Supplementary Material

Diagnostic Performance of Automated MRI Volumetry by icobrain dm for Alzheimer's Disease in a Clinical Setting: A REMEMBER Study

Supplementary Table 1. Description on scanner field and model specifications. Magnet strength in Tesla (T) (**Field**) and number of subjects (**#**) were reported.

Vendor	***Model***	***Field (T)***	**#**
GE medical systems	Sigma	1.5	80
GE medical systems	Discovery	3.0	42
Philips	Achieva	1.5	124
Philips	Intera	1.5	92
Philips	Achieva	3.0	47
Philips	Intera	3.0	24
Siemens	Aera	1.5	10
Siemens	Avanto	1.5	44
Siemens	Symphony	1.5	63
Siemens	Allegra	3.0	100
Siemens	TrioTrim	3.0	123
Siemens	Skyra	3.0	21
Siemens	Prisma	3.0	50

Supplementary Table 2. Exploratory study: Disease stage group division according to slice thickness resolution.

Resolution	HC-SCD	MCI	ADD
High (ST < 1 mm)	81	172	145
Middle (1 mm ≤ ST ≤ 1.6 mm)	99	151	110
Low (ST > 1.6 mm)	9	51	56

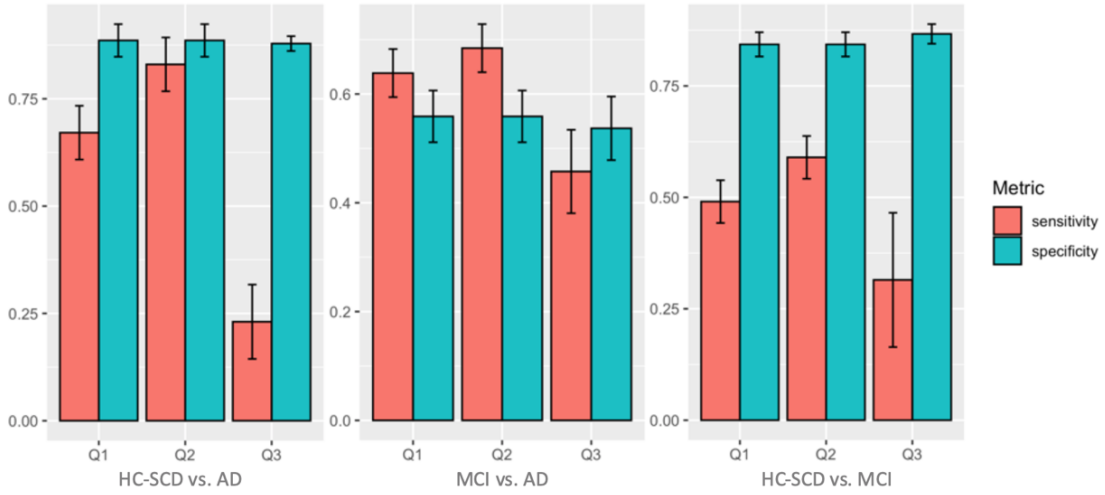
Subjects were split into three groups according to T1 image resolution. ST, slice thickness; HC, cognitively healthy controls; SCD, subjective cognitive decline; MCI, mild cognitive impairment; ADD, Alzheimer's disease dementia. High resolution (High, ST < 1 mm), middle resolution (Middle, 1 mm ≤ ST ≤ 1.6 mm), and low resolution images (Low, ST > 1.6 mm). The cognitively healthy controls and subjective cognitive decline subjects were taken together as a diagnostic group due to the low number of low resolution images available.

Supplementary Table 3. Exploratory study: icobrain dm's diagnostic performance regarding differences in slice thickness resolution.

Resolution	HC-SCD versus MCI AUC [95% CI]	HC-SCD versus ADD AUC [95% CI]	MCI versus ADD AUC [95% CI]
High (ST < 1 mm)	0.741 [0.735-0.747]	0.865 [0.852-0.877]	0.629 [0.615-0.643]
Middle (1 mm ≤ ST ≤ 1.6 mm)	0.757 [0.746-0.769]	0.895 [0.889-0.900]	0.677 [0.663-0.690]
Low (ST > 1.6 mm)	0.731 [0.716-0.747]	0.666 [0.644-0.687]	0.539 [0.529-0.551]

