

Table 1: Previous approaches to WMH segmentation with respect to image sources and reported performance.

#	Ref.	Year	Authors	MRI Sequences	I	S	SI
1	[21]	2015	Harmouche et al.	T1, T2, PD, FLAIR	100	35	0.56
2	[33]	2012	Samaille et al.	T1, FLAIR	67	6	0.72
3	[28]	2016	Knight et al.	FLAIR	15	3	0.7
4	[5]	2004	Anbeek et al.	T1, T2, PD, FLAIR, IR	20	1	0.61
5	[4]	2005	Anbeek et al.	T1, T2, PD, FLAIR, IR	10	1	0.78
6	[15]	2011	García-Lorenzo et al.	T1, T2, FLAIR	10	1	0.65
7	[42]	2013	Sweeney et al.	T1, T2, PD, FLAIR	111	1	0.61
8	[16]	2011	Geremia et al.	T1, T2, FLAIR	20	2	
9	[44]	2017	Valverde et al.	T1, FLAIR	33	2	
10	[45]	2001	Van Leemput et al.	T1, T2, PD	20	1	0.51
11	[38]	2011	Smart et al.	T1, FLAIR	30	1	
12	[29]	2006	Lao et al.	T1, T2, PD, FLAIR	45	1	
13	[27]	2008	Khayati et al.	FLAIR	20	1	0.75
14	[9]	2017	Dadar et al.	T1, FLAIR	80	3	0.62
15	[25]	2014	Khademi et al.	FLAIR	25	1	0.78
16	[47]	2008	Wels et al.	T1, T2, FLAIR	6	1	0.57
17	[19]	2015	Guizard et al.	T1, T2, PD, FLAIR	108	32	0.6
18	[48]	2006	Wu et al.	T1, T2, PD	12	1	
19	[2]	2005	Admiraal-Behloul et al.	T2, PD, FLAIR	100	1	0.75
20	[22]	2008	Herskovits et al.	T1, T2, PD, FLAIR	42	2	0.6
21	[26]	2012	Khademi et al.	FLAIR	24	1	0.83
22	[24]	2015	Jain et al.	T1, FLAIR	20	1	0.67
23	[43]	2015	Tomas-Fernandez et al.	T1, T2, FLAIR	51	2	
24	[7]	2008	Bricq et al.	T2, FLAIR	25	2	
25	[46]	2015	Wang et al.	T1, T2, FLAIR	70	2	0.84
26	[30]	2016	Mechrez et al.	T1, T2, FLAIR	20	2	0.31
27	[31]	2015	Roy et al.	FLAIR	38	3	0.56
28	[12]	2008	Dyrby et al.	T1, T2, FLAIR	362	10	0.56
29	[6]	2009	Boer et al.	T1, PD, FLAIR	20	2	0.72
30	[17]	2010	Gibson et al.	T1, T2, FLAIR	18	1	0.81
31	[8]	2015	Brosch et al.	T1, T2, FLAIR	20	2	0.36
32	[32]	2006	Sajja et al.	T2, PD, FLAIR	23	1	0.78
33	[13]	2015	Fartaria et al.	FLAIR	39	1	0.55
34	[37]	2010	Shiee et al.	T1, FLAIR	10	1	0.63
35	[39]	2008	Souplet et al.	T1, T2, FLAIR	25	2	
36	[10]	2013	Datta et al.	T1, T2, FLAIR	90	3	
37	[14]	2009	García-Lorenzo et al.	T1, T2, PD	10	1	0.63
38	[34]	2012	Schmidt et al.	T1, FLAIR	53	1	0.75
39	[51]	2002	Zijdenbos et al.	T1, T2	10	1	0.6
40	[3]	2009	Akselrod-Ballin et al.	T1, T2, PD, FLAIR	41	1	0.53
41	[41]	2016	Strumia et al.	T1, FLAIR	20	3	0.52
42	[23]	2001	Jack et al.	FLAIR	39	1	
43	[20]	2006	Harmouche et al.	T1, T2, PD	10	1	0.61
44	[1]	2012	Abdullah et al.	T1, T2, FLAIR	61	3	
45	[36]	2010	Scully et al.	T1, T2, FLAIR	17	1	
46	[18]	2016	Griffanti et al.	T1, FLAIR	130	2	0.76
47	[49]	2014	Yoo et al.	FLAIR	32	2	0.76
48	[11]	2015	Deshpande et al.	T1, T2, PD, FLAIR	52	1	0.5
49	[40]	2013	Steenwijk et al.	T1, FLAIR	40	2	0.8
50	[]			T1, FLAIR	20	2	0.34
51	[35]	2009	Schwarz et al.	T1, T2, PD	165	2	
52	[50]	2017	Zhan et al.	T1, T2, FLAIR	50	2	0.76

Abbreviations. I: number of MR image sets used for validation; S: number of MRI scanners used for validation; SI: reported validation similarity index.

