Quantitative analysis of human brain MR images at ultrahigh field strength

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References

[1] A. E. Guttmacher, F. S. Collins, R. L. Nussbaum, and C. E. Ellis, "Alzheimer's disease and parkinson's disease," *N Engl J Med*, vol. 348, no. 14, pp. 1356–1364, 2003.

[2] D. E. Barnes and K. Yaffe, "The projected effect of risk factor reduction on Alzheimer's disease prevalence," *The Lancet Neurology*, vol. 10, no. 9, pp. 819–828, 2011.

[3] A. Association, "2012 Alzheimer's disease facts and figures," *Alzheimers Dement*, vol. 8, no. 2, pp. 131–168, 2012.

[4] G. B. Frisoni, N. C. Fox, C. R. Jack, P. Scheltens, and P. M. Thompson, "The clinical use of structural MRI in Alzheimer disease," *Nat Rev Neurol*, vol. 6, no. 2, pp. 67–77, 2010.

[5] N. Fayed, P. J. Modrego, G. R. Salinas, and J. Gazulla, "Magnetic resonance imaging based clinical research in Alzheimer's disease," *J Alzheimers Dis*, vol. 31, pp. S5–S18, 2012.

[6] R. Roos, "Huntington's disease: a clinical review," *Orphanet J Rare Dis*, vol. 5, no. 1, p. 40, 2010.

[7] M. J. Novak and S. J. Tabrizi, "Huntington's disease: clinical presentation and treatment," *Int Rev Neurobiol*, vol. 98, pp. 297–323, 2011.

[8] C. A. Ross and S. J. Tabrizi, "Huntington's disease: from molecular pathogenesis to clinical treatment," *The Lancet Neurology*, vol. 10, no. 1, pp. 83–98, 2011.

[9] D. W. Weir, A. Sturrock, and B. R. Leavitt, "Development of biomarkers for Huntington's disease," *The Lancet Neurology*, vol. 10, no. 6, pp. 573–590, 2011.

[10] S. van den Bogaard, E. Dumas, J. van der Grond, M. van Buchem, and R. Roos, "MRI biomarkers in Huntington's disease," *Front Biosci (Elite Ed)*, vol. 4, pp. 1910–1925, 2012.

[11] T. G. Beach, S. E. Monsell, L. E. Phillips, and W. Kukull, "Accuracy of the clinical diagnosis of Alzheimer disease at National Institute on Aging Alzheimer Disease Centers, 2005-2010," *J Neuropathol Exp Neurol*, vol. 71, no. 4, pp. 266–273, 2012.

[12] L. Guzmán-Martínez, G. A. Farías, and R. B. Maccioni, "Emerging noninvasive biomarkers for early detection of Alzheimer's disease," *Arch Med Res*, vol. 43, no. 8, pp. 663–666, 2012.

[13] G. Bartzokis and T. A. Tishler, "MRI evaluation of basal ganglia ferritin iron and neurotoxicity in Alzheimer's and huntingon's disease," *Cell Mol Biol (Noisy-le-grand)*, vol. 46, no. 4, pp. 821–833, 2000.

[14] L. Zecca, M. B. H. Youdim, P. Riederer, J. R. Connor, and R. R. Crichton, "Iron, brain ageing and neurodegenerative disorders," *Nat Rev Neurosci*, vol. 5, no. 11, pp. 863–873, 2004.

[15] M. Fukunaga, T.-Q. Li, P. van Gelderen, J. A. de Zwart, K. Shmueli, B. Yao, J. Lee, D. Maric, M. A. Aronova, G. Zhang, R. D. Leapman, J. F. Schenck, H. Merkle, and J. H. Duyn, "Layer-specific variation of iron content in cerebral cortex as a source of MRI contrast," *Proc Natl Acad Sci U S A*, vol. 107, no. 8, pp. 3834–3839, 2010.

[16] I. Bohanna, N. Georgiou-Karistianis, A. J. Hannan, and G. F. Egan, "Magnetic resonance imaging as an approach towards identifying neuropathological biomarkers for Huntington's disease," *Brain Research Reviews*, vol. 58, no. 1, pp. 209–225, 2008.

[17] E. H. Aylward, "Change in MRI striatal volumes as a biomarker in preclinical Huntington's disease," *Brain Res Bull*, vol. 72, no. 2, pp. 152–158, 2007.

[18] S. J. Tabrizi, D. R. Langbehn, B. R. Leavitt, R. A. Roos, A. Durr, D. Craufurd, C. Kennard, S. L. Hicks, N. C. Fox, R. I. Scahill, B. Borowsky, A. J. Tobin, H. D. Rosas, H. Johnson, R. Reilmann, B. Landwehrmeyer, and J. C. Stout, "Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study: cross-sectional analysis of baseline data," *The Lancet Neurology*, vol. 8, no. 9, pp. 791–801, 2009.

[19] J. S. Paulsen, P. C. Nopoulos, E. Aylward, C. A. Ross, H. Johnson, V. A. Magnotta, A. Juhl, R. K. Pierson, J. Mills, D. Langbehn, and M. Nance, "Striatal and white matter predictors of estimated diagnosis for Huntington disease," *Brain Res Bull*, vol. 82, no. 3-4, pp. 201–207, 2010.

[20] S. van den Bogaard, E. Dumas, T. Acharya, H. Johnson, D. Langbehn, R. Scahill, S. Tabrizi, M. van Buchem, J. van der Grond, and R. Roos, "Early atrophy of pallidum and accumbens nucleus in Huntington's disease," *J Neurol*, vol. 258, no. 3, pp. 412–420, 2011.

[21] S. van den Bogaard, E. Dumas, L. Ferrarini, J. Milles, M. van Buchem, J. van der Grond, and R. Roos, "Shape analysis of subcortical nuclei in Huntington's disease, global versus local atrophy - results from the TRACK-HD study," *J Neurol Sci*, vol. 307, no. 1-2, pp. 60–68, 2011.

[22] E. M. Dumas, M. J. Versluis, S. J. van den Bogaard, M. J. van Osch, E. P. Hart, W. M. van Roon-Mom, M. A. van Buchem, A. G. Webb, J. van der Grond, and R. A. Roos, "Elevated brain iron is independent from atrophy in Huntington's disease," *Neuroimage*, vol. 61, no. 3, pp. 558–564, 2012.

[23] G. B. Chavhan, P. S. Babyn, B. Thomas, M. M. Shroff, and E. M. Haacke, "Principles, techniques, and applications of T2*-based MR imaging and its special applications," *Radiographics*, vol. 29, no. 5, pp. 1433–1449, 2009.

[24] M. Versluis, J. van der Grond, M. van Buchem, P. van Zijl, and A. Webb, "High-field imaging of neurodegenerative diseases," *Neuroimaging Clin N Am*, vol. 22, no. 2, pp. 159–171, 2012.

[25] Y. Wang, Y. Yu, D. Li, K. T. Bae, J. J. Brown, W. Lin, and E. M. Haacke, "Artery and vein separation using susceptibility-dependent phase in contrast-enhanced MRA," *J Magn Reson Imaging*, vol. 12, no. 5, pp. 661–670, 2000.

[26] B. Yao, T.-Q. Li, P. v. Gelderen, K. Shmueli, J. A. de Zwart, and J. H. Duyn, "Susceptibility contrast in high field MRI of human brain as a function of tissue iron content," *Neuroimage*, vol. 44, no. 4, pp. 1259–1266, 2009.

[27] B. P. Thomas, E. B. Welch, B. D. Niederhauser, W. O. Whetsell, A. W. Anderson, J. C. Gore, M. J. Avison, and J. L. Creasy, "High-resolution 7T MRI of the human hippocampus in vivo," *J Magn Reson Imaging*, vol. 28, no. 5, pp. 1266–1272, 2008.

