Supplemental Information for:

First PET Imaging Studies with ^{63}Zn-Zinc Citrate in Healthy Subjects and Alzheimer's Disease Patients

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Table S1. SUVs of ^{63}Zn-zinc Citrate in Brain Regions at Early Time Points*

	PET scan at 10-15 min		PET scan at 25-30 min	
Tissue	Healthy Subjects (n=6)	AD Patients (n=6)	Healthy Subjects (n=6)	AD Patients (n=6)
AD-global	0.497±0.050	0.443±0.084	0.422±0.049	0.390±0.080
L parietal	0.456±0.047	0.399±0.073	0.392±0.039	0.355±0.077
R parietal	0.472±0.045	0.426±0.067	0.398±0.041	0.378±0.078
Cingulate precuneus	0.525±0.060	0.455±0.072	0.447±0.059	0.408±0.071
L prefrontal cortex	0.475±0.051	0.401±0.047	0.422±0.088	0.370±0.082
R prefrontal cortex	0.479±0.053	0.406±0.050	0.434±0.085	0.383±0.075
Orbitofrontal	0.518±0.080	0.419±0.077	0.447±0.079	0.376±0.086
L lateral temporal	0.515±0.050	0.427±0.047	0.444±0.085	0.379±0.082
R lateral temporal	0.518±0.043	0.432±0.048	0.461±0.098	0.393±0.088
Primary visual cortex	0.624±0.059	0.543±0.067	0.557±0.116	0.508±0.103
Cerebellum	0.599±0.055	0.517±0.057	0.560±0.116	0.497±0.104
Anterior cingulate	0.497±0.069	0.405±0.065	0.397±0.091	0.329±0.094
Occipital cortex	0.537±0.059	0.474±0.059	0.486±0.096	0.443±0.090
L medial temporal	0.585±0.056	0.448±0.070	0.517±0.065	0.392±0.056
R medial temporal	0.567±0.038	0.437±0.043	0.508±0.065	0.387±0.082
Pons	0.581±0.060	0.510±0.081	0.540±0.100	0.481±0.098

*No statistically significant differences were found in comparing AD and healthy groups at these time points.

Clinical Laboratory Tests for Safety of ^{63}Zn-zinc Citrate Administration

In order to assess the safety of administration of ^{63}Zn-zinc citrate, venous blood samples were withdrawn prior to administration of ^{63}Zn-zinc citrate and ~130 min post-injection. Table S2 shows the clinical laboratory tests performed on the samples, with pre- and post-administration values.

The vast majority of the clinical laboratory parameters were within the normal range, and those outside the range were largely consistent between pre- and post-administration values. The two diabetic subjects had abnormally high plasma glucose concentrations. Subject 9, who was obese (BMI=36.8), showed a number of abnormalities, but these were consistent between pre- and post-administration values.

Table S2. Clinical laboratory tests for safety assessment

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Albumin	g/dL	3.5-5.0	1 2 3 4 5 6 7 8 9 10 11 12	4.4 4.6 4.2 4.7 4.5 4.1 4.7 5 5.3 4.1 4.2 4.7	3.9 4.1 3.7 4.3 4.4 4.1 4.3 4.3 4.5 3.9 3.7 3.9
Alk. Phosphatase	U/L	50-130	1 2 3 4 5 6 7 8 9 10 11 12	81 74 78 93 57 55 77 61 121 54 81 100	82 67 70 85 58 52 72 55 96 50 77 87

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
ALT (GPT)	U/L	7-45	1 2 3 4 5 6 7 8 9 10 11 12	49 17 23 21 26 19 24 35 22 12 14 22	44 17 21 20 25 14 23 32 20 13 13 22
AST (GOT)	U/L	8-43	1 2 3 4 5 6 7 8 9 10 11 12	33 22 19 22 34 24 25 22 21 19 19 16	33 23 17 19 29 27 23 24 16 19 18 15
Basophils	$X10^9/L$	0-0.03	1 2 3 4 5 6 7 8 9 10 11 12	0.03 0.02 0.01 0.03 M 0.03 0.03 0.02 0.03 0.02 0.01 0.01	0.04 0.03 0.01 0.02 M 0.04 0.02 0.02 0.03 0.01 0 0.01

