Assessing Brain Volumes Using MorphoBox Prototype

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Introduction

Brain morphometry from routine structural MR images is useful to detect abnormal regional brain volumes that may be indicative of a disease [1]. For instance, hippocampus atrophy is known to be associated with memory impairment commonly experienced by individuals with dementia [2]. When combined with other volumetric measurements such as frontal lobe atrophy and white matter lesions, it may help diagnose a particular form of dementia (Alzheimer's disease, fronto-temporal or vascular dementia among others).

The MorphoBox algorithm[1] was developed by the Advanced Clinical Imaging Technology group in Lausanne in close collaboration with the University Hospital's Radiology Department. As an integral part of a Siemens prototype sequence, it automatically estimates a number of brain volumes from a single T1-weighted MR image acquired with the MPRAGE sequence, and compares these volumes with normative ranges adjusted for head size, age, and sex. The results are presented to the user in the form of a DICOM report, where brain structures that are found to be abnormally small (or abnormally large, e.g. for ventricular structures) are indicated with an asterisk.

Owing to its full incorporation into the MRI system, MorphoBox runs during image reconstruction. Results can be read with the *syngo* standard viewers or sent to the PACS system in order to seamlessly integrate into the radiological workflow. As of early 2016, more than 10,000 patients had benefited from this prototype worldwide.

[1] WIP, the product is currently under development and is not for sale in the US and in other countries. Its future availability cannot be ensured.

Methodology

Image processing

MorphoBox implements a processing pipeline consisting of several steps, as outlined in Figure 1. After the incoming MR scan has been checked for protocol compliance with a widely accepted standard for MPRAGE sequences [3], it is

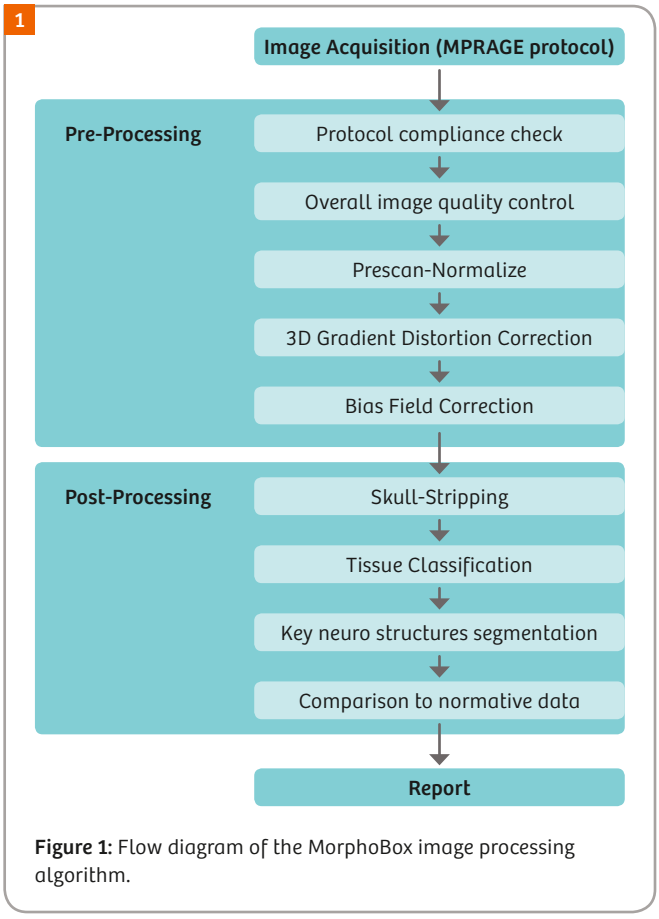
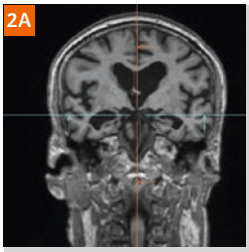
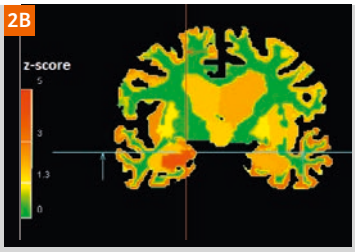


Figure 1: Flow diagram of the MorphoBox image processing algorithm.