[28] A. M. Abduljalil, P. Schmalbrock, V. Novak, and D. W. Chakeres, "Enhanced gray and white matter contrast of phase susceptibility-weighted images in ultra-high-field magnetic resonance imaging," *J Magn Reson Imaging*, vol. 18, no. 3, pp. 284–290, 2003.

[29] D. H. Salat, S. Y. Lee, A. J. van der Kouwe, D. N. Greve, B. Fischl, and H. D. Rosas, "Age-associated alterations in cortical gray and white matter signal intensity and gray to white matter contrast," *Neuroimage*, vol. 48, no. 1, pp. 21–28, 2009.

[30] K. Hopp, B. F. G. Popescu, R. P. E. McCrea, S. L. Harder, C. A. Robinson, M. E. Haacke, A. H. Rajput, A. Rajput, and H. Nichol, "Brain iron detected by SWI high pass filtered phase calibrated with synchrotron X-ray fluorescence," *J Magn Reson Imaging*, vol. 31, no. 6, pp. 1346–1354, 2010.

[31] J. H. Duyn, "The future of ultra-high field MRI and fMRI for study of the human brain," *Neuroimage*, vol. 62, no. 2, pp. 1241–1248, 2012.

[32] E. Moser, F. Stahlberg, M. E. Ladd, and S. Trattnig, "7-T MR–from research to clinical applications?" *NMR Biomed*, vol. 25, no. 5, pp. 695–716, 2012.

[33] M. S. de Oliveira, M. L. F. Balthazar, A. D'Abreu, C. L. Yasuda, B. P. Damasceno, F. Cendes, and G. Castellano, "MR imaging texture analysis of the corpus callosum and thalamus in amnestic mild cognitive impairment and mild Alzheimer disease," *AJNR Am J Neuroradiol*, vol. 32, pp. 60–66, 2010.

[34] B. Julész, E. N. Gilbert, L. A. Shepp, and H. L. Frisch, "Inability of humans to discriminate between visual textures that agree in second-order statistics-revisited," *Perception*, vol. 2, no. 4, pp. 391–405, 1973.

[35] A. Kassner and R. E. Thornhill, "Texture analysis: a review of neurologic MR imaging applications," *AJNR Am J Neuroradiol*, vol. 31, no. 5, pp. 809–816, 2010.

[36] A. Materka, M. Strzelecki *et al.*, "Texture analysis methods-a review," *Technical University of Lodz, Institute of Electronics, COST B11 Report*, 1998.

[37] J.-K. Kamarainen, V. Kyrki, and H. Kalviainen, "Invariance properties of Gabor filter-based features-overview and applications," *IEEE Trans Image Process*, vol. 15, no. 5, pp. 1088 –1099, 2006.

[38] S. Drabycz, R. G. Stockwell, and J. R. Mitchell, "Image texture characterization using the discrete orthonormal S-transform," *J Digit Imaging*, vol. 22, no. 6, pp. 696–708, 2009.

[39] P. M. Szczypinski, M. Strzelecki, A. Materka, and A. Klepaczko, "MaZda–A software package for image texture analysis," *Comput Methods Programs Biomed*, vol. 94, no. 1, pp. 66–76, 2009.

[40] R. G. Stockwell, L. Mansinha, and R. P. Lowe, "Localization of the complex spectrum: The S transform," *IEEE Trans Signal Process*, vol. 44, no. 4, pp. 998–1001, 1996.

[41] R. M. Haralick, K. Shanmugam, and I. H. Dinstein, "Textural features for image classification," *IEEE Trans Syst, Man, Cybern*, vol. 3, no. 6, pp. 610–621, 1973.

[42] W. Chen, M. L. Giger, H. Li, U. Bick, and G. M. Newstead, "Volumetric texture analysis of breast lesions on contrast-enhanced magnetic resonance images," *Magn Reson Med*, vol. 58, no. 3, pp. 562–571, 2007.

[43] M. E. Mayerhoefer, P. Szomolanyi, D. Jirak, A. Materka, and S. Trattnig, "Effects of MRI acquisition parameter variations and protocol heterogeneity on the results of texture analysis and pattern discrimination: an application-oriented study," *Med Phys*, vol. 36, no. 4, pp. 1236–1243, 2009.

[44] S. Duchesne, N. Bernasconi, A. Bernasconi, and D. Collins, "MR-based neurological disease classification methodology: Application to lateralization of seizure focus in temporal lobe epilepsy," *Neuroimage*, vol. 29, no. 2, pp. 557–566, 2006.

[45] S. Duchesne, A. Caroli, C. Geroldi, C. Barillot, G. B. Frisoni, and D. L. Collins, "MRI-based automated computer classification of probable AD versus normal controls," *IEEE Trans Med Imaging*, vol. 27, no. 4, pp. 509–520, 2008.

[46] S. Duchesne, C. Bocti, K. De Sousa, G. B. Frisoni, H. Chertkow, and D. L. Collins, "Amnestic MCI future clinical status prediction using baseline MRI features," *Neurobiol Aging*, vol. 31, no. 9, pp. 1606–1617, 2010.

[47] H. C. Achterberg, F. Lijn, T. Heijer, A. Lugt, M. M. B. Breteler, W. J. Niessen, and M. Bruijne, "Prediction of dementia by hippocampal shape analysis," in *Machine Learning in Medical Imaging*. Springer, 2010, vol. 6357, pp. 42–49.

[48] S. V. Bharath Kumar, "Textural content in 3T MR: an image-based marker for Alzheimer's disease," in *Medical Imaging*, 2005, pp. 1366–1376.

[49] P. A. Freeborough and N. C. Fox, "MR image texture analysis applied to the diagnosis and tracking of Alzheimer's disease," *IEEE Trans Med Imaging*, vol. 17, no. 3, pp. 475–479, 1998.

[50] Y. Liu, L. Teverovskiy, O. Carmichael, R. Kikinis, M. Shenton, C. Carter, V. Stenger, S. Davis, H. Aizenstein, and J. Becker, "Discriminative MR image feature analysis for automatic schizophrenia and Alzheimer's disease classification," in *Medical Image Computing and Computer-Assisted Intervention – MICCAI*, vol. 3216, 2004, pp. 393–401.

[51] Y. Peng, Z. Wu, and J. Jiang, "A novel feature selection approach for biomedical data classification," *J Biomed Inform*, vol. 43, no. 1, pp. 15–23, 2010.

[52] J. Zhang, L. Tong, L. Wang, and N. Li, "Texture analysis of multiple sclerosis: a comparative study," *Magn Reson Imaging*, vol. 26, no. 8, pp. 1160–1166, 2008.

[53] J. Zhang, C. Yu, G. Jiang, W. Liu, and L. Tong, "3D texture analysis on MRI images of Alzheimer's disease," *Brain Imaging and Behavior*, vol. 6, no. 1, pp. 61–69, 2012.

[54] S. B. Antel, D. Collins, N. Bernasconi, F. Andermann, R. Shinghal, R. E. Kearney, D. L. Arnold, and A. Bernasconi, "Automated detection of focal cortical dysplasia lesions using computational models of their MRI characteristics and texture analysis," *Neuroimage*, vol. 19, no. 4, pp. 1748–1759, 2003.

[55] P. Georgiadis, D. Cavouras, I. Kalatzis, D. Glotsos, E. Athanasiadis, S. Kostopoulos, K. Sifaki, M. Malamas, G. Nikiforidis, and E. Solomou, "Enhancing the discrimination accuracy between metastases, gliomas and meningiomas on brain MRI by volumetric textural features and ensemble pattern recognition methods," *Magn Reson Imaging*, vol. 27, no. 1, pp. 120–130, 2009.

