups. Fortunately, the 300 quadratic terms are minimal in most regions, indicating that the relationship is nearly linear for 301 the age range in this study and the impact of age differences at the scanning is relatively minor. 302 At the moment of this analysis, information regarding comorbidities, lifestyle, cognition, AD risk 303 factors, and other relevant factors presented in Table 2 were not included as covariates in the 304 analysis, which could influence the change trajectory of brain morphometrics and will be subject 305 of future study.

306 Our study also identified some limitations regarding the acquired datasets at both 3T and 307 7T. Firstly, FreeSurfer segmentations could fail when the cortex, occipital lobe specifically, had 308 insufficient grey matter to white matter contrast sometimes observed in the 3T datasets. Control 309 points were placed to aid the re-run of FreeSurfer segmentation. In the case of poor global 310 contrast caused in conjunction with motion artifact, the subject is excluded. Cortical thickness 311 measurements could also be biased due to the inconsistent tissue boundary due to the lack of 312 white to gray matter contrast. Secondly, due to the altered T1 relaxation time, blood vessels, 313 otherwise invisible at 3T, are marked with ultra bright contrast on 7T MPRAGE images. These 314 blood vessels distinguish themselves with the surrounding tissue drastically, creating challenges 315 for FreeSurfer algorithms which are tailored to lower field strengths image contrast. Major blood 316 vessels such as the middle cerebral artery and pericallosal artery, were oftentimes included in the 317 segmentation of their surrounding brain regions such as the anterior cingulate cortex, the 318 parahippocampal cortex, the entorhinal cortex, the insula cortex, and the transverse temporal 319 cortex in the 7T image segmentations. These regions were found to be either insignificant or 320 having a weak and inconsistent correlation with age, which could be explained by inaccurate

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

segmentation. We have excluded the most effected regions from this analysis. Another tissue that 321 322 was more visible at 7T was the dura. While deep learning-based brain extraction provided consistent results across magnet strength and scanning procedure for our dataset, the survival rate 323 324 of dura after brain stripping remained inconsistent, resulting in inconsistent over-classification of 325 surface temporal cortical regions in the 7T segmentations. The effect of dura is manifested in the 326 positive correlation between parahippocampal, entorhinal cortex thickness and age. The 327 worsened susceptibility effects at 7T also gave rise to the air-tissue interface distortion artifact 328 near the sinus in about half of the subjects, mainly presented in the inferior border of the orbital

- 329 front cortex with extreme hyperintensity, veiling the cortex's true boundary. While the impact to
- 330 the volume measurement was limited, the susceptibility artifact appeared as an inevitable
- 331 obstacle in calculating the true morphometrics of the region. Regarding the drawbacks
- encountered when segmenting the entorhinal and parahippocampal cortex with FreeSurfer,
- efforts have been made to address this issue: for instance, with the ASHS package and ASHS-
- PMC-T1 atlas, it is potentially possible to distinguish the complex tissues around the region and
 to generate more precise cortical/subcortical segmentations of the middle temporal lobe regions
- 336 (Xie et al., 2016; Yushkevich et al., 2015).

337 Conclusion

- 338 In this cohort of 352 participants with paired 3T and 7T scans, we compared the statistical
- performance in assessing age-related brain morphological changes. Our study reaffirmed the
- inverse correlation between brain volumes and cortical thicknesses and age and highlighted
- 341 varying correlations in different brain regions at 3T and 7T. Compared to 3T, 7T has stronger
- 342 correlations of total grey matter, subcortical, and white matter volumes, and mean cortical
- thickness with age, and shows more brain regions in which they volumes and cortical thicknesses
- have statistically significant correlations with age. For comparable statistical power at 3T, the
- required sample size for 7T is reduced for cortical and subcortical volumes, and substantially
- 346 reduced for cortical thickness.

347 Acknowledgements

- 348 This research was supported by the National Institutes of Health (NIH-R56AG074467, NIH-
- 349 R01AG053504, NIH-P01AG025204, NIH-RF1AG053504, NIH-R01MH111265, NIH-
- 350 P01HL040962, and NIH-R01DK110041) and in part by the University of Pittsburgh Center for
- 351 Research Computing, RRID:SCR 022735, through the resources provided. Specifically, this
- 352 work used the HTC cluster, which is supported by NIH award number S100D028483.

