Improved Alzheimer's disease diagnostic performance using structural MRI: validation of the MRI combination biomarker that won the CADDementia challenge

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Purpose

Improved Alzheimer's disease (AD) diagnosis using a single structural MRI scan requires analysis of many aspects of the acquired scan. Our combination MRI biomarker recently won the Computer-Aided Diagnosis of Dementia based on Structural MRI data (CADDementia) challenge [1] (see Fig. 1). In an effort to further validate this marker and its clinical applicability, we report its diagnostic performance on two recognized reference datasets.

Images for this section:

Original results table presented on 18 September 2014 at the MICCAI workshop.

Algorithm	Rank accuracy	Accuracy [CI] (%)	TPF_{CN} [CI] (%)	TPF_{MCI} [CI] (%)	TPF_{AD} [CI] (%)	Rank AUC	AUC_{all} [CI] (%)	AUC_{CN} [CI] (%)	AUC_{MCI} [CI] (%)	AUC_{AD} [CI] (%)	Date	Documentation
Soerensen-equal	1.0	63.0 [57.9 - 67.5]	96.9 [92.9 - 99.2]	28.7 [21.3 - 37.4]	61.2 [51.6 - 69.8]	1.5	78.8 [75.6 - 82.0]	86.3 [81.8 - 89.3]	63.1 [56.6 - 68.3]	87.5 [83.4 - 91.1]	15/06/2014	Paper | Wiki | Pres.
Soerensen-optimized	2.0	59.9 [54.8 - 64.7]	70.5 [62.8 - 77.8]	41.0 [33.3 - 50.0]	68.9 [59.6 - 77.2]	1.5	78.8 [75.5 - 82.1]	86.3 [81.9 - 89.3]	62.7 [56.8 - 68.4]	86.7 [82.3 - 90.4]	15/06/2014	Paper | Wiki | Pres.
Wachinger-enetNorm	3.0	59.0 [54.0 - 63.6]	72.1 [63.4 - 79.2]	51.6 [43.5 - 61.3]	51.5 [41.5 - 61.2]	4.0	77.0 [73.6 - 80.3]	83.3 [78.5 - 87.0]	59.4 [52.9 - 65.5]	88.2 [83.8 - 91.4]	15/06/2014	Paper | Wiki | Pres.
Ledig-ALL	4.0	57.9 [52.5 - 62.7]	89.1 [83.7 - 93.8]	41.0 [32.4 - 49.6]	38.8 [30.7 - 50.0]	5.0	76.7 [73.6 - 79.8]	86.6 [82.7 - 89.8]	59.7 [53.3 - 65.1]	84.9 [79.7 - 88.7]	15/06/2014	Paper | Wiki | Pres.
Moradi	5.0	57.6 [52.3 - 62.4]	57.4 [48.7 - 66.1]	59.8 [51.3 - 68.1]	55.3 [46.7 - 65.2]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Franke	6.0	56.2 [50.8 - 61.3]	58.9 [50.4 - 67.5]	43.4 [34.8 - 51.7]	68.0 [58.8 - 77.1]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Ledig-CORT	7.5	55.1 [49.7 - 59.9]	68.2 [60.5 - 76.0]	45.1 [35.3 - 53.4]	50.5 [41.2 - 60.5]	12.0	73.7 [69.9 - 77.2]	79.6 [75.0 - 84.2]	58.9 [52.9 - 64.9]	82.4 [76.7 - 87.3]	15/06/2014	Paper | Wiki | Pres.