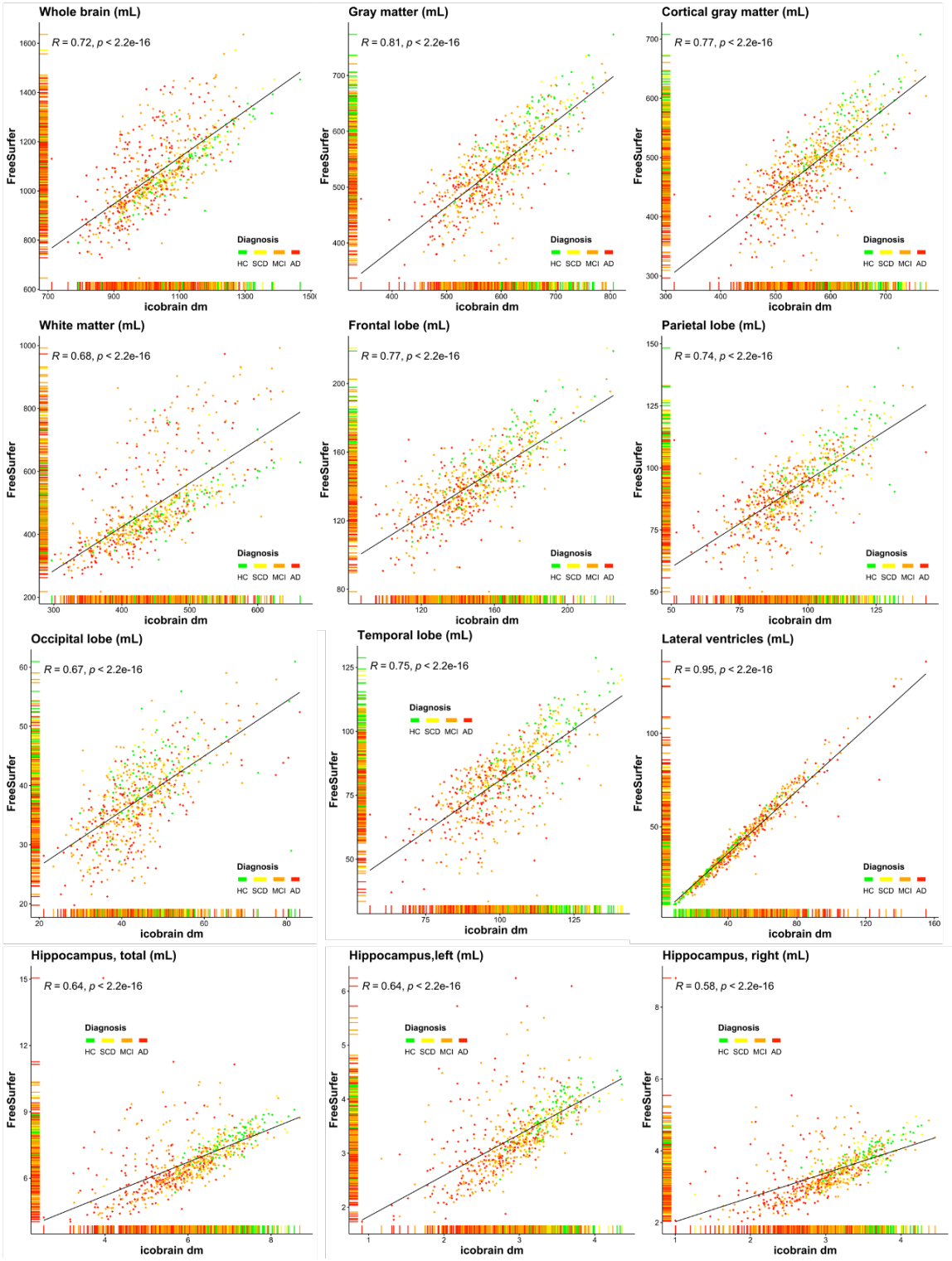
ST, slice thickness; HC, cognitively healthy controls; SCD, subjective cognitive decline; MCI, mild cognitive impairment; ADD, Alzheimer's disease dementia. For estimating the AUC (area under the curve) distribution, a 50 repetition bootstrap resampling procedure was performed over the training set (the high ST resolution group) and the fitted models were evaluated over the 2 testing sets (the middle and low ST resolution groups). Data reported as mean and 95% AUC confidence intervals. Model input: whole brain, gray matter, cortical gray matter, white matter, left hippocampus, right hippocampus, frontal, parietal, temporal, and occipital cortices.

Supplementary Figure 1. Exploratory study: Effect of slice thickness resolution on diagnostic performance of icobrain dm



Resolution model performance for classification between AD stages. ST, slice thickness; HC, cognitively healthy controls; SCD, subjective cognitive decline; MCI, mild cognitive impairment; AD, Alzheimer's disease dementia. Sensitivity (red) and specificity (blue) were reported for high resolution (Q1, ST <1 mm), middle resolution (Q2, 1 mm ≤ ST ≤ 1.6 mm), and low resolution (Q3, ST > 1.6 mm) pairwise comparisons. Model input: whole brain, gray matter, cortical gray matter, white matter, left hippocampus, right hippocampus, frontal, parietal, temporal, and occipital cortices.

Supplementary Figure 2. Correlations between icobrain dm and FreeSurfer brain volumes



Regional brain volumes are presented in milliliter (mL). Cognitively healthy controls (HC) are depicted in green. Subjective cognitive decline subjects (SCD) are depicted in yellow. Mild cognitive impairment (MCI) patients are depicted in orange. Alzheimer's disease dementia (AD) patients are depicted in red. R, Pearson's correlation coefficient. p, *p* value.