353 Conflict of interest statement

The authors declare no conflict of interest.

355 References

- 356 Andrea N Sajewski, T. S., Anthony DeFranco, Boris Keil, Hecheng Jin, Jacob Berardinelli,
- Jinghang Li, Cong Chu, Tiago Martins, and Tamer S Ibrahim. (2023). *An Open* 60-
- 358 channel Tx/ 32-channel Rx RF Coil System for Routine Use at 7T ISMRM,
- Barisano, G., Sepehrband, F., Ma, S., Jann, K., Cabeen, R., Wang, D. J., Toga, A. W., & Law,
- 360 M. (2019). Clinical 7 T MRI: Are we there yet? A review about magnetic resonance

361	imaging at ultra-high field. Br J Radiol, 92(1094), 20180492.					
362	https://doi.org/10.1259/bjr.20180492					
363	Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and					
364	Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society. Series					
365	B (Methodological), 57(1), 289-300.					
366	http://www.jstor.org.pitt.idm.oclc.org/stable/2346101					
367	Choi, U. S., Kawaguchi, H., & Kida, I. (2020). Cerebral artery segmentation based on					
368	magnetization-prepared two rapid acquisition gradient echo multi-contrast images					
369	in 7 Tesla magnetic resonance imaging. <i>Neuroimage</i> , 222, 117259.					
370	https://doi.org/10.1016/j.neuroimage.2020.117259					
371	Dickerson, B. C., Bakkour, A., Salat, D. H., Feczko, E., Pacheco, J., Greve, D. N., Grodstein,					
372	F., Wright, C. I., Blacker, D., Rosas, H. D., Sperling, R. A., Atri, A., Growdon, J. H.,					
373	Hyman, B. T., Morris, J. C., Fischl, B., & Buckner, R. L. (2009). The cortical signature					
374	of Alzheimer's disease: regionally specific cortical thinning relates to symptom					
375	severity in very mild to mild AD dementia and is detectable in asymptomatic					
376	amyloid-positive individuals. Cereb Cortex, 19(3), 497-510.					
377	https://doi.org/10.1093/cercor/bhn113					
378	Fiedler, T. M., Ladd, M. E., & Bitz, A. K. (2018). SAR Simulations & Safety. <i>Neuroimage</i> , 168,					
379	33-58. <u>https://doi.org/10.1016/j.neuroimage.2017.03.035</u>					
380	Fischl, B. (2012). FreeSurfer. <i>Neuroimage</i> , 62(2), 774-781.					
381	https://doi.org/10.1016/j.neuroimage.2012.01.021					
382	Fjell, A. M., McEvoy, L., Holland, D., Dale, A. M., Walhovd, K. B., & Alzheimer's Disease					
383	Neuroimaging, I. (2013). Brain changes in older adults at very low risk for					
384	Alzheimer's disease. <i>J Neurosci, 33</i> (19), 8237-8242.					
385	https://doi.org/10.1523/JNEUROSCI.5506-12.2013					
386	Fjell, A. M., McEvoy, L., Holland, D., Dale, A. M., Walhovd, K. B., & Alzheimer's Disease					
387	Neuroimaging, I. (2014). What is normal in normal aging? Effects of aging, amyloid					
388	and Alzheimer's disease on the cerebral cortex and the hippocampus. <i>Prog</i>					
389	Neurobiol, 117, 20-40. <u>https://doi.org/10.1016/j.pneurobio.2014.02.004</u>					
390	Fjell, A. M. W., Kristine B. (2010). Structural Brain Changes in Aging: Courses, Causes and					
391	Cognitive Consequences. Reviews in the Neurosciences.					
392	Hoopes, A., Mora, J. S., Dalca, A. V., Fischl, B., & Hoffmann, M. (2022). SynthStrip: skull-					
393	stripping for any brain image. <i>Neuroimage</i> , 260, 119474.					
394	https://doi.org/10.1016/j.neuroimage.2022.119474					
395	Ibrahim, T. S., Mitchell, C., Abraham, R., & Schmalbrock, P. (2007). In-depth study of the					
396	electromagnetics of ultrahigh-field MRI. NMR Biomed, 20(1), 58-68.					
397	https://doi.org/10.1002/nbm.1094					
398	Ibrahim, T. S., & Tang, L. (2007). Insight into RF power requirements and B1 field					
399	homogeneity for human MRI via rigorous FDTD approach. J Magn Reson Imaging,					
400	25(6), 1235-1247. <u>https://doi.org/10.1002/jmri.20919</u>					
401	Kim, J., Krishnamurthy, N., Santini, T., Zhao, Y., Zhao, T., Bae, K. T., & Ibrahim, T. S. (2016).					
402	Experimental and numerical analysis of B1(+) field and SAR with a new transmit					
403	array design for 7T breast MRI. <i>J Magn Reson, 2</i> 69, 55-64.					
404	https://doi.org/10.1016/j.jmr.2016.04.012					