Sensi	7.5	55.1 [50.0 - 60.2]	71.3 [63.6 - 78.8]	40.2 [31.2 - 49.6]	52.4 [42.7 - 62.0]	11.0	73.8 [70.2 - 77.5]	81.7 [77.1 - 85.8]	55.0 [48.8 - 61.0]	83.9 [78.8 - 87.7]	15/06/2014	Paper | Wiki | Pres.
Wachinger-step1	9.5	54.0 [48.9 - 59.0]	68.2 [60.2 - 75.4]	41.0 [31.9 - 50.9]	51.5 [42.2 - 61.1]	8.0	74.6 [70.8 - 78.1]	79.1 [73.5 - 83.1]	55.0 [48.5 - 61.4]	89.2 [85.3 - 92.3]	15/06/2014	Paper | Wiki | Pres.
Ledig-GRAD	9.5	54.0 [48.9 - 59.3]	87.6 [81.7 - 92.6]	37.7 [29.3 - 47.5]	31.1 [22.4 - 40.4]	6.0	75.4 [72.4 - 78.6]	85.6 [81.5 - 88.9]	60.3 [53.9 - 66.5]	81.7 [76.3 - 86.1]	15/06/2014	Paper | Wiki | Pres.
Wachinger-step2	12.5	53.7 [47.5 - 58.8]	66.7 [58.1 - 74.1]	38.5 [30.1 - 48.1]	55.3 [45.5 - 65.0]	13.0	72.7 [68.9 - 76.4]	79.3 [74.0 - 83.5]	51.9 [45.3 - 58.7]	86.5 [81.9 - 90.3]	15/06/2014	Paper | Wiki | Pres.
Abdulkadir	12.5	53.7 [48.3 - 58.2]	45.7 [37.0 - 53.6]	65.6 [56.1 - 73.0]	49.5 [39.4 - 58.8]	3.0	77.7 [74.2 - 81.0]	85.6 [81.4 - 89.0]	59.9 [54.1 - 66.4]	86.7 [82.3 - 90.3]	15/06/2014	Paper | Wiki | Pres.
Sarica	12.5	53.7 [48.3 - 58.8]	65.9 [57.4 - 74.2]	39.3 [30.0 - 48.2]	55.3 [44.9 - 64.9]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Wachinger-step1Norm	12.5	53.7 [48.6 - 58.8]	63.6 [54.9 - 71.9]	47.5 [38.4 - 56.6]	48.5 [39.6 - 59.1]	9.5	74.3 [70.5 - 77.9]	79.3 [74.1 - 83.5]	55.5 [48.5 - 61.6]	87.7 [83.7 - 91.1]	15/06/2014	Paper | Wiki | Pres.
Ledig-MBL	15.0	53.4 [47.7 - 57.9]	82.9 [76.0 - 88.7]	43.4 [35.1 - 52.9]	28.2 [20.2 - 37.4]	7.0	75.2 [72.0 - 78.1]	82.5 [77.8 - 86.0]	57.3 [50.9 - 63.6]	86.4 [81.4 - 89.9]	15/06/2014	Paper | Wiki | Pres.
Wachinger-man	16.0	53.1 [47.7 - 57.9]	61.2 [53.5 - 69.6]	60.7 [51.7 - 70.0]	34.0 [25.7 - 44.7]	9.5	74.3 [70.9 - 77.9]	80.6 [75.7 - 84.9]	56.3 [49.7 - 63.0]	86.1 [81.7 - 90.0]	15/06/2014	Paper | Wiki | Pres.