## References

- [1] Bassem a Abdullah, Akmal a Younis, and Nigel M John. “Multi-Sectional Views Textural Based SVM for MS Lesion Segmentation in Multi-Channels MRIs”. eng. In: *The open biomedical engineering journal* 6 (2012), pp. 56–72. ISSN: 1874-1207. DOI: 10.2174/1874230001206010056.
- [2] F. Admiraal-Behloul et al. “Fully automatic segmentation of white matter hyperintensities in MR images of the elderly”. In: *NeuroImage* 28.3 (2005), pp. 607–617. ISSN: 10538119. DOI: 10.1016/j.neuroimage.2005.06.061.
- [3] Ayelet Akselrod-Ballin et al. “Automatic Segmentation and Classification of Multiple Sclerosis in Multichannel MRI”. In: *IEEE Transactions on Biomedical Engineering* 56.10 (2009), pp. 2461–2469. ISSN: 00189294.
- [4] Petronella Anbeek et al. “Probabilistic segmentation of brain tissue in MR imaging”. In: *NeuroImage* 27.4 (Oct. 2005), pp. 795–804. ISSN: 1053-8119. DOI: 10.1016/j.neuroimage.2005.05.046.
- [5] Petronella Anbeek et al. “Probabilistic segmentation of white matter lesions in MR imaging”. In: *NeuroImage* 21.3 (Mar. 2004), pp. 1037–44. ISSN: 1053-8119. DOI: 10.1016/j.neuroimage.2003.10.012.
- [6] Renske de Boer et al. “White matter lesion extension to automatic brain tissue segmentation on MRI”. In: *NeuroImage* 45.4 (May 2009), pp. 1151–61. ISSN: 1095-9572. DOI: 10.1016/j.neuroimage.2009.01.011.
- [7] S Bricq, Christophe Collet, and Jean-Paul Armspach. “MS Lesion Segmentation based on Hidden Markov Chains”. In: *The MIDAS Journal - MS Lesion Segmentation (MICCAI 2008 Workshop)*. 2008.
- [8] Tom Brosch et al. *Deep Convolutional Encoder Networks for Multiple Sclerosis Lesion Segmentation*. Vol. 9556. 2015, pp. 144–155. DOI: 10.1007/978-3-319-30858-6.
- [9] Mahsa Dadar et al. “Validation of a Regression Technique for Segmentation of White Matter Hyperintensities in Alzheimer’s Disease”. In: *IEEE Transactions on Medical Imaging* 99.PP (2017), pp. 1–1. ISSN: 0278-0062. DOI: 10.1109/TMI.2017.2693978.
- [10] Sushmita Datta and Ponnada A. Narayana. “A comprehensive approach to the segmentation of multichannel three-dimensional MR brain images in multiple sclerosis”. In: *NeuroImage: Clinical* 2 (2013), pp. 184–196. DOI: 10.1016/j.nicl.2012.12.007.
- [11] Hrishikesh Deshpande, Pierre Maurel, and Christian Barillot. “Classification of multiple sclerosis lesions using adaptive dictionary learning”. In: *Computerized Medical Imaging and Graphics* 46 (2015), pp. 2–10. ISSN: 18790771. DOI: 10.1016/j.compmedimag.2015.05.003.