Supplementary Table 4. Effect of segmentation technique on brain structure volume calculation

Brain structures	Estimate	Std. error	z-value	Adjusted p (Bonferroni)
Whole brain				
FreeSurfer – icobrain dm == 0	44.673	5.936	7.525	<0.001
Gray matter				
FreeSurfer – icobrain dm == 0	-61.140	3.034	-20.15	<0.001
Cortical gray matter				
FreeSurfer – icobrain dm == 0	-83.665	2.942	-28.44	<0.001
White matter				
FreeSurfer – icobrain dm == 0	56.134	4.979	11.28	<0.001
Frontal cortex				
FreeSurfer – icobrain dm == 0	-7.7290	0.9787	-7.897	<0.001
Parietal cortex				
FreeSurfer – icobrain dm == 0	-3.3545	0.6338	-5.293	<0.001
Temporal cortex				
FreeSurfer – icobrain dm == 0	-20.592	0.6374	-32.30	<0.001
Occipital cortex				
FreeSurfer – icobrain dm == 0	-6.6748	0.3848	-17.35	<0.001
Hippocampus, total				
FreeSurfer – icobrain dm == 0	0.84136	0.05225	16.10	<0.001
Hippocampus, left				
FreeSurfer – icobrain dm == 0	0.42075	0.02677	15.71	<0.001
Hippocampus, right				
FreeSurfer – icobrain dm == 0	0.42061	0.02869	14.66	<0.001
Lateral ventricles				
FreeSurfer – icobrain dm == 0	-6.1584	0.9256	-6.653	<0.001

Supplementary Table 5. Diagnostic performance of icobrain dm for all pairwise comparisons

	versus SCD				versus MCI				versus ADD			
icobrain dm	AUC	Specificity (%)	Sensitivity (%)	Threshold*	AUC	Specificity (%)	Sensitivity (%)	Threshold*	AUC	Specificity (%)	Sensitivity (%)	Threshold*
WB												
HC	0.644	65.2	62.9	0.497	0.720	65.2	72.8	0.759	**0.749**	65.2	75.6	0.697
SCD					0.569	24.7	89.1	0.733	0.615	91.0	26.8	0.798
MCI									0.548	79.1	31.6	0.460
GM												
HC	0.623	75.0	52.3	0.524	0.661	86.4	48.2	0.814	**0.726**	86.4	57.4	0.729
SCD					0.558	90.9	24.6	0.813	0.634	84.1	44.1	0.742
MCI									0.573	69.7	44.1	0.413
CGM												
HC	0.601	89.8	32.9	0.560	0.639	89.8	40.3	0.823	**0.686**	89.8	49.0	0.749
SCD					0.540	89.8	20.5	0.809	0.597	85.3	33.8	0.743
MCI									0.555	72.9	39.7	0.411
WM												
HC	0.562	56.8	58.0	0.504	0.582	75.0	44.5	0.795	**0.562**	75.0	44.1	0.709
SCD					0.530	75.0	36.0	0.787	0.484	96.5	13.7	0.700
MCI									0.512	63.4	45.6	0.393
Frontal cortex												
HC	0.505	79.5	33.0	0.492	0.631	85.2	45.4	0.805	**0.685**	82.9	51.5	0.721
SCD					0.614	77.2	45.1	0.806	0.664	53.4	73.0	0.664
MCI									0.543	32.2	80.0	0.361
Parietal cortex												
HC	0.612	63.6	57.9	0.515	0.661	88.6	43.5	0.831	**0.725**	88.6	50.0	0.758
SCD					0.554	90.9	22.1	0.816	0.630	90.9	33.8	0.766
MCI									0.578	73.2	40.2	0.422
Occipital cortex												
HC	0.433	50.0	51.1	0.508	0.455	53.4	51.4	0.786	**0.464**	70.4	32.8	0.693
SCD					0.526	85.2	29.6	0.797	0.471	78.4	28.4	0.671
MCI									0.495	44.4	61.3	0.393
Temporal cortex												
HC	0.586	86.4	34.1	0.551	0.732	60.3	74.8	0.743	**0.790**	65.9	78.0	0.640
SCD					0.628	45.5	78.3	0.737	0.706	90.9	40.2	0.797
MCI									0.600	83.3	36.8	0.452
Lateral ventricles												
HC	0.579	63.6	55.7	0.490	0.666	62.5	67.5	0.749	**0.763**	65.9	77.4	0.610
SCD					0.587	53.4	63.4	0.764	0.680	59.1	70.6	0.647