Eskildsen-ADNI1	17.5	52.0 [46.6 - 56.8]	65.1 [56.9 - 73.2]	32.0 [24.1 - 40.9]	59.2 [49.5 - 68.3]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Eskildsen-FACEADNI1	17.5	52.0 [46.9 - 57.1]	65.1 [56.6 - 73.1]	36.1 [28.1 - 45.5]	54.4 [44.6 - 63.6]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Eskildsen-Combined	19.0	51.1 [45.5 - 56.2]	64.3 [56.2 - 72.3]	35.2 [27.1 - 44.3]	53.4 [43.0 - 62.9]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Dolph	20.0	49.7 [44.6 - 54.8]	84.5 [77.9 - 90.4]	23.0 [16.4 - 31.2]	37.9 [28.9 - 47.3]	17.0	63.0 [59.6 - 67.2]	66.2 [61.3 - 70.3]	55.4 [50.0 - 60.0]	65.8 [60.6 - 71.3]	15/06/2014	Paper | Wiki | Pres.
Routier-adni	21.0	49.2 [43.5 - 54.2]	94.6 [89.8 - 97.7]	11.5 [6.2 - 17.7]	36.9 [27.4 - 46.5]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Routier-train	22.5	48.3 [42.9 - 53.4]	48.1 [39.8 - 56.9]	21.3 [14.8 - 29.0]	80.6 [72.2 - 87.3]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Eskildsen-FACEADNI2	22.5	48.3 [43.2 - 53.4]	48.8 [40.5 - 57.4]	42.6 [33.9 - 51.3]	54.4 [45.5 - 64.0]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Eskildsen-ADNI2	24.5	47.7 [42.1 - 52.8]	59.7 [51.2 - 68.4]	38.5 [29.9 - 47.3]	43.7 [33.7 - 53.8]	-	-	-	-	-	15/06/2014	Paper | Wiki | Pres.
Ledig-VOL	24.5	47.7 [42.1 - 52.8]	66.7 [57.1 - 74.1]	36.9 [28.9 - 45.9]	36.9 [28.6 - 47.2]	14.0	68.4 [64.5 - 72.5]	75.7 [70.3 - 81.0]	50.1 [44.1 - 56.4]	79.0 [73.3 - 83.5]	15/06/2014	Paper | Wiki | Pres.
Amoroso	26.0	46.9 [41.5 - 52.3]	67.4 [58.5 - 75.2]	42.6 [33.6 - 51.1]	26.2 [18.3 - 35.4]	15.0	67.2 [63.3 - 71.3]	73.4 [67.8 - 78.7]	56.0 [49.7 - 61.9]	72.3 [66.2 - 77.5]	15/06/2014	Paper | Wiki | Pres.
Tangaro	27.0	46.6 [41.0 - 51.4]	68.2 [60.2 - 76.5]	37.7 [29.2 - 46.3]	30.1 [21.7 - 39.0]	16.0	67.1 [63.2 - 71.0]	73.1 [67.8 - 78.0]	52.6 [45.9 - 58.6]	75.8 [70.2 - 80.6]	15/06/2014	Paper | Wiki | Pres.
Cardenas-Pena	28.0	39.0 [33.9 - 43.8]	50.4 [41.5 - 59.1]	28.7 [21.6 - 38.5]	36.9 [27.4 - 46.8]	18.0	55.9 [51.2 - 59.9]	57.8 [51.6 - 63.4]	50.0 [43.9 - 57.1]	59.8 [53.5 - 65.7]	15/06/2014	Paper | Wiki | Pres.
Smith	29.0	32.2 [27.4 - 36.7]	48.1 [39.6 - 57.1]	20.5 [13.9 - 28.3]	26.2 [18.3 - 35.0]	19.0	50.4 [46.7 - 54.6]	54.1 [48.0 - 60.0]	50.6 [45.0 - 57.1]	46.6 [40.0 - 53.6]	15/06/2014	Paper | Wiki | Pres.

