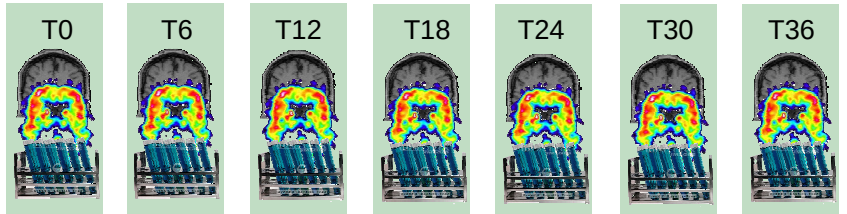
The pilot European Alzheimer's Disease Neuroimaging Initiative (E-ADNI) of the European Alzheimer's Disease Consortium

GB Frisoni, WJP Henneman, MW Weiner, Ph Scheltens, B Vellas, E Reynish, J Hudecova, S Galluzzi, H Hampel, K Burger, K Blennow, G Waldemar, P Johannsen, L-O Wahlund, G Zito, PM Rossini, B Winblad, F Barkhof, H Zetterberg, M Ewers, and the Alzheimer's Disease Neuroimaging Initiative

BACKGROUND

The US Alzheimer's Disease Neuroimaging Initiative (ADNI)



Mild Cognitive Impairment N=400

Alzheimer's Disease N=200

Normal older persons N=200

AIMS

1. To test the feasibility of the ADNI methods for imaging+biomarker collection in academic centres in Europe

2. To test the validity of the ADNI platform by comparing clinical and instrumental features of EU and US study groups

METHODS
The EADC academic centres

City	*Principal Investigator*	*Institution*
Amsterdam	Ph Scheltens	VU Medical Center, Amsterdam, The Netherlands
Brescia	GB Frisoni	IRCCS Fatebenefratelli, Brescia, Italy
Copenhagen	G Waldemar	MDRU, Rigshospitalet, Copenhagen, Denmark
Munich	H Hampel	Ludwig-Maximilian Univ, Munich, Germany
Roma	PM Rossini	Ospedale S Giovanni Calibita, Isola Tiberina, Roma
Stockholm	L-O Wahlund	Huddinge Hospital, Sweden
Toulouse	B Vellas	Centre Hospitalier Univ Toulouse, France

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METHODS
Assessment & disease markers

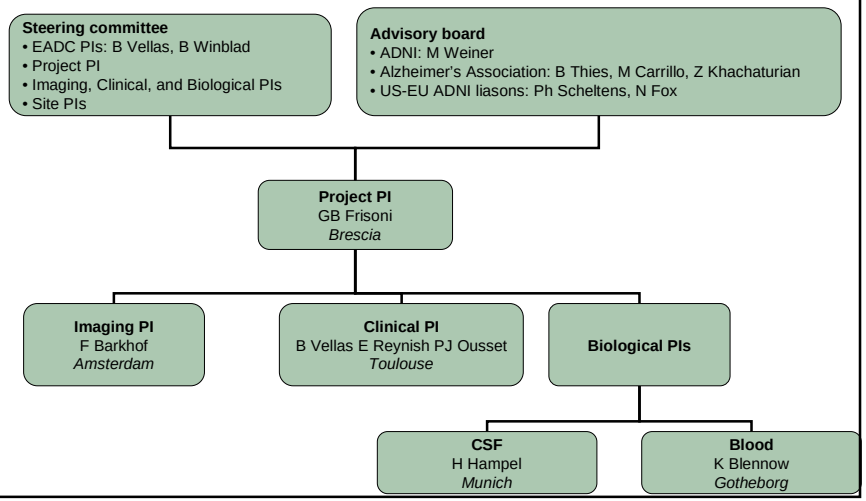
SUBJECTS
3 AD, 3 MCI, 3 CTR per centre

CASE REPORT FORM
ADNI CRF including npsy tests: Italian, German, French, Danish, Swedish, Dutch

MR
- **Human phantoms (3 travelling volunteers)**
- **Volumetric 1.5T ADNI seq.s (GE, Philips, Siemens)**
- **Diffusion imaging**
- **resting fMRI**

CSF & blood
- **ADNI collection protocol**

METHODS
The decision structure



ELSEVIER

Alzheimer's & Dementia 4 (2008) 255–264

Alzheimer's & Dementia

Featured Articles

The pilot European Alzheimer's Disease Neuroimaging Initiative of the European Alzheimer's Disease Consortium