MCI								0.598	54.3	62.7	0.371	
Hippocampus, total												
HC	0.608	65.9	54.5	0.511	0.753	85.3	59.0	0.815	**0.871**	89.8	72.5	0.736
SCD					0.667	78.4	51.0	0.802	0.802	78.4	71.6	0.682
MCI									0.646	69.1	53.4	0.414
Hippocampus, left												
HC	0.591	72.7	45.5	0.527	0.737	87.5	52.4	0.831	**0.849**	97.7	58.3	0.836
SCD					0.660	80.6	47.6	0.810	0.788	80.7	65.2	0.710
MCI									0.633	66.6	54.9	0.400
Hippocampus, right												
HC	0.607	47.7	70.5	0.475	0.748	79.5	61.8	0.800	**0.862**	84.1	75.5	0.703
SCD					0.660	62.5	68.5	0.765	0.794	83.0	65.2	0.719
MCI									0.649	51.4	72.0	0.350

Area under the curve (AUC), specificity and sensitivity values were documented for each of the pairwise comparisons between disease stages (SCD versus HC, MCI versus HC, ADD versus HC, ADD versus SCD and ADD versus MCI). Specificity (%) and sensitivity (%) outcomes were calculated based on the combined smallest Euclidian distance, using the Youden index to determine the threshold* for each disease stage comparison. AUC values for HC versus ADD are highlighted in bold. HC, cognitively healthy controls; SCD, subjective cognitive decline; MCI, mild cognitive impairment; ADD, Alzheimer's disease dementia; WB, whole brain; GM, gray matter; CGM, cortical gray matter; WM, white matter.

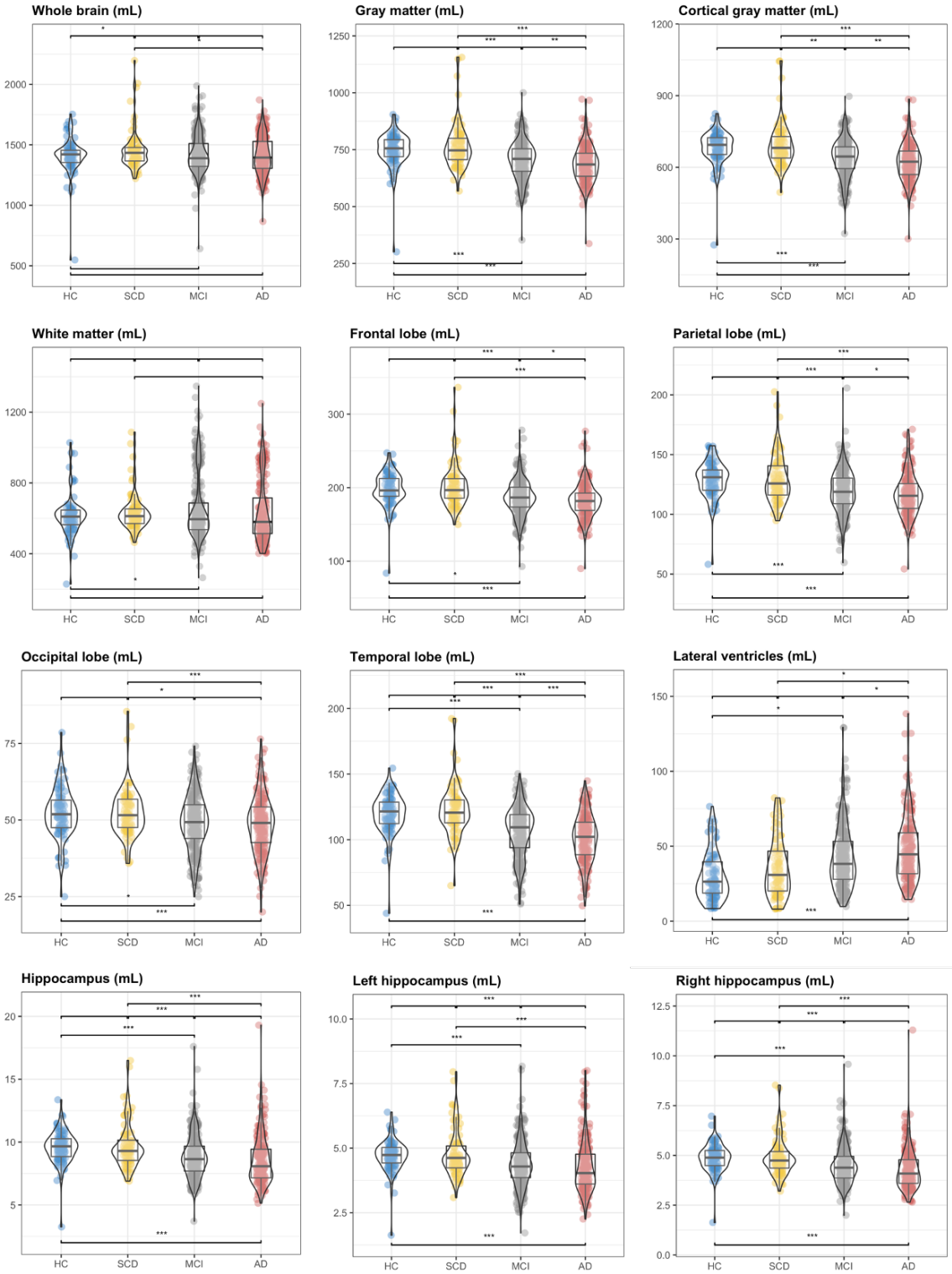
Supplementary Table 6. Diagnostic performance of FreeSurfer for all pairwise comparisons