[56] P. Theocharakis, D. Glotsos, I. Kalatzis, S. Kostopoulos, P. Georgiadis, K. Sifaki, K. Tsakouridou, M. Malamas, G. Delibasis, D. Cavouras, and G. Nikiforidis, "Pattern recognition system for the discrimination of multiple sclerosis from cerebral microangiopathy lesions based on texture analysis of magnetic resonance images," *Magn Reson Imaging*, vol. 27, no. 3, pp. 417–422, 2009.

[57] T. Sankar, N. Bernasconi, H. Kim, and A. Bernasconi, "Temporal lobe epilepsy: Differential pattern of damage in temporopolar cortex and white matter," *Hum Brain Mapp*, vol. 29, no. 8, pp. 931–944, 2008.

[58] K. Jafari-Khouzani, K. Elisevich, S. Patel, B. Smith, and H. Soltanian-Zadeh, "FLAIR signal and texture analysis for lateralizing mesial temporal lobe epilepsy," *Neuroimage*, vol. 49, no. 2, pp. 1559–1571, 2010.

[59] Y. Zhang, H. Zhu, J. R. Mitchell, F. Costello, and L. M. Metz, "T2 MRI texture analysis is a sensitive measure of tissue injury and recovery resulting from acute inflammatory lesions in multiple sclerosis," *Neuroimage*, vol. 47, no. 1, pp. 107–111, 2009.

[60] M. d. C. Alegro, A. V. Silva, S. Y. Bando, R. d. D. Lopes, L. H. Martins de Castro, W. HungTsu, C. A. Moreira-Filho, and E. Amaro, "Texture analysis of high resolution MRI allows discrimination between febrile and afebrile initial precipitating injury in mesial temporal sclerosis," *Magn Reson Med*, vol. 68, pp. 1647–1653, 2012.

[61] M. Sikiö, K. K. Holli, L. C. Harrison, H. Ruottinen, M. Rossi, M. T. Helminen, P. Ryymin, R. Paalavuo, S. Soimakallio, H. J. Eskola, I. Elovaara, and P. Dastidar, "Parkinson's disease: Interhemispheric textural differences in MR images," *Acad Radiol*, vol. 18, no. 10, pp. 1217–1224, 2011.

[62] M. R. Sabuncu, R. S. Desikan, J. Sepulcre, B. T. Yeo, H. Liu, N. J. Schmansky, M. Reuter, M. W. Weiner, R. L. Buckner, R. A. Sperling, B. Fischl, and for the Alzheimer's Disease Neuroimaging Initiative, "The dynamics of cortical and hippocampal atrophy in Alzheimer disease," *Arch Neurol*, vol. 68, no. 8, pp. 1040–1048, 2011.

[63] L. de Jong, K. van der Hiele, I. Veer, J. Houwing, R. Westendorp, E. Bollen, P. de Bruin, H. Middelkoop, M. van Buchem, and J. van der Grond, "Strongly reduced volumes of putamen and thalamus in Alzheimer's disease: an MRI study," *Brain*, vol. 131, no. 12, pp. 3277–3285, 2008.

[64] E. Cavedo, M. Boccardi, R. Ganzola, E. Canu, A. Beltramello, C. Caltagirone, P. M. Thompson, and G. B. Frisoni, "Local amygdala structural differences with 3T MRI in patients with Alzheimer disease," *Neurology*, vol. 76, no. 8, pp. 727–733, 2011.

[65] L. Ferrarini, W. M. Palm, H. Olofsen, R. van der Landen, M. A. van Buchem, J. H. C. Reiber, and F. Admiraal-Behloul, "Ventricular shape biomarkers for Alzheimer's disease in clinical MR images," *Magn Reson Med*, vol. 59, no. 2, pp. 260–267, 2008.

[66] J. Ashburner, C. Hutton, R. Frackowiak, I. Johnsrude, C. Price, and K. Friston, "Identifying global anatomical differences: Deformation-based morphometry," *Hum Brain Mapp*, vol. 6, no. 5-6, pp. 348–357, 1998.

[67] S. Klein, M. Loog, F. van der Lijn, T. den Heijer, A. Hammers, M. de Bruijne, A. van der Lugt, R. Duin, M. Breteler, and W. Niessen, "Early diagnosis of dementia based on intersubject whole-brain dissimilarities," in *Biomedical Imaging: From Nano to Macro, 2010 IEEE International Symposium on*, 2010, pp. 249 –252.

[68] J. J. M. Zwanenburg, M. J. Versluis, P. R. Luijten, and N. Petridou, "Fast high resolution whole brain T2* weighted imaging using echo planar imaging at 7T," *Neuroimage*, vol. 56, pp. 1902–1907, 2011.

[69] T.-Q. Li, P. van Gelderen, H. Merkle, L. Talagala, A. P. Koretsky, and J. Duyn, "Extensive heterogeneity in white matter intensity in high-resolution T2*-weighted MRI of the human brain at 7.0 T," *Neuroimage*, vol. 32, no. 3, pp. 1032–1040, 2006.

[70] J. Hagemeier, B. Weinstock-Guttman, N. Bergsland, M. H. Brown, E. Carl, C. Kennedy, C. Magnano, D. Hojnacki, M. G. Dwyer, and R. Zivadinov, "Iron deposition on SWI-filtered phase in the subcortical deep gray matter of patients with clinically isolated syndrome may precede structure-specific atrophy," *AJNR Am J Neuroradiol*, vol. 33, pp. 1596–1601, 2012.

[71] R. Zivadinov, M. Heininen-Brown, C. V. Schirda, G. U. Poloni, N. Bergsland, C. R. Magnano, J. Durfee, C. Kennedy, E. Carl, J. Hagemeier, R. H. Benedict, B. Weinstock-Guttman, and M. G. Dwyer, "Abnormal subcortical deep-gray matter susceptibility-weighted imaging filtered phase measurements in patients with multiple sclerosis: A case-control study," *Neuroimage*, vol. 59, no. 1, pp. 331–339, 2012.

[72] J. H. Duyn, P. van Gelderen, T.-Q. Li, J. A. de Zwart, A. P. Koretsky, and M. Fukunaga, "High-field MRI of brain cortical substructure based on signal phase," *Proc Natl Acad Sci U S A*, vol. 104, no. 28, pp. 11 796–11 801, 2007.

[73] W. Zhu, W. Zhong, W. Wang, C. Zhan, C. Wang, J. Qi, J. Wang, and T. Lei, "Quantitative MR phase-corrected imaging to investigate increased brain iron deposition of patients with Alzheimer disease," *Radiology*, vol. 253, no. 2, pp. 497–504, 2009.

[74] R. Roos and G. Bots, "Nuclear membrane indentations in Huntington's chorea," *J Neurol Sci*, vol. 61, no. 1, pp. 37–47, 1983.

[75] R. A. Roos, J. F. Pruyt, J. de Vries, and G. T. Bots, "Neuronal distribution in the putamen in Huntington's disease," *J Neurol Neurosurg Psychiatry*, vol. 48, no. 5, pp. 422–425, 1985.

[76] J. P. Vonsattel and M. DiFiglia, "Huntington disease," *J Neuropathol Exp Neurol*, vol. 57, no. 5, pp. 369–384, 1998.

[77] D. T. Dexter, A. Carayon, F. Javoy-Agid, Y. Agid, F. R. Wells, S. E. Daniel, A. J. Lees, P. Jenner, and C. D. Marsden, "Alterations in the levels of iron, ferritin and other trace metals in Parkinson's disease and other neurodegenerative diseases affecting the basal ganglia," *Brain*, vol. 114, no. 4, pp. 1953–1975, 1991.