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Bicarbonate	mmol/L	22-29	1 2 3 4 5 6 7 8 9 10 11 12	25 25 28 28 28 29 28 28 25 32 30 25	28 24 27 28 31 25 28 28 24 27 27 24
Bilirubin	mg/dL	0.1-1.0	1 2 3 4 5 6 7 8 9 10 11 12	0.5 0.4 0.8 0.5 1.2 0.6 0.9 0.4 0.4 0.4 0.5 0.4	0.5 0.4 0.6 0.5 1.1 0.6 0.9 0.4 0.3 0.4 0.5 0.4
Blood Urea Nitrogen (BUN)	mg/dL	6-21	1 2 3 4 5 6 7 8 9 10 11 12	15 15 17 16 17 16 17 15 20 13 16 15	14 14 15 15 16 14 15 13 17 12 14 14

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Calcium	mg/dL	8.9-10.1	1 2 3 4 5 6 7 8 9 10 11 12	9.7 9.2 9.5 9.1 9.1 9.5 9.7 10 10.9* 9.2 9.4 9.7	9.7 9 8.7 9 9.2 9.2 9.3 9.4 9.7 8.9 9 9
Chloride	mg/dL	100-108	1 2 3 4 5 6 7 8 9 10 11 12	100 99* 101 100 98* 103 104 100 100 102 104 100	108 104 105 104 100 105 107 102 103 104 107 104
Cholesterol	mg/dL		1 2 3 4 5 6 7 8 9 10 11 12	244 145 199 205 116 178 209 125 185 201 209 300	240 130 173 187 115 174 208 118 155 196 193 275

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Creatinine	mg/dL	0.6-1.1	1 2 3 4 5 6 7 8 9 10 11 12	0.8 0.8 1 0.9 1 1.2 0.8 0.6 0.7 0.8 0.8 0.9	0.7 0.8 0.9 0.9 1 1.1 0.8 0.6 0.6 0.7 0.8 0.9
Eosinophils	$X10^9/L$	0.05-0.5	1 2 3 4 5 6 7 8 9 10 11 12	0.12 0.34 0.18 0.23 M 0.07 0.04* 0.43 0.44 0.05 0.04* 0.07	0.11 0.3 0.18 0.19 M 0.06 0.03* 0.32 0.31 0.07 0.05 0.05
Erythrocytes	$X10^{12}/L$	3.9-5.03	1 2 3 4 5 6 7 8 9 10 11 12	4.63 3.91 4.63 4.76 5.12* 4.63 4.47 5.13* 4.75 4.17 4.7 4.56	4.57 3.67* 4.29 4.49 5.04* 4.72 4.49 4.9 4.18 4.03 4.53 4.35

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
G-Glutamyltfrase	U/L	6-29	1 2 3 4 5 6 7 8 9 10 11 12	73* 10 24 18 16 14 10 22 16 13 26 15	71* 10 20 16 16 13 8 19 14 12 25 14
Glucose	mg/dL	70-100	1 2 3 4 5 6 7 8 9 10 11 12	75 165* 99 85 83 94 92 104* 237* 93 97 92	76 129* 89 81 74 92 87 90 181* 85 84 97
Hematocrit	%	34.9-44.5	1 2 3 4 5 6 7 8 9 10 11 12	40.4 36.2 41.7 42.9 44.5 43.4 42.4 43.9 41.9 38.5 41.7 44.7*	40.5 34* 39.6 40.3 44 43 41.5 43.3 37.8 37.1 40.1 42.5

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Hemoglobin	g/dL	12-15.5	1 2 3 4 5 6 7 8 9 10 11 12	13.4 12.1 14.3 14.8 16.2* 14.5 13.7 14.8 14.6 12.6 14 14.8	13.1 11.4 13.2 13.9 16* 14.8 13.7 14.3 12.8 12.1 13.6 13.9
IgA	mg/dL	61-356	1 2 3 4 5 6 7 8 9 10 11 12	47* 197 218 258 175 137 119 267 191 72 136 147	38* 185 180 192 168 146 118 258 163 69 151 116
IgG	mg/dL	767-1590	1 2 3 4 5 6 7 8 9 10 11 12	1090 1060 702 1230 1070 821 1140 987 971 660* 1010 811	1010 943 581* 967 1040 822 1050 980 798 618* 943 690*