	versus SCD				versus MCI				versus ADD			
FreeSurfer	**AUC**	**Specificity (%)**	**Sensitivity (%)**	**Threshold***	**AUC**	**Specificity (%)**	**Sensitivity (%)**	**Threshold***	**AUC**	**Specificity (%)**	**Sensitivity (%)**	**Threshold***
WB												
HC	0.596	83.1	42.7	0.515	0.561	83.1	41.7	0.790	**0.564**	83.1	45.6	0.745
SCD					0.514	71.9	39.8	0.786	0.503	86.5	34.8	0.734
MCI									0.501	68.8	39.2	0.438
GM												
HC	0.515	95.5	18.2	0.548	0.613	73.8	49.5	0.789	**0.705**	73.9	63.7	0.699
SCD					0.621	93.2	27.4	0.843	0.703	69.3	61.3	0.718
MCI									0.578	50.5	65.7	0.382
CGM												
HC	0.509	93.2	21.6	0.535	0.607	85.2	36.9	0.804	**0.695**	86.4	49.5	0.733
SCD					0.610	90.9	27.7	0.838	0.692	73.9	53.9	0.730
MCI									0.576	60.3	55.9	0.390
WM												
HC	0.591	56.8	58.0	0.491	0.453	61.4	45.1	0.764	**0.486**	92.0	23.0	0.652
SCD					0.525	64.8	49.5	0.772	0.548	97.8	27.5	0.678
MCI									0.539	89.3	24.5	0.403
Frontal cortex												
HC	0.525	62.5	50.0	0.500	0.575	92.0	26.8	0.807	**0.637**	88.6	35.8	0.736
SCD					0.596	47.7	67.8	0.771	0.651	55.7	67.6	0.689
MCI									0.554	45.1	65.7	0.384
Parietal cortex												
HC	0.530	93.2	22.7	0.483	0.604	84.1	42.9	0.803	**0.670**	81.8	52.9	0.773
SCD					0.574	70.5	42.9	0.805	0.627	68.2	54.1	0.721
MCI									0.554	70.3	43.6	0.401
Occipital cortex												
HC	0.502	18.2	90.9	0.489	0.555	70.5	41.3	0.792	**0.557**	78.5	35.3	0.719
SCD					0.549	90.9	26.2	0.809	0.565	88.6	30.8	0.732
MCI									0.512	71.0	33.8	0.395
Temporal cortex												
HC	0.528	84.1	28.4	0.527	0.675	72.7	57.4	0.781	**0.759**	76.1	70.1	0.685
SCD					0.691	68.1	61.8	0.781	0.707	73.9	71.0	0.694
MCI									0.585	48.6	69.6	0.371
Lateral ventricles												
HC	0.597	84.1	36.4	0.554	0.636	63.6	59.3	0.767	**0.733**	65.9	71.6	0.646
SCD					0.539	42.0	67.8	0.770	0.633	51.1	71.6	0.649

MCI									0.596	47.6	68.6	0.362
Hippocampus, total												
HC	0.537	48.9	64.8	0.500	0.656	85.2	47.6	0.804	**0.711**	87.5	56.9	0.725
SCD					0.625	71.6	54.3	0.799	0.688	85.2	52.0	0.742
MCI									0.574	66.6	52.0	0.403
Hippocampus, left												
HC	0.538	67.0	48.9	0.494	0.647	76.1	55.5	0.791	**0.696**	87.5	54.9	0.723
SCD					0.616	78.4	47.0	0.806	0.671	78.4	57.4	0.721
MCI									0.563	70.9	47.0	0.400
Hippocampus, right												
HC	0.526	89.8	21.6	0.485	0.660	80.6	50.8	0.799	**0.732**	89.8	55.9	0.735
SCD					0.637	68.2	58.7	0.793	0.710	77.3	61.3	0.723
MCI									0.588	72.6	45.1	0.416

Area under the curve (AUC), specificity and sensitivity values were documented for each of the pairwise comparisons between disease stages (SCD versus HC, MCI versus HC, ADD versus HC, ADD versus SCD and ADD versus MCI). Specificity (%) and sensitivity (%) outcomes were calculated based on the combined smallest Euclidian distance, using the Youden index to determine the threshold* for each disease stage comparison. AUC values for HC versus ADD are highlighted in bold. WB, whole brain; GM, gray matter; CGM, cortical gray matter; WM, white matter.

