Objective
To quantify the impact of the differences among Magnetic Resonance Imaging (MRI)-based hippocampal segmentation protocols on volume estimates of Alzheimer’s disease (AD)-related atrophy, in order to support evidence-based decisions for an internationally harmonized protocol.

Background
A harmonized procedure is required, since quantitative MRI should help diagnosis and tracking of AD. A survey of segmentation protocols allowed the identification of anatomical sources of heterogeneity in volume estimates.

Methods
We operationalized landmark differences among protocols into segmentation units (SUs), through extraction of landmarks, semantic harmonization, and convergence of similar variants, in order to achieve a limited number of well defined portions of the hippocampus, that are differentially segmented in different existing protocols (Fig. 1). A power analysis was carried out on a preliminary sample of 20 ADNI subjects (4 by each degree of severity of hippocampal atrophy at the visual scale by Scheltens et al., 1992), to define the sample size allowing reliable computation. Then, we manually traced each SU within the right and left hippocampi of a sample of 77 Alzheimer’s Disease Neuroimaging Initiative (ADNI) participants, which included Mild Cognitive Impairment (MCI) patients who subsequently converted to AD and AD patients, all with abnormal Cerebrospinal Fluid (CSF) Aβ levels, and controls (CTRL), with normal CSF Aβ levels (Tab. 1).

Results
We defined four SUs: Minimum Hippocampus (MinH), Alveus/Fimbria, Tail, and Subiculum. The power analysis indicated a required sample size for the quantification of SUs impact on AD-related volume differences of n=77 (31 CTRL, 23 MCI, 23 AD). All Sus had good ICC values (Tab 2). The average volume difference between patients and controls was 538 mm³, with Minimum Hippocampus (red SU in Figures) contributing to over 66% of this difference, Tail (blue SUs in Figures) over 20%, Alveus/Fimbria (yellow SU in Figures) 6%, Subiculum (green SUs in Figures) over 5%. The SU volume differences between patients and controls were significant for all SUs except the Subiculum (Tab 3).