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
IgM	mg/dL	37-286	1 2 3 4 5 6 7 8 9 10 11 12	86 78 45 132 55 56 74 91 94 55 93 62	77 70 34* 130 55 55 66 86 82 48 90 50
Leukocytes	$X10^9/L$	3.5-10.5	1 2 3 4 5 6 7 8 9 10 11 12	4.6 5.7 5.6 4.3 5.5 5.2 5.3 6.9 9.2 3.5 6.7 5.3	5.5 5.5 5.7 4.3 6 5.2 4.5 6.9 7 3.4 6.7 5.4
Lymphocytes	$x10^9/L$	0.9-2.9	1 2 3 4 5 6 7 8 9 10 11 12	1.61 1.7 1.88 1.48 M 1 1.3 2.87 2.49 1.02 1.59 1.75	1.52 1.88 1.8 1.71 M 1.03 1.21 2.68 2.12 1.18 1.92 1.73

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Magnesium	mg/dL	1.7-2.3	1 2 3 4 5 6 7 8 9 10 11 12	1.9 1.4* 2.2 2.1 2 2.1 2 2.1 1.5* 2.1 2 1.6*	2 1.3* 2.1 1.9 1.9 2 1.9 2.2 1.4* 2.2 2.1 1.5*
Mean Corpuscular Hemoglobin (MCH)	pg/cell	27-31	1 2 3 4 5 6 7 8 9 10 11 12	28.9 30.9 30.96 31.1 31.6 31.3 30.6 28.8 30.7 30.2 29.8 32.5*	28.7 31.1 30.8 31.0 31.7 31.4 30.5 29.2 30.6 30.0 30.0 32.0
Mean Corpuscular Hemoglobin Conc. (MCHC)	g/dL	32-36	1 2 3 4 5 6 7 8 9 10 11 12	33.2 33.4 34.3 34.5 36.4 33.4 32.3 33.7 34.8 31.7 33.6 33.1	32.3 33.5 33.3 34.5 36.4 34.4 33.0 33.0 33.9 32.6 33.9 32.7

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Mean Corpuscular Volume (MCV)	fL	81.6-98.3	1 2 3 4 5 6 7 8 9 10 11 12	87.3 92.6 90.1 90.1 86.9 93.7 94.9 85.6 88.2 92.3 88.7 98	88.6 92.6 92.3 89.8 87.3 91.1 92.4 88.4 90.4 92.1 88.5 97.7
Monocytes	$x10^9/L$	0.3-0.9	1 2 3 4 5 6 7 8 9 10 11 12	0.29* 0.6 0.62 0.38 M 0.51 0.32 0.35 0.78 0.27 0.54 0.57	0.24* M 0.56 0.35 M 0.46 0.4 0.32 0.54 0.31 0.62 0.47
Neutrophils	$x10^9/L$	1.7-7.0	1 2 3 4 5 6 7 8 9 10 11 12	2.53 2.72 2.93 2.15 M 3.57 3.64 3.21 5.41 2.16 4.48 2.93	3.56 2.9 3.18 2.05 M 3.62 2.84 3.56 3.95 1.84 4.11 3.11

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Phosphorus	mg/dL	2.5-4.5	1 2 3 4 5 6 7 8 9 10 11 12	3.5 2.9 2.9 2.8 3.1 3.3 3.8 3.5 3.1 4.1 4.1 3.5	3.2 M 3.2 2.7 2.9 3.3 3.5 3.6 2.6 3.7 3.7 3.0
Platelet Count	$x10^9/L$	150-450	1 2 3 4 5 6 7 8 9 10 11 12	248 255 329 170 215 189 255 222 337 182 248 277	257 244 291 163 199 185 245 221 271 179 237 242
Potassium	mmol/L	3.6-5.2	1 2 3 4 5 6 7 8 9 10 11 12	5.3* 4.5 4.3 4.8 3.7 5.4* 4.9 4.3 5.4* 4.5 4.2 4	4.6 4.7 4.4 4.9 3.7 4.5 4.2 4.2 5.3* 4.3 4.3 3.8

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Protein, Total	g/dL	6.3-7.9	1 2 3 4 5 6 7 8 9 10 11 12	6.5 6.8 6.5 7.2 6.9 6.2* 6.8 7.4 8* 6 6.4 7.1	6.2* 6.3 5.4* 6.4 6.7 5.9 6.5 6.9 6.6 5.7 5.8 6.5
Sodium	mmol/L	135-145	1 2 3 4 5 6 7 8 9 10 11 12	140 137 138 138 139 141 144 139 140 141 142 142	145 138 140 140 140 142 145 141 141 142 143 144
Triglycerides	mg/dL		1 2 3 4 5 6 7 8 9 10 11 12	88 109 137 193 87 66 112 92 219 64 67 289	74 92 130 165 82 57 98 78 216 64 61 245

Table S2 (cont.)