Giovanni B. Frisoni[a,*], Wouter J. P. Henneman[b], Michael W. Weiner[c], Philip Scheltens[d], Bruno Vellas[e], Emma Reynish[e,f], Jaroslava Hudecova[a], Harald Hampel[g,h], Katharina Burger[h], Kaj Blennow[i], Gunhild Waldemar[j], Peter Johannsen[j], Lars-Olof Wahlund[k], Giancarlo Zito[l], Paolo M. Rossini[l], Bengt Winblad[k], Frederik Barkhof[b], and the Alzheimer's Disease Neuroimaging Initiative

RESULTS

Subject enrolment and data collection

	AD		MCI		Controls		Total	
	N (%)	Cases/ site	N (%)	Cases/ site	N (%)	Cases/ site	N (%)	Cases/ site
CRF [1]	22 (ref.)	2 to 6	19 (ref.)	0 to 4	18 (ref.)	1 to 4	59 (ref.)	3 to 10
MR scan [2]	22(100%)	2 to 6	19(100%)	0 to 4	18(100%)	1 to 4	59(100%)	3 to 10
Lumb punc [3]	17 (77%)	0 to 6	13 (68%)	0 to 4	15 (83%)	0 to 3	45 (76%)	0 to 10
Blood [4]	19 (86%)	1 to 6	17 (89%)	0 to 4	17 (94%)	1 to 4	53 (90%)	3 to 10

The denominator of percentages is N of the first row, representing 100% (reference). [1] including full neuropsychological battery; [2] at least valid 3D acquisition; [3] with viable CSF reaching safely the collection centre in Munich; [4] with viable blood reaching safely the collection centre in Gothenburg.

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RESULTS

European and US cases had similar general clinical features

		AD		MCI		Controls		Signif. on	
		E	US	E	US	E	US	ANOVA or χ^2	
Number		22	186	19	394	18	229	Site	Int.n
Socdem	Age, yrs	74.6	75.2	68.9	74.7	71.2	75.9	<.0005	n.s.
	Sex, F	50%	47%	47%	36%	22%	48%	n.s.	---
	Education, yrs	10.5	14.7	11.1	15.7	10.8	16.0	<.0005	n.s.
Cognition	MMSE	23.2	23.3	27.3	27.0	29.1	29.1	n.s.	n.s.
	CDR	4.8	4.4	1.3	1.6	0.06	0.03	n.s.	n.s.
	ADAS-Cog	19.8	18.6	11.4	11.6	8.2	6.2	n.s.	n.s.
	Log Mem-DR	1.7	1.2	5.8	3.8	11.6	13.0	---	.005
Behav	GDS	2.4	1.7	2.5	1.6	1.2	.8	<.0005	n.s.
& disab	Func Ass Q.	12.8	13.1	1.6	3.8	0	.1	n.s.	n.s.
	NPI	3.1	3.6	1.6	1.8	.2	.4	n.s.	n.s.

Figures denote number (%) or mean±SD. ANOVA and χ^2 test significance of the "site" main effect (EU *vs.* US) and the interaction of site x diagnosis. In the case of significant main effects.

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RESULTS

Cognitive test scores were also rather close

	AD		MCI		Controls		Sig on ANOVA	
	E	US	E	US	E	US	Site	Interac
Clock								
Drawing	2.6	3.4	3.9	4.2	4.6	4.7	.004	n.s.
Copying	4.4	4.3	4.7	4.7	4.8	4.9	n.s.	n.s.
Categ Fluency								
Category 1	11.4	12.3	18.4	15.9	20.8	19.9	n.s.	n.s.
Category 2	8.0	7.9	12.8	10.8	13.5	14.7	---	.03
Trial Making								
Trial B–A	126	133	98	86	60	53	n.s.	n.s.
Digit Symbol								
Total Score	17.4	26.7	28.1	36.9	39.6	45.7	<.0005	n.s.
Boston Naming								
Without cue	19.6	21.8	23.7	25.0	26.9	27.4	.043	n.s.
With cue	20.7	22.3	24.7	25.5	27.1	27.8	n.s.	n.s.