- [12] Tim B Dyrby et al. “Segmentation of age-related white matter changes in a clinical multi-center study.” In: *NeuroImage* 41.2 (June 2008), pp. 335–345. ISSN: 1053-8119 (Print). DOI: 10.1016/j.neuroimage.2008.02.024.
- [13] Mário João Fartaria et al. “Automated detection of white matter and cortical lesions in early stages of multiple sclerosis”. In: *Journal of magnetic resonance imaging : JMRI* (Nov. 2015). ISSN: 1522-2586. DOI: 10.1002/jmri.25095.
- [14] Daniel García-Lorenzo et al. “Multiple Sclerosis lesion segmentation using an automatic multimodal Graph Cuts”. In: (2009).
- [15] Daniel García-Lorenzo et al. “Trimmed-likelihood estimation for focal lesions and tissue segmentation in multisequence MRI for multiple sclerosis”. In: *IEEE Transactions on Medical Imaging* 30.8 (Aug. 2011), pp. 1455–67. ISSN: 1558-254X. DOI: 10.1109/TMI.2011.2114671.
- [16] Ezequiel Geremia et al. “Spatial decision forests for MS lesion segmentation in multi-channel magnetic resonance images”. eng. In: *NeuroImage* 57.2 (July 2011), pp. 378–390. ISSN: 1095-9572 (Electronic). DOI: 10.1016/j.neuroimage.2011.03.080.
- [17] Erin Gibson et al. “Automatic segmentation of white matter hyperintensities in the elderly using FLAIR images at 3T”. In: *Journal of Magnetic Resonance Imaging* 31.6 (June 2010), pp. 1311–1322. ISSN: 15222586. DOI: 10.1002/jmri.22004.
- [18] Ludovica Griffanti et al. “BIANCA (Brain Intensity AbNormality Alassification Algorithm): A new tool for automated segmentation of white matter hyperintensities”. In: *NeuroImage* 141 (2016), pp. 191–205. ISSN: 10538119. DOI: 10.1016/j.neuroimage.2016.07.018.
- [19] Nicolas Guizard et al. “Rotation-invariant multi-contrast non-local means for MS lesion segmentation”. In: *NeuroImage: Clinical* 8 (2015), pp. 376–389. ISSN: 22131582. DOI: 10.1016/j.nicl.2015.05.001.

- [20] Rola Harmouche et al. “Bayesian MS lesion classification modeling regional and local spatial information”. In: *Proceedings - International Conference on Pattern Recognition*. Vol. 3. IEEE, 2006, pp. 984–987. ISBN: 0769525210. DOI: 10.1109/ICPR.2006.318.
- [21] Rola Harmouche et al. “Probabilistic multiple sclerosis lesion classification based on modeling regional intensity variability and local neighborhood Information”. In: *IEEE Transactions on Biomedical Engineering* 62.5 (2015), pp. 1281–1292. ISSN: 15582531. DOI: 10.1109/TBME.2014.2385635.
- [22] E H Herskovits, R N Bryan, and F Yang. “Automated Bayesian segmentation of microvascular white-matter lesions in the ACCORD-MIND study.” eng. In: *Advances in medical sciences* 53.2 (2008), pp. 182–190. ISSN: 1896-1126 (Print). DOI: 10.2478/v10039-008-0039-3.
- [23] Clifford R Jack et al. “FLAIR histogram segmentation for measurement of leukoaraiosis volume”. In: *Journal of Magnetic Resonance Imaging* 14.6 (Dec. 2001), pp. 668–676. ISSN: 10531807. DOI: 10.1002/jmri.10011. arXiv: NIHMS150003.
- [24] Saurabh Jain et al. “Automatic segmentation and volumetry of multiple sclerosis brain lesions from MR images”. In: *NeuroImage: Clinical* 8 (2015), pp. 367–75. ISSN: 2213-1582. DOI: 10.1016/j.nicl.2015.05.003.
- [25] April Khademi, Anastasios Venetsanopoulos, and Alan R Moody. “Generalized method for partial volume estimation and tissue segmentation in cerebral magnetic resonance images”. In: *Journal of Medical Imaging* 1.1 (Apr. 2014), p. 14002. ISSN: 2329-4302. DOI: 10.1117/1.JMI.1.1.014002.