[78] G. Bartzokis, P. H. Lu, T. A. Tishler, S. M. Fong, B. Oluwadara, J. P. Finn, D. Huang, Y. Bordelon, J. Mintz, and S. Perlman, "Myelin breakdown and iron changes in Huntington's disease: pathogenesis and treatment implications," *Neurochem Res*, vol. 32, no. 10, pp. 1655–1664, 2007.

[79] J. Vymazal, J. Klempíř, R. Jech, J. Zidovská, M. Syka, E. Ruzicka, and J. Roth, "MR relaxometry in Huntington's disease: Correlation between imaging, genetic and clinical parameters," *J Neurol Sci*, vol. 263, no. 1-2, pp. 20–25, 2007.

[80] C. K. Jurgens, R. Jasinschi, A. Ekin, M.-N. W. Witjes-Ané, J. van der Grond, H. Middelkoop, and R. A. Roos, "MRI T2 hypointensities in basal ganglia of premanifest Huntington's disease," *PLoS Curr*, vol. 2, 2010.

[81] B. Belaroussi, J. Milles, S. Carme, Y. M. Zhu, and H. Benoit-Cattin, "Intensity non-uniformity correction in MRI: existing methods and their validation," *Med Image Anal*, vol. 10, no. 2, pp. 234–246, 2006.

[82] J. G. Sled, A. P. Zijdenbos, and A. C. Evans, "A nonparametric method for automatic correction of intensity nonuniformity in MRI data," *IEEE Trans Med Imaging*, vol. 17, no. 1, pp. 87–97, 1998.

[83] M. J. McAuliffe, F. M. Lalonde, D. McGarry, W. Gandler, K. Csaky, and B. L. Trus, "Medical image processing, analysis and visualization in clinical research," in *Computer-Based Medical Systems, 2001. CBMS 2001. Proceedings. 14th IEEE Symposium on*, 2002, pp. 381–386.

[84] B. Patenaude, S. M. Smith, D. N. Kennedy, and M. Jenkinson, "A Bayesian model of shape and appearance for subcortical brain segmentation," *Neuroimage*, vol. 56, no. 3, pp. 907–922, 2011.

[85] S. Klein, M. Staring, K. Murphy, M. A. Viergever, and J. Pluim, "elastix: A toolbox for intensity-based medical image registration," *IEEE Trans Med Imaging*, vol. 29, no. 1, pp. 196–205, 2010.

[86] M. Hollander and D. A. Wolfe, *Nonparametric Statistical Methods*. NY John Wiley & Sons, 1999.

[87] J. P. G. Vonsattel, C. Keller, and E. P. Cortes Ramirez, "Huntington's disease - neuropathology," *Handbook of Clinical Neurology / Edited by P.J. Vinken and G.W. Bruyn*, vol. 100, pp. 83–100, 2011.

[88] H. H. Ruocco, I. Lopes-Cendes, L. M. Li, M. Santos-Silva, and F. Cendes, "Striatal and extrastriatal atrophy in Huntington's disease and its relationship with length of the CAG repeat," *Braz J Med Biol Res*, vol. 39, no. 8, pp. 1129–1136, 2006.

[89] A. Peinemann, S. Schuller, C. Pohl, T. Jahn, A. Weindl, and J. Kassubek, "Executive dysfunction in early stages of Huntington's disease is associated with striatal and insular atrophy: A neuropsychological and voxel-based morphometric study," *J Neurol Sci*, vol. 239, no. 1, pp. 11–19, 2005.

[90] J. Kassubek, F. D. Juengling, D. Ecker, and G. B. Landwehrmeyer, "Thalamic atrophy in Huntington's disease co-varies with cognitive performance: A morphometric MRI analysis," *Cereb Cortex*, vol. 15, no. 6, pp. 846–853, 2005.

[91] J. F. Schenck and E. A. Zimmerman, "High-field magnetic resonance imaging of brain iron: birth of a biomarker?" *NMR Biomed*, vol. 17, no. 7, pp. 433–445, 2004.

[92] H. D. Rosas, A. K. Liu, S. Hersch, M. Glessner, R. J. Ferrante, D. H. Salat, A. van der Kouwe, B. G. Jenkins, A. M. Dale, and B. Fischl, "Regional and progressive thinning of the cortical ribbon in Huntington's disease," *Neurology*, vol. 58, no. 5, pp. 695–701, 2002.

[93] P. C. Nopoulos, E. H. Aylward, C. A. Ross, H. J. Johnson, V. A. Magnotta, A. R. Juhl, R. K. Pierson, J. Mills, D. R. Langbehn, and J. S. Paulsen, "Cerebral cortex structure in prodromal Huntington disease," *Neurobiol Dis*, vol. 40, no. 3, pp. 544–554, 2010.

[94] B. C. Dickerson, A. Bakkour, D. H. Salat, E. Feczko, J. Pacheco, D. N. Greve, F. Grodstein, C. I. Wright, D. Blacker, H. D. Rosas, R. A. Sperling, A. Atri, J. H. Growdon, B. T. Hyman, J. C. Morris, B. Fischl, and R. L. Buckner, "The cortical signature of Alzheimer's disease: regionally specific cortical thinning relates to symptom severity in very mild to mild AD dementia and is detectable in asymptomatic amyloid-positive individuals," *Cereb Cortex*, vol. 19, no. 3, pp. 497–510, 2009.

[95] T. D. Cannon, P. M. Thompson, T. G. M. van Erp, A. W. Toga, V.-P. Poutanen, M. Huttunen, J. Lonnqvist, C.-G. Standerskjold-Nordenstam, K. L. Narr, M. Khaledy, C. I. Zoumalan, R. Dail, and J. Kaprio, "Cortex mapping reveals regionally specific patterns of genetic and disease-specific gray-matter deficits in twins discordant for schizophrenia," *Proc Natl Acad Sci U S A*, vol. 99, no. 5, pp. 3228–3233, 2002.

[96] A. Fornito, M. Yücel, B. Dean, S. J. Wood, and C. Pantelis, "Anatomical abnormalities of the anterior cingulate cortex in schizophrenia: bridging the gap between neuroimaging and neuropathology," *Schizophr Bull*, vol. 35, no. 5, pp. 973–993, 2009.

[97] S. M. Wolosin, M. E. Richardson, J. G. Hennessey, M. B. Denckla, and S. H. Mostofsky, "Abnormal cerebral cortex structure in children with ADHD," *Hum Brain Mapp*, vol. 30, no. 1, pp. 175–184, 2009.

[98] J. A. Duce, A. Tsatsanis, M. A. Cater, S. A. James, E. Robb, K. Wikhe, S. L. Leong, K. Perez, T. Johanssen, M. A. Greenough, H.-H. Cho, D. Galatis, R. D. Moir, C. L. Masters, C. McLean, R. E. Tanzi, R. Cappai, K. J. Barnham, G. D. Ciccotosto, J. T. Rogers, and A. I. Bush, "Iron-export ferroxidase activity of β-amyloid precursor protein is inhibited by zinc in Alzheimer's disease," *Cell*, vol. 142, no. 6, pp. 857–867, 2010.

[99] D. J. Piñero and J. R. Connor, "Iron in the brain: An important contributor in normal and diseased states," *Neuroscientist*, vol. 6, no. 6, pp. 435 –453, 2000.

[100] M. A. Smith, X. Zhu, M. Tabaton, G. Liu, J. McKeel, M. L. Cohen, X. Wang, S. L. Siedlak, B. E. Dwyer, T. Hayashi, M. Nakamura, A. Nunomura, and G. Perry, "Increased iron and free radical generation in preclinical Alzheimer disease and mild cognitive impairment," *J Alzheimers Dis*, vol. 19, no. 1, pp. 363–372, 2010.