Supplementary Figure 3. Violin boxplots per brain region – FreeSurfer.



Differences between groups reported using post-hoc analysis ("Tukey" correction) for normalized brain volumes. *p* values: 0 '***' <0.001 '**' <0.01 '*' <0.05. The absence of a notation corresponds with a non-significant value. HC, cognitively healthy controls. SCD, subjective cognitive decline; MCI, mild cognitive impairment; ADD, Alzheimer's disease dementia.

Supplementary Table 7. Stepwise backward regression model – FreeSurfer for age- and sex-adjusted brain volumes normalized for head size.

FreeSurfer									
Disease Stage	**Final Brain Structures**	**AIC**	**ΔAIC**	**REL.LL**	**Youden Index**	**Threshold**	**Specificity (%)**	**Sensitivity (%)**	**AUC**
SCD versus HC	**WB** and LVENT	235.3	6.57	0.04	0.284	0.482	63.6	64.8	0.679
MCI versus HC	**WB,** FL, **TL**, HIP-L and LVENT	375.8	2.84	0.24	0.448	0.834	90.9	53.9	0.761
ADD versus HC	**WB**, FL, TL, **HIP-R,** and **LVENT**	275.3	3.88	0.14	0.577	0.743	88.6	69.1	0.844
MCI versus SCD	PL, **TL**, and **HIP-L**	384.3	6.25	0.04	0.335	0.815	79.5	53.9	0.713
ADD versus SCD	PL, **TL**, and **HIP-R**	288.7	6.06	0.05	0.480	0.695	75.0	73.0	0.802
ADD versus MCI	**PL,** TL**, HIP-R** and **LVENT**	683.2	2.97	0.23	0.213	0.394	62.5	58.8	0.622

Input brain volumes: whole brain (WB), frontal cortex (FL), parietal cortex (PL), temporal cortex (TL), lateral ventricles (LVENT), left hippocampus (HIP-L), and right hippocampus (HIP-R). Disease stages: HC, cognitively healthy controls; SCD, subjective cognitive decline; MCI, mild cognitive impairment; ADD, Alzheimer's disease dementia. AIC, Akaike Information Criterion; Δ-AIC, Difference between the AIC of the full model (input brain volumes) and the final model (brain volume model with the lowest AIC); REL.LL, relative likelihood measure; AUC, Area under the curve, specificity (%), and sensitivity (%) values were reported. Specificity and sensitivity outcomes are presented as percentages and were calculated based on the combined smallest Euclidian distance, using the Youden index to determine the threshold. Brain structures highlighted in bold are present in the final models of both automated volumetric tools.

Supplementary Table 8. Stepwise backward regression model: contribution of separate brain volumes– icobrain dm.

Disease Stage Comparison	Initial Model	VIF	VIF-2	VIF-3	Start Model	Final Model	Stepwise AIC
SCD versus HC	Whole brain	2.19	1.85	1.79	Whole brain	Whole brain	239.29
	Gray matter	**46.04**	**5.57**				
	Cortical gray matter	**52.21**					
	Frontal cortex	2.83	2.84	2.06	Frontal cortex	Frontal cortex	236.38
	Parietal cortex	2.77	2.77	1.88	Parietal cortex	Parietal cortex	236.33
	Temporal cortex	2.13	2.06	1.75	Temporal cortex		
	Hippocampus, right	1.70	1.69	1.68	Hippocampus, right	Hippocampus, right	234.56
	Hippocampus, left	1.70	1.71	1.67	Hippocampus, left		
	Lateral ventricles	2.17	1.40	1.40	Lateral ventricles		
					AIC*i*: 239.05	**AIC*min:* 233.71**	
MCI versus HC	Whole brain	1.78	1.43	1.35	Whole brain	Whole brain	352.81
	Gray matter	**52.29**	**5.39**				
	Cortical gray matter	**57.00**					
	Frontal cortex	3.27	3.07	1.74	Frontal cortex		
	Parietal cortex	2.31	2.27	1.69	Parietal cortex	Parietal cortex	343.27
	Temporal cortex	1.68	1.66	1.39	Temporal cortex	Temporal cortex	344.99
	Hippocampus, right	2.01	2.00	1.95	Hippocampus, right	Hippocampus, right	363.39
	Hippocampus, left	2.03	1.96	1.95	Hippocampus, left		
	Lateral ventricles	2.08	1.36	1.34	Lateral ventricles		
					AIC*i*: 346.53	**AIC*min:* 342.42**	
ADD versus HC	Whole brain	1.49	1.34	1.30	Whole brain	Whole brain	215.88
	Gray matter	**29.69**	**4.96**				
	Cortical gray matter	**31.61**					
	Frontal cortex	2.54	2.28	1.52	Frontal cortex		
	Parietal cortex	2.33	2.20	1.40	Parietal cortex	Parietal cortex	226.07
	Temporal cortex	1.77	1.84	1.43	Temporal cortex		
	Hippocampus, right	1.67	1.65	1.65	Hippocampus, right	Hippocampus, right	222.84
	Hippocampus, left	1.55	1.52	1.48	Hippocampus, left	Hippocampus, left	224.46
	Lateral ventricles	1.42	1.18	1.18	Lateral ventricles	Lateral ventricles	216.21
					AIC*i*: 218.45	**AIC*min:* 215.35**	
MCI versus SCD	Whole brain	2.07	1.78	1.71	Whole brain		
	Gray matter	**47.95**	**8.63**				