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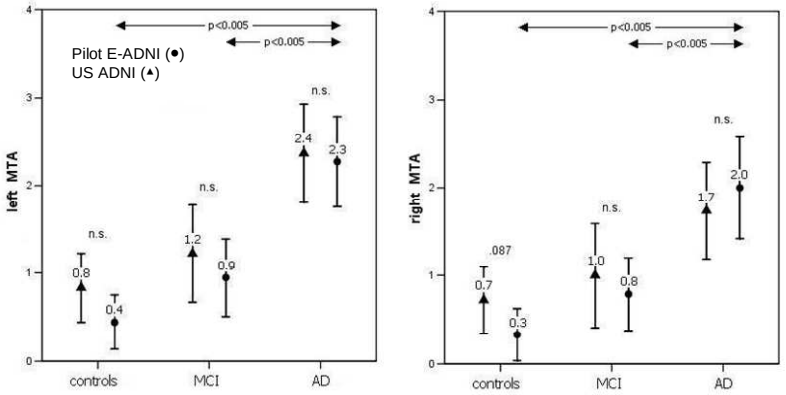
METHODS

Temporal atrophy: increase CTR-MCI-AD. No difference E-ADNI vs US-ADNI



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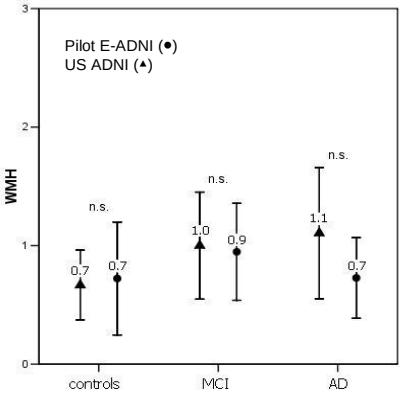
RESULTS

White Matter Changes: similar across groups. No difference E-ADNI vs US-ADNI



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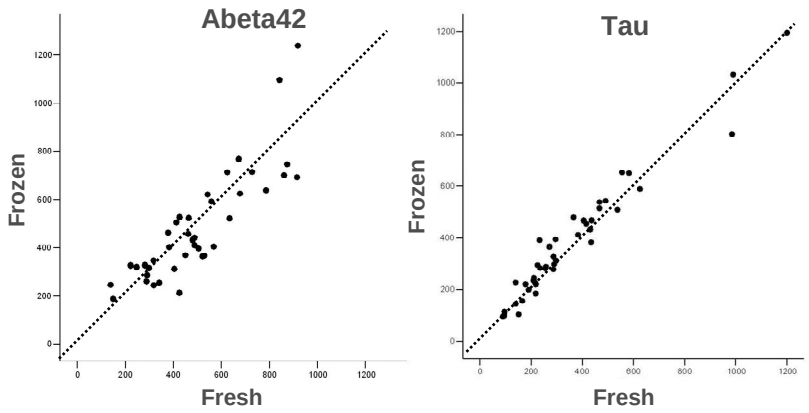
RESULTS
Biomarkers

Multi-Center Reliability and Validation Study of Core Biochemical Marker Candidates in CSF and Plasma
The Pilot European Alzheimer's Disease Neuroimaging Initiative

Katharina Bürger, Giovanni B Frisoni, Olga Uspenskaya, Michael Ewers, Henrik Zetterberg, Cristina Geroldi**,** Gunhild Waldemar, Paolo M Rossini, Lars-Olof Wahlund, Bruno Vellas, Kaj Blennow, Harald Hampel

Submitted

RESULTS
Biomarkers in CSF



RESULTS
Advanced imaging

Hippocampal volumetry, diffusion imaging, and resting fMRI
The Pilot European Alzheimer's Disease Neuroimaging Initiative

Frederick Barkhof & colleagues, Amsterdam

In preparation

CONCLUSIONS

- **Pilot E-ADNI is the first published attempt to closely replicate the multicentre US-ADNI**
- **E-ADNI MCI, AD and CTR have clinical and structural imaging features remarkably similar to US ADNI**
- **Evidence of validity of the ADNI platform**

THE FUTURE

www.neuGRID.eu

- …al initiatives in France, …
- Infrastructures allowing the merge of WW-ADNI datasets (es neuGRID)
- ADNI "step 2": Standard Operational Proce… measurem…

Day: Monday July 28
Time: 5:15 to 6:15 pm
Place: Hyatt McCormick Hotel Room CC11A

Acknowledgments

Alzheimer's Association

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