- [26] April Khademi, Anastasios Venetsanopoulos, and Alan R Moody. “Robust white matter lesion segmentation in FLAIR MRI”. eng. In: *IEEE transactions on bio-medical engineering* 59.3 (Mar. 2012), pp. 860–871. ISSN: 1558-2531 (Electronic). DOI: 10.1109/TBME.2011.2181167.
- [27] Rasoul Khayati et al. “Fully automatic segmentation of multiple sclerosis lesions in brain MR FLAIR images using adaptive mixtures method and Markov random field model”. eng. In: *Computers in biology and medicine* 38.3 (Mar. 2008), pp. 379–390. ISSN: 0010-4825 (Print). DOI: 10.1016/j.compbimed.2007.12.005.
- [28] Jesse Knight and April Khademi. “MS Lesion Segmentation Using FLAIR MRI Only”. In: *Medical Image Computing and Computer-Assisted Intervention - MICCAI*. Athens, Greece, 2016, TBD.
- [29] Z. Lao et al. “Automated Segmentation of White Matter Lesions in 3D Brain MR Images, using Multivariate Pattern Classification”. In: *3rd IEEE International Symposium on Biomedical Imaging: Macro to Nano, 2006*. IEEE, 2006, pp. 307–310. ISBN: 0-7803-9576-X. DOI: 10.1109/ISBI.2006.1624914.
- [30] Roey Mechrez, Jacob Goldberger, and Hayit Greenspan. “Patch-Based Segmentation with Spatial Consistency: Application to MS Lesions in Brain MRI”. In: *International Journal of Biomedical Imaging* 2016 (2016), pp. 1–13. ISSN: 16874196. DOI: 10.1155/2016/7952541.
- [31] Pallab Kanti Roy et al. “Automatic white matter lesion segmentation using contrast enhanced FLAIR intensity and Markov Random Field”. eng. In: *Computerized medical imaging and graphics : the official journal of the Computerized Medical Imaging Society* 45 (Oct. 2015), pp. 102–111. ISSN: 1879-0771 (Electronic). DOI: 10.1016/j.compmedimag.2015.08.005.
- [32] Balasrinivasa Rao Sajja et al. “Unified approach for multiple sclerosis lesion segmentation on brain MRI”. In: *Annals of biomedical engineering* 34.1 (Jan. 2006), pp. 142–51. ISSN: 0090-6964. DOI: 10.1007/s10439-005-9009-0.
- [33] Thomas Samaille et al. “Contrast-based fully automatic segmentation of white matter hyperintensities: method and validation”. eng. In: *PloS one* 7.11 (2012), e48953. ISSN: 1932-6203 (Electronic). DOI: 10.1371/journal.pone.0048953.
- [34] Paul Schmidt et al. “An automated tool for detection of FLAIR-hyperintense white-matter lesions in multiple sclerosis”. eng. In: *Neuroimage* 59.4 (Feb. 2012), pp. 3774–3783. ISSN: 1095-9572 (Electronic). DOI: 10.1016/j.neuroimage.2011.11.032.
- [35] Christopher Schwarz et al. “Fully-automated white matter hyperintensity detection with anatomical prior knowledge and without FLAIR”. In: *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)*. Vol. 5636 LNCS. NIH Public Access, 2009, pp. 239–251. ISBN: 3642024971. DOI: 10.1007/978-3-642-02498-6\_20.
- [36] Mark Scully et al. “An Automated Method for Segmenting White Matter Lesions through Multi-Level Morphometric Feature Classification with Application to Lupus”. In: *Frontiers in human neuroscience* 4.April (2010), p. 27. ISSN: 1662-5161. DOI: 10.3389/fnhum.2010.00027.

- [37] Navid Shiee et al. “A topology-preserving approach to the segmentation of brain images with multiple sclerosis lesions”. In: *NeuroImage* 49.2 (Jan. 2010), pp. 1524–1535. ISSN: 1095-9572. DOI: 10.1016/j.neuroimage.2009.09.005.