	Cortical gray matter	**53.50**					
	Frontal cortex	4.45	3.92	1.81	Frontal cortex	Frontal cortex	397.41
	Parietal cortex	2.82	2.80	1.99	Parietal cortex		
	Temporal cortex	2.42	2.28	1.81	Temporal cortex	Temporal cortex	398.45
	Hippocampus, right	2.08	2.05	2.01	Hippocampus, right		
	Hippocampus, left	2.11	2.07	2.02	Hippocampus, left	Hippocampus, left	408.25
	Lateral ventricles	2.09	1.44	1.47	Lateral ventricles		
					AIC*i*: 402.24	**AIC*min:* 396.99**	
ADD versus SCD	Whole brain	1.74	1.54	1.52	Whole brain		
	Gray matter	**27.13**	**8.15**				
	Cortical gray matter	**32.16**					
	Frontal cortex	3.49	2.87	1.59	Frontal cortex	Frontal cortex	277.97
	Parietal cortex	3.01	2.98	1.68	Parietal cortex		
	Temporal cortex	2.59	2.48	1.71	Temporal cortex	Temporal cortex	277.64
	Hippocampus, right	1.61	1.61	1.68	Hippocampus, right	Hippocampus, right	279.33
	Hippocampus, left	1.59	1.59	1.54	Hippocampus, left	Hippocampus, left	287.58
	Lateral ventricles	1.52	1.33	1.31	Lateral ventricles		
					AIC*i*: 279.48	**AIC*min*: 276.54**	
ADD versus MCI	Whole brain	1.87	1.63	1.50	Whole brain		
	Gray matter	**36.14**	**7.67**				
	Cortical gray matter	**37.61**					
	Frontal cortex	3.47	3.34	1.76	Frontal cortex		
	Parietal cortex	2.92	2.85	1.94	Parietal cortex	Parietal cortex	664.94
	Temporal cortex	2.14	2.12	1.65	Temporal cortex		
	Hippocampus, right	1.94	1.93	1.92	Hippocampus, right	Hippocampus, right	664.83
	Hippocampus, left	1.85	1,82	1.81	Hippocampus, left	Hippocampus, left	661.62
	Lateral ventricles	1.78	1.42	1.42	Lateral ventricles	Lateral ventricles	661.54
					AIC*i*: 664.33	**AIC*min:* 660.98**	

A stepwise backward regression model for age- and sex-adjusted brain volumes normalized for head size computed by ico**brain dm**. Disease stages: HC, cognitively healthy controls; SCD, subjective cognitive decline; MCI, mild cognitive impairment; ADD, Alzheimer's disease dementia. AIC, Akaike Information Criterion; Initial model, odel containing all individual predictors; VIF, Variance inflation factor; VIF-1, Variance inflation factors after exclusion of cortical gray matter from the initial model; VIF-2, Variance inflation factors after exclusion of cortical gray matter and gray matter from the initial model; Start model, Start model with corresponding AIC (AICi) for stepwise AIC analysis after removing variables causing multi-collinearity; Final model, Model containing the lowest AIC (AICmin); Stepwise AIC, Contribution of individual brain volumes to the model visualized as the change in AIC upon removal.

Supplementary Table 9. Stepwise backward regression model: contribution of separate brain volumes – FreeSurfer.