Fig. 1: The final CADDementia challenge results. Algorithms were ranked according to three-class classification accuracy (the second column). We submitted two algorithms (marked in green). Here we validate the algorithm that achieved first place.

Methods and materials

Two T1-weighted structural MRI reference datasets were considered. ADNI: baseline scans from the "complete annual year 2 visit" 1.5T standardized Alzheimer's Disease Neuroimaging Initiative dataset [2] (169 normal controls (CTRL), 234 subjects with mild cognitive impairment (MCI), 101 AD patients). AIBL: baseline scans from the imaging arm of the Australian Imaging, Biomarker & Lifestyle Flagship Study of Aging [3] (88 CTRL, 29 MCI, and 28 AD).

The challenge-winning combination MRI biomarker was applied to each scan. First, the following individual MRI biomarkers were computed:

- cortical thickness using cross-sectional FreeSurfer,
- hippocampal shape using an in-house method,
- hippocampal texture using an in-house method,
- standard volumetry using cross-sectional FreeSurfer as well as an in-house method specifically constructed to segment the hippocampus.

The individual MRI biomarkers were subsequently age-normalized and combined using a regularized linear discriminant analysis classifier (LDA). We refer to [4] for further details.

The method was applied using 10-fold cross-validation stratified on diagnostic group and cohort, and performance on ADNI and AIBL was subsequently investigated separately for the two datasets. Both per-class and three-class receiver operating characteristic (ROC) curves and the associated area under the ROC curve (AUC) were computed [1]. The evaluation python scripts supplied by the CADDementia organizers were used for this purpose.

Results

The method achieved the following three-class AUCs with 95 % confidence intervals: ADNI 0.779 [0.748 0.809] and AIBL 0.803 [0.752 0.857].

The Per-class AUCs for ADNI were as follows (see Fig. 2 for associated ROC-curves): CTRL 0.853, MCI 0.678, and AD 0.819. For AIBL, the AUCs were CTRL 0.895m MCI 0.715, and AD 0.803 (see Fig 3. for associated ROC-curves).

Images for this section:

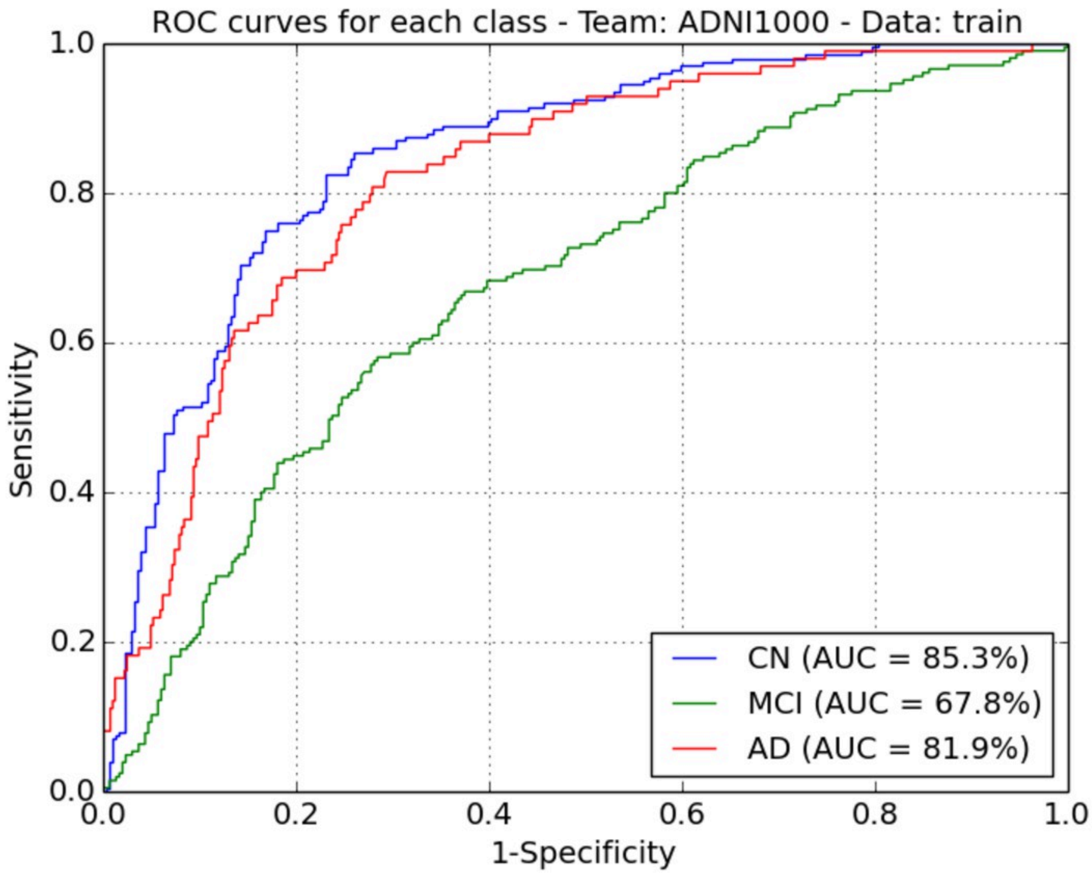

Fig. 2: Per-class ROC-curves for the ADNI data. The ROC-curves were generated using the evaluation scripts supplied by the CADDementia organizers.