Laboratory test variable	units	Normal Range	Subject No.	Pre-administration Value	Post-Administration Value
Tryptase	ng/mL	<11.5	1 2 3 4 5 6 7 8 9 10 11 12	2.5 5.1 6 3.3 1.3 3.5 3.7 3.5 5.1 3 4.4 4.2	2.1 4.4 4.6 2.9 1.1 3.2 3.2 3.3 4.9 2.6 4.6 3.9
Uric Acid	mg/dL	2.7-6.1	1 2 3 4 5 6 7 8 9 10 11 12	6.1 4.2 5.4 6.2* 8* 5.4 4.4 5.8 8.7* 5.1 4.4 7.3*	6.4* M 5.4 6 7.8* 5.1 4.4 5.7 8.5* 4.8 4.4 6.9*

Vital Signs Before and After Administration of ^{63}Zn-zinc Citrate

1. Temperature

Body temperatures were measured prior to administration of ^{63}Zn-zinc citrate and at 115 min post-injection. Table S3 shows body temperatures. No significant changes were observed.

Table S3. Body temperatures (°C)

Subject No.	Pre-administration Value	Post-Administration Value
1	35.5	35.8
2	36.4	36.6
3	35.4	35.5
4	36.7	36.4
5	36.9	36.7
6	36.3	36.4
7	36.7	36.6
8	36.5	36.5
9	36.8	36.8
10	35	34.6
11	36.6	36.8
12	36.4	36.4

2. Heart rate

Heart rates were measured prior to administration of ^{63}Zn-zinc citrate and at 30, 70, and 115 min post-injection. Table S4 shows heart rates. Although small differences in heart rate were measured across time, no dramatic effects on heart rate were observed.

Table S3. Heart rates (BPM)

Subject No.	Pre-administration Value	30 min p.i.	70 min p.i.	115 min p.i.
1	66	71	69	78
2	71	74	77	77
3	58	60	58	57
4	57	52	54	57
5	43	41	44	63
6	52	52	51	56
7	65	63	71	67
8	65	63	62	57
9	78	71	72	73
10	52	51	50	50
11	69	64	65	62
12	73	77	64	71

3. Blood pressures

Blood pressures were measured prior to administration of ^{63}Zn-zinc citrate and at 30, 70, and 115 min post-injection. Table S5 shows blood pressures. Subject 4 showed small changes from pre-injection to 30 min p.i. value, but diastolic pressure dropped from 86 to 61 mm Hg at the 70 min time point. Subject 11 showed a depression in blood pressures after administration of ^{63}Zn-zinc citrate. It is possible that this patient had not yet reached a resting state when the initial measurements were taken.

Table S5. Blood pressures (Systolic/diastolic, mm Hg)

Subject No.	Pre-administration Values	30 min p.i.	70 min p.i.	115 min p.i.
1	140/77	144/74	146/76	148/84
2	155/75	156/75	161/80	154/77
3	161/83	145/88	144/88	143/90
4	136/80	129/86	M	122/78
5	139/65	143/69	134/66	123/65
6	170/73	173/67	156/70	156/78
7	144/61	125/62	139/65	123/60
8	125/67	102/60	117/71	116/67
9	101/52	126/63	112/59	119/66
10	174/78	160/70	168/91	178/80
11	173/86	147/65*	162/65*	140/74
12	141/66	174/76	152/62	131/59

4. Respiratory rate

Respiratory rates were measured prior to administration of ^{63}Zn-zinc citrate and at 30, 70, and 115 min post-injection. Table S6 shows respiratory rates. Respiratory rates were increased greater than 4 min^{-1} in two subjects at the 30 min time point (Subjects 1 and 8).

Table S6. Respiratory rates (min^{-1})

Subject No.	Pre-administration Values	30 min p.i.	70 min p.i.	115 min p.i.
1	16	25	25	25
2	25	20	24	20
3	25	20	16	16
4	18	18	16	17
5	20	20	21	19
6	16	12	12	12
7	20	20	16	20
8	20	25	18	19
9	18	18	18	24
10	15	17	15	16
11	20	20	19	21
12	18	20	19	20