405	Krishnamurthy, N., Santini, T., Wood, S., Kim, J., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S.
406	(2019). Computational and experimental evaluation of the Tic-Tac-Toe RF coil for 7
407	Tesla MRI. <i>PLoS One, 14</i> (1), e0209663.
408	https://doi.org/10.1371/journal.pone.0209663
409	Lusebrink, F., Wollrab, A., & Speck, O. (2013). Cortical thickness determination of the
410	human brain using high resolution 3T and 7T MRI data. Neuroimage, 70, 122-131.
411	https://doi.org/10.1016/j.neuroimage.2012.12.016
412	Okada, T., Fujimoto, K., Fushimi, Y., Akasaka, T., Thuy, D. H. D., Shima, A., Sawamoto, N.,
413	Oishi, N., Zhang, Z., Funaki, T., Nakamoto, Y., Murai, T., Miyamoto, S., Takahashi, R.,
414	& Isa, T. (2022). Neuroimaging at 7 Tesla: a pictorial narrative review. Quant Imaging
415	Med Surg, 12(6), 3406-3435. <u>https://doi.org/10.21037/qims-21-969</u>
416	Otsuka, R., Nishita, Y., Nakamura, A., Kato, T., Ando, F., Shimokata, H., & Arai, H. (2022).
417	Basic lifestyle habits and volume change in total gray matter among community
418	dwelling middle-aged and older Japanese adults. Prev Med, 161, 107149.
419	https://doi.org/10.1016/j.ypmed.2022.107149
420	Perera Molligoda Arachchige, A. S., & Garner, A. K. (2023). Seven Tesla MRI in Alzheimer's
421	disease research: State of the art and future directions: A narrative review. AIMS
422	Neurosci, 10(4), 401-422. <u>https://doi.org/10.3934/Neuroscience.2023030</u>
423	Santini, T., Wood, S., Krishnamurthy, N., Martins, T., Aizenstein, H. J., & Ibrahim, T. S. (2021).
424	Improved 7 Tesla transmit field homogeneity with reduced electromagnetic power
425	deposition using coupled Tic Tac Toe antennas. Sci Rep, 11(1), 3370.
426	<u>https://doi.org/10.1038/s41598-020-79807-9</u>
426 427	https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins,
426 427 428	https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical
426 427 428 429	https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit
426 427 428 429 430	https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i> , <i>13</i> (11), e0206127.
426 427 428 429 430 431	https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i> , <i>13</i> (11), e0206127. https://doi.org/10.1371/journal.pone.0206127
426 427 428 429 430 431 432	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky,
426 427 428 429 430 431 432 433	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based
426 427 428 429 430 431 432 433 434	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>,
426 427 428 430 431 432 433 434 435	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019
426 427 428 429 430 431 432 433 434 435 436	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R.,
426 427 428 429 430 431 432 433 434 435 436 437	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T.
426 427 428 429 430 431 432 433 434 435 436 437 438	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol</i>, <i>51</i>(8), 469-482. https://doi.org/10.1097/RLI.00000000000256
426 427 428 429 430 431 432 433 434 435 436 437 438 439	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol</i>, <i>51</i>(8), 469-482. https://doi.org/10.1097/RLI.0000000000256 Statistical Parametric Mapping: The Analysis of Functional Brain Images. (2006). (K. J. F.
426 427 428 430 431 432 433 434 435 436 437 438 439 440	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol</i>, <i>51</i>(8), 469-482. https://doi.org/10.1097/RLI.0000000000256 Statistical Parametric Mapping: The Analysis of Functional Brain Images. (2006). (K. J. F. William D. Penny, John T. Ashburner, Stefan J. Kiebel, Thomas E. Nichols, Ed. 1 ed.).
426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol</i>, <i>51</i>(8), 469-482. https://doi.org/10.1097/RLI.00000000000256 Statistical Parametric Mapping: The Analysis of Functional Brain Images. (2006). (K. J. F. William D. Penny, John T. Ashburner, Stefan J. Kiebel, Thomas E. Nichols, Ed. 1 ed.). Truong, T. K., Chakeres, D. W., Beversdorf, D. Q., Scharre, D. W., & Schmalbrock, P. (2006).
