Automated and consistent brain atrophy estimation using the boundary shift integral in longitudinal MRI study

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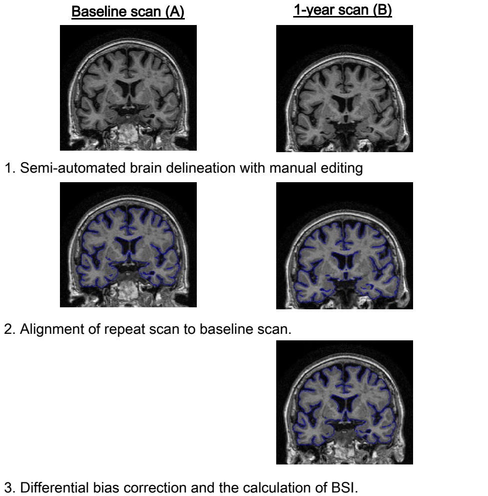
Background

Automated techniques are often used in the measurement of brain atrophy in large imaging studies of Alzheimer's disease (AD). It is however essential that automated measures are as reliable, precise and unbiased as possible. The boundary shift integral (BSI) has been used to measure the brain atrophy in longitudinal MRI studies and clinical trials.

Steps for brain atrophy measurement using the boundary shift integral (BSI)



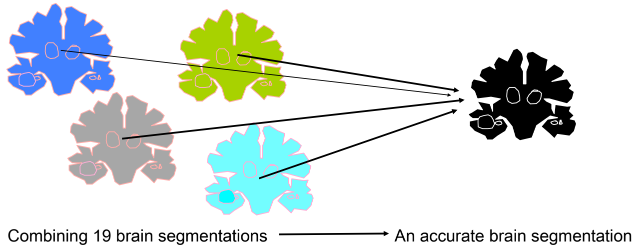
However, the semi-automated brain delineation is time-consuming, and the registration of repeat scans to the baseline scans is asymmetric, which may introduce bias into the measurement:

- BSI (A-to-B) = BSI (B-to-A) ?
- BSI (A-to-B) + BSI (B-to-C) = BSI (A-to-C) ?

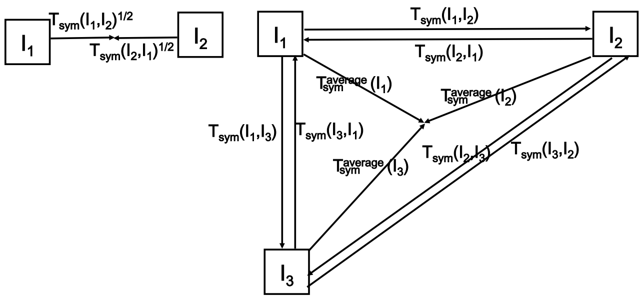
We describe an automated and consistent boundary shift integral (BSI) for multiple time points by combining (1) a multi-atlas propagation and segmentation (MAPS) technique to provide automated brain extraction, and (2) symmetric registration and differential bias correction techniques.

Methods

1. Brain delineation. Brain-MAPS uses non-linear registration of the top 19 best-matched templates from our manually-segmented library of 682 brain scans to generate multiple segmentations, and combines them using the shape based averaging to create an accurate brain segmentation.



2. Consistent image registration. In order to remove the dependency on the order of different time points in the measurement process, we register the baseline and repeat scans using symmetric registration and groupwise registration schemes.



3. Consistent differential bias correction (DBC). The formulation of DBC is extended from two time points into multiple time points by dividing each scan by the geometric mean of the pairwise differential bias.

4. Test of inverse and transitive consistency. We applied our method to the baseline, 12-month and 24-month scans of 439 subjects downloaded from the ADNI website.

	Control (n=138)	MCI (n=211)	AD (n=90)
Mean (SD) age / years	76.1 (4.6)	75.1 (6.9)	75.8 (7.1)
Gender / male (%)	71 (51%)	137 (65%)	50 (56%)
Mean (SD) MMSE / 30	29.2 (0.9)	27.1 (1.7)	23.3 (1.9)

Results and Discussion

1. Test of inverse consistency using two time points. The table shows the mean (SD) of brain volume loss (ml) between the baseline and 24-month scans calculated using asymmetric and symmetric registration schemes. Up to 4.26ml of bias was detected when using an asymmetric registration using linear interpolation. Bias was substantially reduced when using windowed-sinc interpolation.