Disease Stage Comparison	Initial Model	VIF-1	VIF-2	VIF-3	Start Model	Final Model	Stepwise AIC
SCD versus HC	Whole brain	1.54	1.56	1.66	Whole brain	Whole brain	242.41
	Gray matter	**253.89**	**13.75**				
	Cortical gray matter	**236.92**					
	Frontal cortex	4.18	4.12	3.29	Frontal cortex		
	Parietal cortex	4.83	4.77	2.96	Parietal cortex		
	Temporal cortex	4.15	4.09	2.80	Temporal cortex		
	Hippocampus, right	5.60	4.64	4.86	Hippocampus, right		
	Hippocampus, left	4.66	4.41	4.63	Hippocampus, left		
	Lateral ventricles	1.46	1.42	1.36	Lateral ventricles	Lateral ventricles	242.51
					AIC*i*: 241.87	**AIC*min:* 235.31**	
MCI versus HC	Whole brain	1.89	1.79	1.87	Whole brain	Whole brain	387.62
	Gray matter	**26.39**	**18.12**				
	Cortical gray matter	**11.79**					
	Frontal cortex	6.52	5.64	3.81	Frontal cortex	Frontal cortex	378.22
	Parietal cortex	5.76	5.37	3.50	Parietal cortex		
	Temporal cortex	5.54	5.08	2.66	Temporal cortex	Temporal cortex	389.96
	Hippocampus, right	3.44	3.07	3.10	Hippocampus, right		
	Hippocampus, left	3.65	3.28	3.39	Hippocampus, left	Hippocampus, left	384.77
	Lateral ventricles	1.12	1.12	1.10	Lateral ventricles	Lateral ventricles	383.16
					AIC*i*: 378.64	**AIC*min:* 375.83**	
ADD versus HC	Whole brain	1.89	1.75	1.77	Whole brain	Whole brain	283.71
	Gray matter	**327.20**	**18.13**				
	Cortical gray matter	**317.76**					
	Frontal cortex	6.09	6.05	3.35	Frontal cortex	Frontal cortex	278.20
	Parietal cortex	4.56	4.52	2.98	Parietal cortex		
	Temporal cortex	4.76	4.72	2.32	Temporal cortex	Temporal cortex	300.48
	Hippocampus, right	3.75	3.37	3.33	Hippocampus, right	Hippocampus, right	286.71
	Hippocampus, left	3.42	3.29	3.27	Hippocampus, left		
	Lateral ventricles	1.09	1.09	1.08	Lateral ventricles	Lateral ventricles	289.28
					AIC*i*: 279.18	**AIC*min:* 275.29**	
MCI versus SCD	Whole brain	1.86	1.72	1.66	Whole brain	Whole brain	
	Gray matter	**317.08**	**20.76**				

	Cortical gray matter	**323.07**					
	Frontal cortex	6.93	6.59	3.85	Frontal cortex		
	Parietal cortex	6.01	5.66	3.85	Parietal cortex	Parietal cortex	390.56
	Temporal cortex	5.66	5.24	2.66	Temporal cortex	Temporal cortex	385.64
	Hippocampus, right	3.72	3.39	3.24	Hippocampus, right		
	Hippocampus, left	3.63	3.31	3.25	Hippocampus, left	Hippocampus, left	413.56
	Lateral ventricles	1.20	1.17	1.16	Lateral ventricles		
					AIC*i*: 390.55	**AIC*min:* 384.26**	
ADD versus SCD	Whole brain	1.83	1.66	1.64	Whole brain		
	Gray matter	**297.17**	**19.32**				
	Cortical gray matter	**302.70**					
	Frontal cortex	7.07	6.88	3.44	Frontal cortex		
	Parietal cortex	5.34	5.14	3.55	Parietal cortex	Parietal cortex	297.26
	Temporal cortex	4.57	4.34	2.35	Temporal cortex	Temporal cortex	337.19
	Hippocampus, right	3.44	3.21	3.09	Hippocampus, right	Hippocampus, right	295.72
	Hippocampus, left	3.29	3.18	3.14	Hippocampus, left		
	Lateral ventricles	1.18	1.18	1.15	Lateral ventricles		
					AIC*i*: 294.76	**AIC*min:* 288.70**	
ADD versuss MCI	Whole brain	1.53	1.34	1.34	Whole brain		
	Gray matter	**336.98**	**19.25**				
	Cortical gray matter	**362.94**					
	Frontal cortex	6.88	6.62	3.47	Frontal cortex		
	Parietal cortex	4.96	4.69	3.28	Parietal cortex	Parietal cortex	684.37
	Temporal cortex	5.61	5.42	2.73	Temporal cortex	Temporal cortex	690.07
	Hippocampus, right	3.10	2.81	2.76	Hippocampus, right	Hippocampus, right	684.11
	Hippocampus, left	3.06	2.76	2.75	Hippocampus, left		
	Lateral ventricles	1.13	1.13	1.11	Lateral ventricles	Lateral ventricles	690.12
					AIC*i*: 686.17	**AIC*min:* 683.24**	

A stepwise backward regression model for age- and sex-adjusted brain volumes normalized for head size computed by FreeSurfer. Disease stages: HC, cognitively healthy controls; SCD, subjective cognitive decline; MCI, mild cognitive impairment; ADD, Alzheimer's disease dementia. AIC, Akaike Information Criterion; Initial model, Model containing all individual predictors; VIF, Variance inflation factor; VIF-1, Variance inflation factors after exclusion of cortical gray matter from the initial model; VIF-2, Variance inflation factors after exclusion of cortical gray matter and gray matter from the initial model; Start model, Start model with corresponding AIC (AICi) for stepwise AIC analysis after removing variables causing multi-collinearity; Final model, Model containing the lowest AIC (AICmin); Stepwise AIC, Contribution of individual brain volumes to the model visualized as the change in AIC upon removal.