426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol</i>, <i>51</i>(8), 469-482. https://doi.org/10.1097/RLI.0000000000256 Statistical Parametric Mapping: The Analysis of Functional Brain Images. (2006). (K. J. F. William D. Penny, John T. Ashburner, Stefan J. Kiebel, Thomas E. Nichols, Ed. 1 ed.). Truong, T. K., Chakeres, D. W., Beversdorf, D. Q., Scharre, D. W., & Schmalbrock, P. (2006). Effects of static and radiofrequency magnetic field inhomogeneity in ultra-high field
426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol</i>, <i>51</i>(8), 469-482. https://doi.org/10.1097/RLI.000000000000256 Statistical Parametric Mapping: The Analysis of Functional Brain Images. (2006). (K. J. F. William D. Penny, John T. Ashburner, Stefan J. Kiebel, Thomas E. Nichols, Ed. 1 ed.). Truong, T. K., Chakeres, D. W., Beversdorf, D. Q., Scharre, D. W., & Schmalbrock, P. (2006). Effects of static and radiofrequency magnetic field inhomogeneity in ultra-high field magnetic resonance imaging. <i>Magn Reson Imaging</i>, <i>24</i>(2), 103-112.
426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One, 13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage, 113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol, 51</i>(8), 469-482. https://doi.org/10.1097/RLI.00000000000256 Statistical Parametric Mapping: The Analysis of Functional Brain Images. (2006). (K. J. F. William D. Penny, John T. Ashburner, Stefan J. Kiebel, Thomas E. Nichols, Ed. 1 ed.). Truong, T. K., Chakeres, D. W., Beversdorf, D. Q., Scharre, D. W., & Schmalbrock, P. (2006). Effects of static and radiofrequency magnetic field inhomogeneity in ultra-high field magnetic resonance imaging. <i>Magn Reson Imaging, 24</i>(2), 103-112. https://doi.org/10.1016/j.mri.2005.09.013
426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol</i>, <i>51</i>(8), 469-482. https://doi.org/10.1097/RLI.00000000000256 Statistical Parametric Mapping: The Analysis of Functional Brain Images. (2006). (K. J. F. William D. Penny, John T. Ashburner, Stefan J. Kiebel, Thomas E. Nichols, Ed. 1 ed.). Truong, T. K., Chakeres, D. W., Beversdorf, D. Q., Scharre, D. W., & Schmalbrock, P. (2006). Effects of static and radiofrequency magnetic field inhomogeneity in ultra-high field magnetic resonance imaging. <i>Magn Reson Imaging</i>, <i>24</i>(2), 103-112. https://doi.org/10.1016/j.mri.2005.09.013 US FDA. (2024). <i>510(k) Premarket Notification for MAGNETOM Terra; MAGNETOM Terra.X</i>.
426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445 446	 https://doi.org/10.1038/s41598-020-79807-9 Santini, T., Zhao, Y., Wood, S., Krishnamurthy, N., Kim, J., Farhat, N., Alkhateeb, S., Martins, T., Koo, M., Zhao, T., Aizenstein, H. J., & Ibrahim, T. S. (2018). In-vivo and numerical analysis of the eigenmodes produced by a multi-level Tic-Tac-Toe head transmit array for 7 Tesla MRI. <i>PLoS One</i>, <i>13</i>(11), e0206127. https://doi.org/10.1371/journal.pone.0206127 Seiger, R., Hahn, A., Hummer, A., Kranz, G. S., Ganger, S., Kublbock, M., Kraus, C., Sladky, R., Kasper, S., Windischberger, C., & Lanzenberger, R. (2015). Voxel-based morphometry at ultra-high fields. a comparison of 7T and 3T MRI data. <i>Neuroimage</i>, <i>113</i>, 207-216. https://doi.org/10.1016/j.neuroimage.2015.03.019 Springer, E., Dymerska, B., Cardoso, P. L., Robinson, S. D., Weisstanner, C., Wiest, R., Schmitt, B., & Trattnig, S. (2016). Comparison of Routine Brain Imaging at 3 T and 7 T. <i>Invest Radiol</i>, <i>51</i>(8), 469-482. https://doi.org/10.1097/RLI.000000000000256 Statistical Parametric Mapping: The Analysis of Functional Brain Images. (2006). (K. J. F. William D. Penny, John T. Ashburner, Stefan J. Kiebel, Thomas E. Nichols, Ed. 1 ed.). Truong, T. K., Chakeres, D. W., Beversdorf, D. Q., Scharre, D. W., & Schmalbrock, P. (2006). Effects of static and radiofrequency magnetic field inhomogeneity in ultra-high field magnetic resonance imaging. <i>Magn Reson Imaging</i>, <i>24</i>(2), 103-112. https://doi.org/10.1016/j.mri.2005.09.013 US FDA. (2024). <i>510(k) Premarket Notification for MAGNETOM Terra; MAGNETOM Terra.X.</i> Viviani, R., Pracht, E. D., Brenner, D., Beschoner, P., Stingl, J. C., & Stocker, T. (2017).