(a) Linear interpolation

	Control (n=138)	MCI (n=211)	AD (n=90)
L^{asym}_{0-24}	18.14 (8.33)	24.21 (12.79)	32.78 (14.22)
L^{asym}_{24-0}	9.62 (8.62)	17.67 (13.14)	28.24 (13.35)
$(L^{asym}_{0-24}$-$L^{asym}_{24-0})/2$	4.26 (2.71)	3.27 (2.80)	2.27 (2.85)
	[3.80, 4.71], $p < 0.001$	[2.89, 3.65], $p < 0.001$	[1.67, 2.87], $p < 0.001$
L^{sym}_{0-24} and L^{sym}_{24-0}	13.61 (8.10)	20.66 (12.57)	30.09 (13.65)

(b) Sinc interpolation

L^{asym}_{0-24}	13.63 (8.01)	20.67 (12.75)	30.34 (13.77)
L^{asym}_{24-0}	14.25 (8.15)	21.48 (12.77)	31.13 (13.64)
$(L^{asym}_{0-24}$-$L^{asym}_{24-0})/2$	-0.31 (0.58)	-0.40 (0.59)	-0.39 (0.66)
	[-0.41, 0.21], $p < 0.001$	[-0.48, -0.32], $p < 0.001$	[-0.53, -0.25], $p < 0.001$
L^{sym}_{0-24} and L^{sym}_{24-0}	13.93 (8.06)	21.01 (12.74)	30.64 (13.84)

2. Test of transitivity using three time points. The table shows the mean (SD) of brain volume loss (ml) between the baseline and 12-month scans, the 12-month and 24-month scans and the baseline and 24-month scans. Similar bias was detected in asymmetric registration scheme. The SD of the difference showed that the symmetric registration scheme produced more consistent results across three time points.

(a) Linear interpolation.

	Control (n=138)	MCI (n=211)	AD (n=90)
L^{asym}_{0-12}	10.75 (7.54)	14.17 (8.68)	17.94 (8.25)
L^{asym}_{12-24}	11.69 (6.74)	13.27 (9.36)	17.41 (11.07)
L^{asym}_{0-24}	18.14 (8.33)	24.21 (12.79)	32.78 (14.22)
$L^{asym}_{0-12} + L^{asym}_{12-24} - L^{asym}_{0-24}$	4.30 (2.85)	3.23 (2.98)	2.57 (3.14)
	[3.82, 4.78], $p < 0.001$	[2.82, 3.63], $p < 0.001$	[1.91, 3.23], $p < 0.001$
L^{sym}_{0-12}	6.22 (6.73)	10.52 (8.45)	14.85 (7.92)
L^{sym}_{12-24}	7.37 (6.50)	10.14 (8.79)	15.23 (9.79)
L^{sym}_{0-24}	13.61 (8.10)	20.66 (12.57)	30.09 (13.65)
$L^{sym}_{0-12} + L^{sym}_{12-24} - L^{sym}_{0-24}$	-0.02 (0.10)	-0.00 (0.12)	-0.01 (0.14)
	[-0.04, -0.00], $p = 0.04$	[-0.02, 0.01], $p = 0.6$	[-0.04, 0.02], $p = 0.6$

(b) Sinc interpolation.

L^{asym}_{0-12}	5.98 (6.81)	10.56 (8.62)	15.15 (7.97)
L^{asym}_{12-24}	7.34 (6.49)	9.98 (8.97)	15.19 (9.86)
L^{asym}_{0-24}	13.63 (8.01)	20.67 (12.75)	30.34 (13.77)
$L^{asym}_{0-12} + L^{asym}_{12-24} - L^{asym}_{0-24}$	-0.31 (0.86)	-0.13 (1.05)	-0.00 (1.03)
	[-0.45, -0.16], $p < 0.001$	[-0.27, 0.01], $p = 0.07$	[-0.22, 0.21], $p = 1.0$
L^{sym}_{0-12}	6.24 (6.67)	10.75 (8.54)	15.29 (8.01)
L^{sym}_{12-24}	7.68 (6.38)	10.27 (8.88)	15.37 (9.69)
L^{sym}_{0-24}	13.93 (8.06)	21.01 (12.74)	30.64 (13.84)
$L^{sym}_{0-12} + L^{sym}_{12-24} - L^{sym}_{0-24}$	-0.02 (0.13)	0.00 (0.14)	0.02 (0.18)
	[-0.04, 0.01], $p = 0.1$	[-0.02, 0.02], $p = 0.7$	[-0.02, 0.06], $p = 0.3$

Conclusions

Results suggested that the use of windowed-sinc interpolation or a symmetric registration scheme reduced the bias in the BSI processing pipeline. No bias was detected in the two tests when using our proposed symmetric procedures.

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