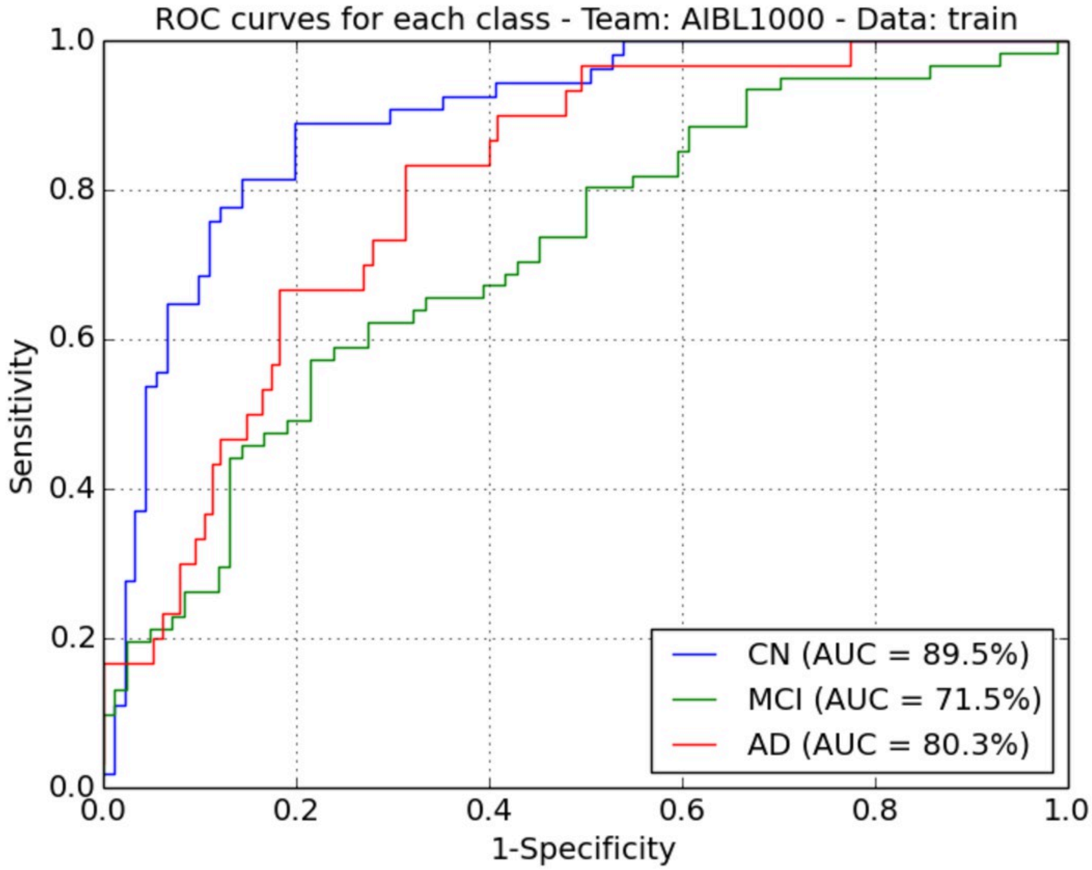

Fig. 3: Per-class ROC-curves for the AIBL data. The ROC-curves were generated using the evaluation scripts supplied by the CADDementia organizers.

Conclusion

The reported diagnostic results were comparable to the challenge-winning results achieved for the CADDementia dataset [1]. This demonstrates that the state-of-the-art performance of the combination MRI marker generalizes to recognized reference datasets, making it a potential marker for improved diagnostic support in clinical assessment of AD.

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