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

448 Dura and Vessels from Cortical Gray Matter. Front Neurosci, 11, 258. 449 https://doi.org/10.3389/fnins.2017.00258 450 Wang, J., Hill-Jarrett, T., Buto, P., Pederson, A., Sims, K. D., Zimmerman, S. C., DeVost, M. 451 A., Ferguson, E., Lacar, B., Yang, Y., Choi, M., Caunca, M. R., La Joie, R., Chen, R., 452 Glymour, M. M., & Ackley, S. F. (2024). Comparison of approaches to control for 453 intracranial volume in research on the association of brain volumes with cognitive 454 outcomes. Hum Brain Mapp, 45(4), e26633. https://doi.org/10.1002/hbm.26633 455 Xie, L., Wisse, L. E. M., Das, S. R., Wang, H., Wolk, D. A., Manjón, J. V., & Yushkevich, P. A. 456 (2016). Accounting for the Confound of Meninges in Segmenting Entorhinal and 457 Perirhinal Cortices in T1-Weighted MRI. In S. Ourselin, L. Joskowicz, M. R. Sabuncu, 458 G. Unal, & W. Wells, Medical Image Computing and Computer-Assisted Intervention 459 - MICCAI 2016 Cham. 460 Yushkevich, P. A., Pluta, J. B., Wang, H., Xie, L., Ding, S. L., Gertje, E. C., Mancuso, L., Kliot, 461 D., Das, S. R., & Wolk, D. A. (2015). Automated volumetry and regional thickness 462 analysis of hippocampal subfields and medial temporal cortical structures in mild 463 cognitive impairment. Hum Brain Mapp, 36(1), 258-287. 464 https://doi.org/10.1002/hbm.22627 465

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

Table 1. T1-weighted Magnetization Prepared RApid Gradient Echo (MPRAGE) sequence

468 parameters at 3T and 7T.