- [38] Sean D Smart, Michael J Firbank, and John T O’Brien. “Validation of automated white matter hyperintensity segmentation”. In: *Journal of aging research* 2011 (Jan. 2011), p. 391783. ISSN: 2090-2212. DOI: 10.4061/2011/391783.
- [39] Jc Souplet et al. “An Automatic Segmentation of T2-FLAIR Multiple Sclerosis Lesions”. In: *MICCAI Grand Challenge Workshop: Multiple Sclerosis Lesion Segmentation Challenge* (2008), pp. 1–11.
- [40] Martijn D Steenwijk et al. “Accurate white matter lesion segmentation by k nearest neighbor classification with tissue type priors (kNN-TTPs)”. In: *NeuroImage: Clinical* 3 (Jan. 2013), pp. 462–9. ISSN: 2213-1582. DOI: 10.1016/j.nicl.2013.10.003.
- [41] Maddalena Strumia et al. “White Matter MS-Lesion Segmentation Using a Geometric Brain Model”. In: *IEEE transactions on medical imaging* PP.99 (2016), p. 1. ISSN: 1558-254X. DOI: 10.1109/TMI.2016.2522178.
- [42] Elizabeth M. Sweeney et al. “OASIS is Automated Statistical Inference for Segmentation, with applications to multiple sclerosis lesion segmentation in MRI”. In: *NeuroImage: Clinical* 2.1 (2013), pp. 402–413. ISSN: 22131582. DOI: 10.1016/j.nicl.2013.03.002.
- [43] Xavier Tomas-Fernandez and Simon K Warfield. “A model of population and subject (MOPS) intensities with application to multiple sclerosis lesion segmentation”. In: *IEEE Transactions on Medical Imaging* 34.6 (June 2015), pp. 1349–1361. ISSN: 1558254X. DOI: 10.1109/TMI.2015.2393853.
- [44] Sergi Valverde et al. “Automated tissue segmentation of MR brain images in the presence of white matter lesions”. In: *Medical Image Analysis* 35 (Aug. 2017), pp. 446–457. ISSN: 1361-8415. DOI: 10.1016/j.media.2016.08.014.
- [45] K. Van Leemput et al. “Automated segmentation of multiple sclerosis lesions by model outlier detection”. In: *IEEE Transactions on Medical Imaging* 20.8 (2001), pp. 677–688. DOI: 10.1109/42.938237.
- [46] Rui Wang et al. “Automatic segmentation and volumetric quantification of white matter hyperintensities on fluid-attenuated inversion recovery images using the extreme value distribution”. eng. In: *Neuroradiology* 57.3 (Mar. 2015), pp. 307–320. ISSN: 1432-1920 (Electronic). DOI: 10.1007/s00234-014-1466-4.
- [47] M. Wels, M. Huber, and J. Hornegger. “Fully automated segmentation of multiple sclerosis lesions in multi-spectral MRI”. In: *Pattern Recognition and Image Analysis* 18.2 (June 2008), pp. 347–350. DOI: 10.1134/S1054661808020235.
- [48] Ying Wu et al. “Automated segmentation of multiple sclerosis lesion subtypes with multichannel MRI”. In: *NeuroImage* 32.3 (Sept. 2006), pp. 1205–1215. ISSN: 10538119. DOI: 10.1016/j.neuroimage.2006.04.211.
- [49] Byung Il Yoo et al. “Application of variable threshold intensity to segmentation for white matter hyperintensities in fluid attenuated inversion recovery magnetic resonance images”. In: *Neuroradiology* 56.4 (2014), pp. 265–281. ISSN: 14321920. DOI: 10.1007/s00234-014-1322-6.
- [50] Tianming Zhan et al. “Multimodal spatial-based segmentation framework for white matter lesions in multi-sequence magnetic resonance images”. In: *Biomedical Signal Processing and Control* 31 (2017), pp. 52–62. DOI: 10.1016/j.bspc.2016.06.016.
- [51] Alex P Zijdenbos, Reza Forghani, and Alan C Evans. “Automatic pipeline analysis of 3-D MRI data for clinical trials: application to multiple sclerosis”. In: *IEEE transactions on medical imaging* 21.10 (Oct. 2002), pp. 1280–91. DOI: 10.1109/TMI.2002.806283.