[101] M. D. Meadowcroft, J. R. Connor, M. B. Smith, and Q. X. Yang, "MRI and histological analysis of beta-amyloid plaques in both human Alzheimer's disease and APP/PS1 transgenic mice," *J Magn Reson Imaging*, vol. 29, no. 5, pp. 997–1007, 2009.

[102] A. M. Dale, B. Fischl, and M. I. Sereno, "Cortical surface-based analysis. I. segmentation and surface reconstruction," *Neuroimage*, vol. 9, no. 2, pp. 179–194, 1999.

[103] X. Zeng, L. H. Staib, R. T. Schultz, and J. S. Duncan, "Segmentation and measurement of the cortex from 3-D MR images using coupled-surfaces propagation," *IEEE Trans Med Imaging*, vol. 18, no. 10, pp. 927–937, 2002.

[104] D. MacDonald, N. Kabani, D. Avis, and A. C. Evans, "Automated 3-D extraction of inner and outer surfaces of cerebral cortex from MRI," *Neuroimage*, vol. 12, no. 3, pp. 340–356, 2000.

[105] C. R. Jack, M. A. Bernstein, N. C. Fox, P. Thompson, G. Alexander, D. Harvey, B. Borowski, P. J. Britson, J. L. Whitwell, C. Ward, A. M. Dale, J. P. Felmlee, J. L. Gunter, D. L. Hill, R. Killiany, N. Schuff, S. Fox-Bosetti, C. Lin, C. Studholme, C. S. DeCarli, G. Krueger, H. A. Ward, G. J. Metzger, K. T. Scott, R. Mallozzi, D. Blezek, J. Levy, J. P. Debbins, A. S. Fleisher, M. Albert, R. Green, G. Bartzokis, G. Glover, J. Mugler, and M. W. Weiner, "The Alzheimer's disease neuroimaging initiative (ADNI): MRI methods," *J Magn Reson Imaging*, vol. 27, no. 4, pp. 685–691, 2008.

[106] P. Bourgeat, J. Fripp, P. Stanwell, S. Ramadan, and S. Ourselin, "MR image segmentation of the knee bone using phase information," *Med Image Anal*, vol. 11, no. 4, pp. 325–335, 2007.

[107] D. S. J. Pandian, C. Ciulla, E. M. Haacke, J. Jiang, and M. Ayaz, "Complex threshold method for identifying pixels that contain predominantly noise in magnetic resonance images," *J Magn Reson Imaging*, vol. 28, no. 3, pp. 727–735, 2008.

[108] A. K. Jain and R. C. Dubes, *Algorithms for Clustering Data*. Prentice-Hall, Inc., 1988.

[109] R. C. Gonzalez and R. E. Woods, *Digital Image Processing, 2nd ed.* Prentice Hall, 2002.

[110] L. Vincent, "Morphological grayscale reconstruction in image analysis: applications and efficient algorithms," *IEEE Trans Image Process*, vol. 2, no. 2, pp. 176–201, 1993.

[111] I. Santillán, A. M. Herrera-Navarro, J. D. Mendiola-Santibáñez, and I. R. Terol-Villalobos, "Morphological connected filtering on viscous lattices," *J Math Imaging Vis*, vol. 36, no. 3, pp. 254–269, 2009.

[112] I. R. Terol-Villalobos and D. Vargas-Vázquez, "Openings and closings by reconstruction using propagation criteria," in *Computer Analysis of Images and Patterns*. Springer, 2001, pp. 502–509.

[113] I. R. Terol-Villalobos, J. D. Mendiola-Santibáñez, and S. L. Canchola-Magdaleno, "Image segmentation and filtering based on transformations with reconstruction criteria," *J Vis Commun Image R*, vol. 17, no. 1, pp. 107–130, 2006.

[114] M. J. Versluis, J. M. Peeters, S. van Rooden, J. van der Grond, M. A. van Buchem, A. G. Webb, and M. J. P. van Osch, "Origin and reduction of motion and f0 artifacts in high resolution T2*-weighted magnetic resonance imaging: application in Alzheimer's disease patients," *Neuroimage*, vol. 51, no. 3, pp. 1082–1088, 2010.

[115] L. R. Dice, "Measures of the amount of ecologic association between species," *Ecology*, vol. 26, no. 3, pp. 297–302, 1945.

[116] J. M. Bland and D. G. Altman, "Statistical methods for assessing agreement between two methods of clinical measurement," *Int J Nurs Stud*, vol. 47, no. 8, pp. 931–936, 2010.

[117] P. A. Yushkevich, J. Piven, H. C. Hazlett, R. G. Smith, S. Ho, J. C. Gee, and G. Gerig, "User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability," *Neuroimage*, vol. 31, no. 3, pp. 1116–1128, 2006.

[118] S. Magnaldi, M. Ukmar, A. Vasciaveo, R. Longo, and R. Pozzi-Mucelli, "Contrast between white and grey matter: MRI appearance with ageing," *Eur Radiol*, vol. 3, no. 6, pp. 513–519, 1993.

[119] B. Hallgren and P. Sourander, "The effect of age on the non-haemin iron in the human brain," *J Neurochem*, vol. 3, no. 1, pp. 41–51, 1958.

[120] D. H. Salat, R. L. Buckner, A. Z. Snyder, D. N. Greve, R. S. R. Desikan, E. Busa, J. C. Morris, A. M. Dale, and B. Fischl, "Thinning of the cerebral cortex in aging," *Cereb Cortex*, vol. 14, no. 7, pp. 721–730, 2004.

[121] X. Xu, Q. Wang, and M. Zhang, "Age, gender, and hemispheric differences in iron deposition in the human brain: An in vivo MRI study," *Neuroimage*, vol. 40, no. 1, pp. 35–42, 2008.

[122] J. Zhang, Y. Zhang, J. Wang, P. Cai, C. Luo, Z. Qian, Y. Dai, and H. Feng, "Characterizing iron deposition in Parkinson's disease using susceptibility-weighted imaging: an in vivo MR study," *Brain Res*, vol. 1330, pp. 124–130, 2010.

[123] N. T. Doan, S. van Rooden, M. J. Versluis, A. G. Webb, J. van der Grond, M. A. van Buchem, J. H. C. Reiber, and J. Milles, "Combined magnitude and phase-based segmentation of the cerebral cortex in 7T MR images of the elderly," *J Magn Reson Imaging*, vol. 36, no. 1, pp. 99–109, 2012.

[124] R. J. Ogg, J. W. Langston, E. M. Haacke, R. G. Steen, and J. S. Taylor, "The correlation between phase shifts in gradient-echo MR images and regional brain iron concentration," *Magn Reson Imaging*, vol. 17, no. 8, pp. 1141–1148, 1999.

[125] S. van Rooden, M. J. Versluis, M. K. Liem, J. Milles, A. B. Maier, A. M. Oleksik, A. G. Webb, M. A. van Buchem, and J. van der Grond, "Cortical phase changes in Alzheimer's disease at 7T MRI: A novel imaging marker," *Alzheimers Dement*, vol. 10, no. 1, pp. e19–e26, 2014.

[126] D. L. Collins, P. Neelin, T. M. Peters, and A. C. Evans, "Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space," *J Comput Assist Tomogr*, vol. 18, no. 2, pp. 192–205, 1994.

[127] B. Fischl and A. M. Dale, "Measuring the thickness of the human cerebral cortex from magnetic resonance images," *Proc Natl Acad Sci U S A*, vol. 97, no. 20, pp. 11 050–11 055, 2000.

