Alternatives for standard T_1-weighted images in brain atrophy measurements in Multiple Sclerosis using SIENA and SIENAX

V. Neacsu[1], B. Jasperse[2], T. Korteweg[1], D. L. Knol[3], P. Valsasina[4], M. Filippi[4], F. Barkhof[1], M. Rovaris[4], and H. Vrenken[5]

[1]Department of Radiology, VU University Medical Center, Amsterdam, Netherlands, [2]Department of Neurology, VU University Medical Center, Amsterdam, Netherlands, [3]Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, Netherlands, [4]Department of Neurology, Neuroimaging Research Unit, Scientific Institute and University Ospedale San Raffaele, Milan, Italy, [5]Department of Physics and Medical Technology, VU University Medical Center, Amsterdam, Netherlands

Introduction

Neurodegeneration is an important component of multiple sclerosis (MS). In the brain, it can be quantified using MR imaging by measuring brain volumes, and within-patient changes thereof. At several research centers, (large) cohorts of MS patients now exist that have been followed over longer periods of time, using both clinical measures and MR imaging of the brain. In principle, these cohorts would provide the opportunity to investigate the development of brain atrophy through the course of the disease, as well as the relation between brain atrophy on the one hand, and clinical and cognitive decline on the other.

To study brain atrophy in large patient groups, (semi)automated methods are preferred over completely manual methods. A widely used automated method is that developed by the FSL group (http://www.fmrib.ox.ac.uk/fsl), consisting of SIENA for measurement of brain volume change over time, and SIENAX for brain volume measurement at a single timepoint[1]. However, the MR imaging protocols previously applied in the MS patient cohorts did not always include the T_1-weighted images without contrast agent for which SIENA and SIENAX have been validated. In order to determine whether SIENA and SIENAX can be used in the retrospective assessment of these valuable existing patient datasets, it is of great importance to investigate the performance of SIENA and SIENAX using other types of MR images as input.

Methods

MR Imaging: From an ongoing study into the natural history of MS, we randomly selected 46 patients (17 male, mean age at baseline ± SD 39.3 ± 9.4 y; 36 patients with relapsing-remitting MS, seven with primary progressive MS and two with secondary progressive MS) who had undergone an identical MR scan twice, with a time interval between the two scans of approximately 2 years. MR imaging was performed using a Siemens Magnetom Impact scanner operating at 1.0T (Siemens, Erlangen, Germany). At each timepoint, the scanning protocol included a fast spin-echo sequence (TR/TE1/TE2=2700/45/90 ms, number of excitations (NEX)=1) yielding proton density- (PD) and T_2-weighted images, as well as two identical series of spin-echo T_1-weighted images (TR/TE=700/15 ms, NEX=2), of which one was acquired before, and one after administration of a Gd-DTPA contrast agent (Magnevist, Schering, Germany). All scans consisted of 25 oblique axial slices acquired at a slice thickness of 5 mm with a 0.5 mm inter-slice gap, a 260 mm rectangular field-of-view, and 1.0*1.0 mm in-plane pixels. *Analysis:* We created an additional image type, "pseudo-T1-weighted" images, by subtracting each T2-weighted image from the corresponding PD-weighted image[2]. Then, T2-weighted, post-contrast (Gd-enhanced) T1-weighted, pseudo-T1-weighted images, and the "gold standard" pre-contrast T1-weighted images were analyzed. First, automated removal of non-brain tissue was perfected manually. Then, using FSL 3.1.1, we applied SIENAX to all baseline cross-sectional scans to obtain normalized brain volumes (NBV), and SIENA to all scanpairs of the same image type to obtain percentage brain volume change (PBVC) values. We analyzed agreement between the results from the T2, post-contrast T1 and pseudo-T1 weighted images on the one hand, and the pre-contrast T1 weighted images on the other, through variance component analysis. From the variance components, we calculated absolute agreement as the concordance correlation coefficient (CCC) and relative agreement as the intra-class correlation coefficient (ICC)[3].

Results

Table 1 lists mean values for baseline NBV and PBVC. For pre-contrast T1 weighted images, PBVC values were compatible with previously reported atrophy rates in MS[4]. Absolute values differed between input image types, but rank orders of subjects were comparable, as was confirmed by the variance component analysis (Table 2). Absolute agreement (CCC) with pre-contrast T1 results was high for post-contrast T1 and pseudo-T1, but lower for T2 weighted images. Relative agreement (ICC) with pre-contrast T1 was relatively good for all three types.

Table 1. Mean (SD) values of normalized brain volume (NBV) and percentage brain volume change (PBVC)

Image type	Baseline NBV [mL]	PBVC [%] over two-year interval
pre-contrast T1	1473.7 (75.1)	-2.05 (1.66)
post-contrast T1	1515.7 (85.5)	-2.09 (1.83)
T2	1315.9 (55.8)	-0.94 (1.10)
Pseudo-T1	1498.0 (64.3)	-1.52 (1.46)

Table 2. Absolute (CCC) and relative (ICC) agreement with T1 results as calculated from variance component analysis

Sequences compared	Baseline NBV		PBVC	
	CCC	ICC	CCC	ICC
pre-contrast T1 vs post-contrast T1	0.76	0.86	0.77	0.77
pre-contrast T1 vs T2	0.19	0.72	0.45	0.58
pre-contrast T1 vs pseudo T1	0.65	0.68	0.79	0.83

Discussion

Our results suggest that other image types may be used to replace standard T1-weighted images if these are not consistently available. If consistently available, post-contrast T1 weighted images should be used as this gives best agreement with pre-contrast T1. In our data-set, pseudo-T1 weighted images performed well, but this is likely to change when different echo times are used in the PD/T2 sequence. Absolute NBV and PBVC values obtained from T2-weighted images were markedly different from the other values and from previously reported values[4], most likely due to misclassification of MS lesions.

Because pre-contrast T1 weighted images do not necessarily best reflect the "true" values, relative agreement may be more important than absolute agreement.

References

1. S.M. Smith et al., NeuroImage 2002; 17: 479-489. **2.** S.J. Hickman et al., Multiple Sclerosis 2002; 8: 433-435. **3.** J.L. Carrasco and L. Jover, Biometrics 2003; 59: 849-858. **4.** V.M. Anderson et al., J Magn Reson Imaging 2006; 23: 605-618.