	3T			7T	
Scanner	Siemens Trio	Siemens Prisma		Siemens Magnetom	
Coil	Transmit: Body Coil			Transmit: 1st generation Tic-Tac- Toe head coil, 16 channels	Transmit: 2nd generation Tic-Tac- Toe head coil, 60 channels
	Receive: 32-channels		Receive: 32-channels		
Resolution	1 mm iso	0.5 x 0.5 x 1 mm	0.8 mm iso	0.75 mm iso	0.75 mm iso
Repetition time (ms)	1500	3650	2400	3000	3000
Echo time (ms)	3.19	2.53	2.22	2.17	1.96
Inversion time (ms)	800	1200	1000	1200	1200
Grappa	0	2	2	2	2
Acquisition time (min)	04:48	09:55	6:35	5:02	5:02
Number of scans after quality control	144	160	48	264	88

7T VS 3T BRAIN MORPHOMETRICS WITH AGE

470 **Table 2.** Demographics and medical history of 352 participants. SD stands for standard

471 deviation.

	3T	7T		
Sample size, n	352			
Sex female, n (%)	210 (59.7)			
Race white, n (%)	308 (87.5)			
Years of education, mean (SD)	17.3 (2.7)			
High blood pressure, n (%)	5 (1.4)			
Heart murmur, n (%)	10 (2.8)			
Heart surgery, n (%)	0			
Diabetes, n (%)	2 (0.6)			
Depression, n (%)	1 (0.3)			
Panic attacks, n (%)	3 (0.9)			
Other anxiety disorder, n (%)	12 (3.4)			
Post traumatic disorder, n (%)	0			
Age at scan, mean (SD)	45.7 (9.2)	50.9 (9.3)		
Intracranial volume mm ³ , mean (SD)	1.5521e+06 (1.4695e+05)	1.4912e+06 (1.3767e+05)		





Figure 1. 7T has a stronger inverse correlation of total cortical grey matter volume, total
subcortical grey matter volume, total white matter volume, and mean cortical thickness
with age. Brain morphometric correlations with age using 352 pairs of 3T and 7T MPRAGE
scans, including the raw volumes (No Correction) and corrected for ICV using either residuals
from regression model (Residual method) or division by ICV (Proportional method). Correlation
between the ICV derived from 3T and 7T was shown to demonstrate consistent brain stripping
results.

7T VS 3T BRAIN MORPHOMETRICS WITH AGE



481



483 mean cortical thickness with age. Cortical regions corrected for ICV using Residual method

and sex and found significant after FDR correction are shown with their respective Pearson

485 correlation coefficient (positive correlation, blue; insignificant, grey; inverse correlation, red).

486 Vessel-affected regions were removed. Cortical thicknesses were only corrected for sex.

7T VS 3T BRAIN MORPHOMETRICS WITH AGE





488 Figure 3. 7T reduces required sample size in all regions, cortical volumes, subcortical

489 **volumes, and cortical thickness.** Number of significant regions in raw volumes (no correction)

and corrected for ICV using both the Residual and Proportional methods observed with

491 increasing sample size significantly differed between 3T and 7T.

7T VS 3T BRAIN MORPHOMETRICS WITH AGE



493 Figure 4. 7T-derived ICV is consistent with that derived from 3T but more accurate in

494 **regional volumes.** Comparison between the ICV value calculated at 3T and 7T as well as the

- 495 effect of different ICV correction (Residual and Proportional) methods. Ideal correction should
- 496 result in no correlation between total cortical volume and ICV. Dashed lines represent 95%
- 497 confidence intervals. For the Residual method, both correlations showed no significant non-zero
- 498 slope. For the Proportional method, 7T data showed no significant non-zero slope (p = 0.17)
- 499 while the 3T data showed non-zero slope (p < 0.0001).

7T VS 3T BRAIN MORPHOMETRICS WITH AGE



- 501 Figure 5. Mean cortical volume annual rate of change measured at 0.32% for both 3T and
- 502 7T. Cortical volumes were corrected for ICV using the Residual method, and the median age of
- the population used for this analysis is 52 years old.