[128] N. Tzourio-Mazoyer, B. Landeau, D. Papathanassiou, F. Crivello, O. Etard, N. Delcroix, B. Mazoyer, and M. Joliot, "Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain," *Neuroimage*, vol. 15, no. 1, pp. 273–289, 2002.

[129] H. B. Mann and D. R. Whitney, "On a test of whether one of two random variables is stochastically larger than the other," *Ann Math Statist*, vol. 18, no. 1, pp. 50–60, 1947.

[130] R. C. Blair and W. Karniski, "An alternative method for significance testing of waveform difference potentials," *Psychophysiology*, vol. 30, no. 5, pp. 518–524, 1993.

[131] T. E. Nichols and A. P. Holmes, "Nonparametric permutation tests for functional neuroimaging: a primer with examples," *Hum Brain Mapp*, vol. 15, no. 1, pp. 1–25, 2002.

[132] L. Ferrarini, W. M. Palm, H. Olofsen, M. A. van Buchem, J. H. C. Reiber, and F. Admiraal-Behloul, "Shape differences of the brain ventricles in Alzheimer's disease," *Neuroimage*, vol. 32, no. 3, pp. 1060–1069, 2006.

[133] L. T. Westlye, K. B. Walhovd, A. M. Dale, T. Espeseth, I. Reinvang, N. Raz, I. Agartz, D. N. Greve, B. Fischl, and A. M. Fjell, "Increased sensitivity to effects of normal aging and Alzheimer's disease on cortical thickness by adjustment for local variability in gray/white contrast: a multi-sample MRI study," *Neuroimage*, vol. 47, no. 4, pp. 1545–1557, 2009.

[134] C. Langkammer, N. Krebs, W. Goessler, E. Scheurer, K. Yen, F. Fazekas, and S. Ropele, "Susceptibility induced gray-white matter MRI contrast in the human brain," *Neuroimage*, vol. 59, no. 2, pp. 1413–1419, 2012.

[135] J. Lee, Y. Hirano, M. Fukunaga, A. C. Silva, and J. H. Duyn, "On the contribution of deoxy-hemoglobin to MRI gray-white matter phase contrast at high field," *Neuroimage*, vol. 49, no. 1, pp. 193–198, 2010.

[136] J. Lee, K. Shmueli, B.-T. Kang, B. Yao, M. Fukunaga, P. van Gelderen, S. Palumbo, F. Bosetti, A. C. Silva, and J. H. Duyn, "The contribution of myelin to magnetic susceptibility-weighted contrasts in high-field MRI of the brain," *Neuroimage*, vol. 59, no. 4, pp. 3967–3975, 2012.

[137] E. R. Sowell, B. S. Peterson, P. M. Thompson, S. E. Welcome, A. L. Henkenius, and A. W. Toga, "Mapping cortical change across the human life span," *Nat Neurosci*, vol. 6, no. 3, pp. 309–315, 2003.

[138] O. Piguet, K. Double, J. Kril, J. Harasty, V. Macdonald, D. McRitchie, and G. Halliday, "White matter loss in healthy ageing: a postmortem analysis," *Neurobiol Aging*, vol. 30, no. 8, pp. 1288–1295, 2009.

[139] A. Giorgio, L. Santelli, V. Tomassini, R. Bosnell, S. Smith, N. De Stefano, and H. Johansen-Berg, "Age-related changes in grey and white matter structure throughout adulthood," *Neuroimage*, vol. 51, no. 3, pp. 943–951, 2010.

[140] G. Bartzokis, P. H. Lu, K. Tingus, M. F. Mendez, A. Richard, D. G. Peters, B. Oluwadara, K. A. Barrall, J. P. Finn, P. Villablanca, P. M. Thompson, and J. Mintz, "Lifespan trajectory of myelin integrity and maximum motor speed," *Neurobiol Aging*, vol. 31, no. 9, pp. 1554–1562, 2010.

[141] G. Bartzokis, P. H. Lu, P. Heydari, A. Couvrette, G. J. Lee, G. Kalashyan, F. Freeman, J. W. Grinstead, P. Villablanca, J. P. Finn, J. Mintz, J. R. Alger, and L. L. Altshuler, "Multimodal magnetic resonance imaging assessment of white matter aging trajectories over the lifespan of healthy individuals," *Biol Psychiatry*, vol. 72, no. 12, pp. 1026–1034, 2012.

[142] P. Vasudevaraju, Bharathi, J. T, N. M. Shamasundar, K. Subba Rao, B. M. Balaraj, R. Ksj, and S. R. T S, "New evidence on iron, copper accumulation and zinc depletion and its correlation with DNA integrity in aging human brain regions," *Indian J Psychiatry*, vol. 52, no. 2, pp. 140–144, 2010.

[143] A. Deistung, A. Schäfer, F. Schweser, U. Biedermann, R. Turner, and J. R. Reichenbach, "Toward in vivo histology: A comparison of quantitative susceptibility mapping (QSM) with magnitude-, phase-, and R2*-imaging at ultra-high magnetic field strength," *Neuroimage*, vol. 65, pp. 299–314, 2013.

[144] C. Langkammer, T. Liu, M. Khalil, C. Enzinger, M. Jehna, S. Fuchs, F. Fazekas, Y. Wang, and S. Ropele, "Quantitative susceptibility mapping in multiple sclerosis," *Radiology*, vol. 267, pp. 551–559, 2013.

[145] C. P. Ferri, M. Prince, C. Brayne, H. Brodaty, L. Fratiglioni, M. Ganguli, K. Hall, K. Hasegawa, H. Hendrie, Y. Huang, A. Jorm, C. Mathers, P. R. Menezes, E. Rimmer, M. Scazufca, and for Alzheimer's Disease International, "Global prevalence of dementia: a Delphi consensus study," *Lancet*, vol. 366, no. 9503, pp. 2112–2117, 2005.

[146] L. Minati, T. Edginton, M. G. Bruzzone, and G. Giaccone, "Current concepts in Alzheimer's disease: a multidisciplinary review," *Am J Alzheimers Dis Other Demen*, vol. 24, no. 2, pp. 95–121, 2009.

[147] T. Imamura, Y. Takatsuki, M. Fujimori, N. Hirono, Y. Ikejiri, T. Shimomura, M. Hashimoto, H. Yamashita, and E. Mori, "Age at onset and language disturbances in Alzheimer's disease," *Neuropsychologia*, vol. 36, no. 9, pp. 945–949, 1998.

[148] D. Jacobs, M. Sano, K. Marder, K. Bell, F. Bylsma, G. Lafleche, M. Albert, J. Brandt, and Y. Stern, "Age at onset of Alzheimer's disease: relation to pattern of cognitive dysfunction and rate of decline," *Neurology*, vol. 44, no. 7, pp. 1215–1220, 1994.

[149] E. Koss, S. Edland, G. Fillenbaum, R. Mohs, C. Clark, D. Galasko, and J. C. Morris, "Clinical and neuropsychological differences between patients with earlier and later onset of Alzheimer's disease: A CERAD analysis, Part XII," *Neurology*, vol. 46, no. 1, pp. 136–141, 1996.

[150] F. Sá, P. Pinto, C. Cunha, R. Lemos, L. Letra, M. Simões, and I. Santana, "Differences between early and late-onset Alzheimer's disease in neuropsychological tests," *Front Neurol*, vol. 3, p. 81, 2012.

[151] L. L. Smits, Y. A. L. Pijnenburg, E. L. G. E. Koedam, A. E. van der Vlies, I. E. W. Reuling, T. Koene, C. E. Teunissen, P. Scheltens, and W. M. van der Flier, "Early onset Alzheimer's disease is associated with a distinct neuropsychological profile," *J Alzheimers Dis*, vol. 30, no. 1, pp. 101–108, 2012.

[152] A. E. van der Vlies, E. L. G. E. Koedam, Y. A. L. Pijnenburg, J. W. R. Twisk, P. Scheltens, and W. M. van der Flier, "Most rapid cognitive decline in APOE ϵ4 negative Alzheimer's disease with early onset," *Psychol Med*, vol. 39, no. 11, pp. 1907–1911, 2009.

[153] M. Balasa, E. Gelpi, A. Antonell, M. J. Rey, R. Sánchez-Valle, J. L. Molinuevo, A. Lladó, and Neurological Tissue Bank/University of Barcelona/Hospital Clínic NTB/UB/HC Collaborative Group, "Clinical features and APOE genotype of pathologically proven early-onset Alzheimer disease," *Neurology*, vol. 76, no. 20, pp. 1720–1725, 2011.

[154] E. L. G. E. Koedam, V. Lauffer, A. E. van der Vlies, W. M. van der Flier, P. Scheltens, and Y. A. L. Pijnenburg, "Early-versus late-onset Alzheimer's disease: more than age alone," *J Alzheimers Dis*, vol. 19, no. 4, pp. 1401–1408, 2010.

[155] G. B. Frisoni, M. Pievani, C. Testa, F. Sabattoli, L. Bresciani, M. Bonetti, A. Beltramello, K. M. Hayashi, A. W. Toga, and P. M. Thompson, "The topography of grey matter involvement in early and late onset Alzheimer's disease," *Brain*, vol. 130, no. 3, pp. 720–730, 2007.

[156] C. Möller, H. Vrenken, L. Jiskoot, A. Versteeg, F. Barkhof, P. Scheltens, and W. M. van der Flier, "Different patterns of gray matter atrophy in early- and late-onset Alzheimer's disease," *Neurobiol Aging*, vol. 34, no. 8, pp. 2014–2022, 2013.

[157] E. J. Kim, S. S. Cho, Y. Jeong, K. C. Park, S. J. Kang, E. Kang, S. E. Kim, K. H. Lee, and D. L. Na, "Glucose metabolism in early onset versus late onset Alzheimer's disease: an SPM analysis of 120 patients," *Brain*, vol. 128, no. 8, pp. 1790–1801, 2005.

[158] R. Ossenkoppele, M. D. Zwan, N. Tolboom, D. M. E. van Assema, S. F. Adriaanse, R. W. Kloet, R. Boellaard, A. D. Windhorst, F. Barkhof, A. A. Lammertsma, P. Scheltens, W. M. van der Flier, and B. N. M. van Berckel, "Amyloid burden and metabolic function in early-onset Alzheimer's disease: parietal lobe involvement," *Brain*, vol. 135, no. 7, pp. 2115–2125, 2012.

[159] G. D. Rabinovici, A. J. Furst, A. Alkalay, C. A. Racine, J. P. O'Neil, M. Janabi, S. L. Baker, N. Agarwal, S. J. Bonasera, E. C. Mormino, M. W. Weiner, M. L. Gorno-Tempini, H. J. Rosen, B. L. Miller, and W. J. Jagust, "Increased metabolic vulnerability in early-onset Alzheimer's disease is not related to amyloid burden," *Brain*, vol. 133, no. 2, pp. 512–528, 2010.

[160] H. Cho, S. Jeon, S. J. Kang, J.-M. Lee, J.-H. Lee, G. H. Kim, J. S. Shin, C. H. Kim, Y. Noh, K. Im, S. T. Kim, J. Chin, S. W. Seo, and D. L. Na, "Longitudinal changes of cortical thickness in early-versus late-onset Alzheimer's disease," *Neurobiol Aging*, vol. 34, no. 7, pp. 1921.e9–1921.e15, 2013.

[161] N. C. Kaiser, R. J. Melrose, C. Liu, D. L. Sultzer, E. Jimenez, M. Su, L. Monserratt, and M. F. Mendez, "Neuropsychological and neuroimaging markers in early versus late-onset Alzheimer's disease," *Am J Alzheimers Dis Other Demen*, vol. 27, no. 7, pp. 520–529, 2012.

[162] E. H. Bigio, L. S. Hynan, E. Sontag, S. Satumtira, and C. L. White, "Synapse loss is greater in presenile than senile onset Alzheimer disease: implications for the cognitive reserve hypothesis," *Neuropathol Appl Neurobiol*, vol. 28, no. 3, pp. 218–227, 2002.

[163] G. J. Ho, L. A. Hansen, M. F. Alford, K. Foster, D. P. Salmon, D. Galasko, L. J. Thal, and E. Masliah, "Age at onset is associated with disease severity in lewy body variant and Alzheimer's disease," *Neuroreport*, vol. 13, no. 14, pp. 1825–1828, 2002.

[164] G. A. Marshall, L. A. Fairbanks, S. Tekin, H. V. Vinters, and J. L. Cummings, "Early-onset Alzheimer's disease is associated with greater pathologic burden," *J Geriatr Psychiatry Neurol*, vol. 20, no. 1, pp. 29–33, 2007.

[165] I. H. Choo, D. Y. Lee, J. W. Kim, E. H. Seo, D. S. Lee, Y. K. Kim, S. G. Kim, S. Y. Park, J. I. Woo, and E. J. Yoon, "Relationship of amyloid-β burden with age-at-onset in Alzheimer disease," *Am J Geriatr Psychiatry*, vol. 19, no. 7, pp. 627–634, 2011.

[166] T. Nakada, H. Matsuzawa, H. Igarashi, Y. Fujii, and I. L. Kwee, "In vivo visualization of senile-plaque-like pathology in alzheimer's disease patients by MR microscopy on a 7T system," *J Neuroimaging*, vol. 18, no. 2, pp. 125–129, 2008.

[167] N. T. Doan, S. van Rooden, M. J. Versluis, M. Buijs, A. G. Webb, J. van der Grond, M. A. van Buchem, J. H. C. Reiber, and J. Milles, "Group-wise cortical feature analysis using high field T2*-weighted MR images highlights local differences between young and elderly healthy subjects," *Neuroimage*, 2013, submitted.

[168] N. Lynöe, M. Sandlund, G. Dahlqvist, and L. Jacobsson, "Informed consent: study of quality of information given to participants in a clinical trial," *Br Med J*, vol. 303, no. 6803, pp. 610–613, 1991.

[169] G. McKhann, D. Drachman, M. Folstein, R. Katzman, D. Price, and E. M. Stadlan, "Clinical diagnosis of Alzheimer's disease: report of the nincds-adrda work group under the auspices of department of health and human services task force on Alzheimer's disease," *Neurology*, vol. 34, no. 7, pp. 939–944, 1984.

[170] M. Schär, S. Kozerke, S. E. Fischer, and P. Boesiger, "Cardiac SSFP imaging at 3 Tesla," *Magn Reson Med*, vol. 51, no. 4, pp. 799–806, 2004.

[171] E. M. Haacke, Y. Xu, Y.-C. N. Cheng, and J. R. Reichenbach, "Susceptibility weighted imaging (SWI)," *Magn Reson Med*, vol. 52, no. 3, pp. 612–618, 2004.

[172] P. Lei, S. Ayton, D. I. Finkelstein, L. Spoerri, G. D. Ciccotosto, D. K. Wright, B. X. W. Wong, P. A. Adlard, R. A. Cherny, L. Q. Lam, B. R. Roberts, I. Volitakis, G. F. Egan, C. A. McLean, R. Cappai, J. A. Duce, and A. I. Bush, "Tau deficiency induces parkinsonism with dementia by impairing app-mediated iron export," *Nat Med*, vol. 18, no. 2, pp. 291–295, 2012.

[173] M. A. Smith, P. L. Harris, L. M. Sayre, and G. Perry, "Iron accumulation in Alzheimer disease is a source of redox-generated free radicals," *Proc Natl Acad Sci U S A*, vol. 94, no. 18, pp. 9866–9868, 1997.

[174] S. van Rooden, M. L. C. Maat-Schieman, R. J. A. Nabuurs, L. van der Weerd, S. van Duijn, S. G. van Duinen, R. Natté, M. A. van Buchem, and J. van der Grond, "Cerebral amyloidosis: postmortem detection with human 7.0-T MR imaging system," *Radiology*, vol. 253, no. 3, pp. 788–796, 2009.

[175] E. M. Haacke, N. Y. C. Cheng, M. J. House, Q. Liu, J. Neelavalli, R. J. Ogg, A. Khan, M. Ayaz, W. Kirsch, and A. Obenaus, "Imaging iron stores in the brain using magnetic resonance imaging," *Magn Reson Imaging*, vol. 23, no. 1, pp. 1–25, 2005.

[176] E. M. Haacke, M. Ayaz, A. Khan, E. S. Manova, B. Krishnamurthy, L. Gollapalli, C. Ciulla, I. Kim, F. Petersen, and W. Kirsch, "Establishing a baseline phase behavior in magnetic resonance imaging to determine normal vs. abnormal iron content in the brain," *J Magn Reson Imaging*, vol. 26, no. 2, pp. 256–264, 2007.

[177] E. Canu, G. B. Frisoni, F. Agosta, M. Pievani, M. Bonetti, and M. Filippi, "Early and late onset Alzheimer's disease patients have distinct patterns of white matter damage," *Neurobiol Aging*, vol. 33, no. 6, pp. 1023–1033, 2012.

[178] K. Ishii, T. Kawachi, H. Sasaki, A. K. Kono, T. Fukuda, Y. Kojima, and E. Mori, "Voxel-based morphometric comparison between early-and late-onset mild Alzheimer's disease and assessment of diagnostic performance of z score images," *AJNR Am J Neuroradiol*, vol. 26, no. 2, pp. 333–340, 2005.

[179] G. Karas, P. Scheltens, S. Rombouts, R. van Schijndel, M. Klein, B. Jones, W. van der Flier, H. Vrenken, and F. Barkhof, "Precuneus atrophy in early-onset Alzheimer's disease: a morphometric structural MRI study," *Neuroradiology*, vol. 49, no. 12, pp. 967–976, 2007.

[180] R. Nabuurs, S. van Rooden, S. van Duijn, M. Versluis, B. Emmer, M. Liem, J. Milles, A. Webb, M. Frosch, S. van Duinen, R. Natte, J. van der Grond, L. van der Weerd, and M. van Buchem, "Detection of cortical changes in Alzheimer's disease at ultra-high field MRI," *Ann Neurol*, 2013, submitted.

[181] G. Frisoni, C. Testa, F. Sabattoli, A. Beltramello, H. Soininen, and M. Laakso, "Structural correlates of early and late onset Alzheimer's disease: voxel based morphometric study," *J Neurol Neurosurg Psychiatry*, vol. 76, no. 1, pp. 112–114, 2005.

[182] S. Sakamoto, K. Ishii, M. Sasaki, K. Hosaka, T. Mori, M. Matsui, N. Hirono, and E. Mori, "Differences in cerebral metabolic impairment between early and late onset types of Alzheimer's disease," *J Neurol Sci*, vol. 200, no. 1, pp. 27–32, 2002.

[183] W. Li, B. Wu, A. Batrachenko, V. Bancroft-Wu, R. A. Morey, V. Shashi, C. Langkammer, M. D. De Bellis, S. Ropele, A. W. Song, and C. Liu, "Differential developmental trajectories of magnetic susceptibility in human brain gray and white matter over the lifespan." *Hum Brain Mapp*, vol. 35, no. 6, pp. 2698–2713, 2014.

[184] S. Yang, W. Lu, D.-S. Zhou, and Y. Tang, "Enriched environment and white matter in aging brain," *Anat Rec (Hoboken)*, vol. 295, no. 9, pp. 1406–1414, 2012.

[185] J. H. Duyn, "Study of brain anatomy with high-field MRI: recent progress," *Magn Reson Imaging*, vol. 28, no. 8, pp. 1210–1215, 2010.

[186] E. Fornari, P. Maeder, R. Meuli, J. Ghika, and M. G. Knyazeva, "Demyelination of superficial white matter in early Alzheimer's disease: a magnetization transfer imaging study," *Neurobiol Aging*, vol. 33, no. 2, pp. 428.e7–428.e19, 2012.

[187] L. Svennerholm and C. G. Gottfries, "Membrane lipids, selectively diminished in Alzheimer brains, suggest synapse loss as a primary event in early-onset form (type I) and demyelination in late-onset form (type II)," *J Neurochem*, vol. 62, no. 3, pp. 1039–1047, 1994.

[188] P. Aljabar, K. Bhatia, M. Murgasova, J. Hajnal, J. Boardman, L. Srinivasan, M. Rutherford, L. Dyet, A. Edwards, and D. Rueckert, "Assessment of brain growth in early childhood using deformation-based morphometry," *Neuroimage*, vol. 39, no. 1, pp. 348–358, 2008.

[189] D. S. Marcus, A. F. Fotenos, J. G. Csernansky, J. C. Morris, and R. L. Buckner, "Open access series of imaging studies (OASIS): longitudinal MRI data in nondemented and demented older adults," *J Cogn Neurosci*, vol. 22, no. 12, pp. 2677–2684, 2010.

[190] D. L. Collins, A. P. Zijdenbos, V. Kollokian, J. G. Sled, N. J. Kabani, C. J. Holmes, and A. C. Evans, "Design and construction of a realistic digital brain phantom," *IEEE Trans Med Imaging*, vol. 17, no. 3, pp. 463–468, 1998.

[191] A. Rauscher, M. Barth, K.-H. Herrmann, S. Witoszynskyj, A. Deistung, and J. R. Reichenbach, "Improved elimination of phase effects from background field inhomogeneities for susceptibility weighted imaging at high magnetic field strengths," *Magn Reson Imaging*, vol. 26, no. 8, pp. 1145–1151, 2008.

[192] F. Schweser, A. Deistung, B. W. Lehr, and J. R. Reichenbach, "Quantitative imaging of intrinsic magnetic tissue properties using MRI signal phase: an approach to in vivo brain iron metabolism?" *Neuroimage*, vol. 54, no. 4, pp. 2789–2807, 2011.

[193] M. Jenkinson, "Fast, automated, N-dimensional phase-unwrapping algorithm," *Magn Reson Med*, vol. 49, no. 1, pp. 193–197, 2003.

[194] M. Pievani, M. Bocchetta, M. Boccardi, E. Cavedo, M. Bonetti, P. M. Thompson, and G. B. Frisoni, "Striatal morphology in early-onset and late-onset Alzheimer's disease: a preliminary study," *Neurobiol Aging*, vol. 34, no. 7, pp. 1728–1739, 2013.

[195] J. P. Lerch, J. C. Pruessner, A. Zijdenbos, H. Hampel, S. J. Teipel, and A. C. Evans, "Focal decline of cortical thickness in Alzheimer's disease identified by computational neuroanatomy," *Cereb Cortex*, vol. 15, no. 7, pp. 995–1001, 2005.

[196] S. M. LeVine, "Iron deposits in multiple sclerosis and Alzheimer's disease brains," *Brain Res*, vol. 760, no. 1-2, pp. 298–303, 1997.