2C

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Lobar GM/structure	Absolute [ml]	Normalized^ [%]	Normative Range^^ [%]
Frontal lobe			
GM left	67.4	* 4.93	[5.27 - 6.47]
GM right	64.2	* 4.69	[5.20 - 6.35]
Parietal lobe			
GM left	49.2	3.59	[3.48 - 4.46]
GM right	47.7	3.49	[3.41 - 4.31]
Occipital lobe			
GM left	15.4	* 1.12	[1.21 - 1.80]
GM right	15.9	* 1.16	[1.37 - 1.98]
Temporal lobe			
GM left	39.4	* 2.88	[3.32 - 4.00]
GM right	42.4	* 3.09	[3.52 - 4.30]
Cingulate gyrus			
GM left	6.3	0.46	[0.44 - 0.59]
GM right	6.5	0.47	[0.43 - 0.56]
Insula			
Left	3.8	* 0.28	[0.30 - 0.40]
Right	4.1	* 0.30	[0.34 - 0.44]

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Figure 2: Screenshots of MorphoBox results on the *syngo* viewer for an Alzeimer's Disease patient. **(2A)** an MRI coronal slice, **(2B)** the corresponding deviation map, and **(2C)** three pages from the report.

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Patient Demographics	80 yrs	Male	
Image quality	high	0.72	[0 - 0.82]
Segmentation Quality	high	0.82	[0.7 - 1]

Tissue	Absolute [ml]	Normalized^ [%]	Normative Range^^ [%]
TIV	1368.4		
GM	474.8	* 34.7	[37.6 - 43.9]
cortical GM	349.5	* 25.5	[28.3 - 33.6]
WM	426.3	31.2	[26.0 - 31.4]
WMab	0.3	0.0	
CSF	467.3	34.2	[26.7 - 35.3]

^ Percentage of TIV (Total Intracranial Volume)
^^ 10th and 90th percentiles of healthy age-matched population
* Out-of-range volumes

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Structure	Absolute [ml]	Normalized^ [%]	Normative Range^^ [%]
Hippocampus	4.3	* 0.31	[0.38 - 0.48]
Hippocampus left	2.3	* 0.17	[0.19 - 0.24]
Hippocampus right	2.0	* 0.14	[0.19 - 0.24]
Ventricles	107.4	* 7.85	[1.94 - 5.38]
lateral ventricle left	55.3	* 4.04	[0.81 - 2.56]
lateral ventricle right	44.1	* 3.22	[0.79 - 2.41]
3rd ventricle	4.6	* 0.34	[0.14 - 0.29]
4th ventricle	3.5	0.25	[0.13 - 0.26]

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submitted to different image quality checks based on both signal-to-noise ratio and contrast-to-noise ratio assessments as well as motion-/aliasing-related artifact detection [4]. Subsequently, the images are corrected for gradient distortion [5] and radio-frequency field inhomogeneity [6, 7]. A tissue classification algorithm [8] is applied to the corrected image, the results of which are combined with a deformed anatomical template to segment various brain structures in the image [9], including: lobe-wise gray and white matter, insula, cingulate, hippocampi, central nuclei, subcortical white matter, corpus callosum, ventricular system, cerebellum, and different brainstem structures. Volumes are computed for each segmented structure.

Normative range analysis

A cohort of 437 subjects with balanced sex and age ranging from 19 to 91 years was used to construct normative ranges for each brain volume measure output by MorphoBox. Specifically, the volumes produced by MorphoBox on the normative cohort were divided by the corresponding total intra-cranial volume, also estimated by MorphoBox, and regressed against age and sex using a log-linear model [9]. The normative ranges were then defined depending on age and sex by the regression prediction intervals corresponding, respectively, to the 10th and 90th percentiles of the TIV-normalized volume distribution, as seen in Figures 2–7 for various brain structures.

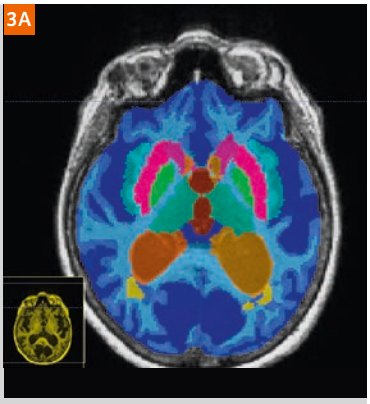
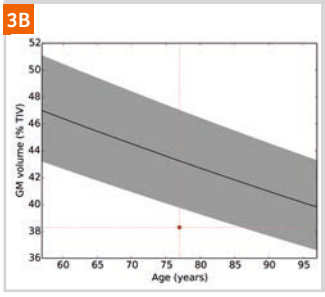
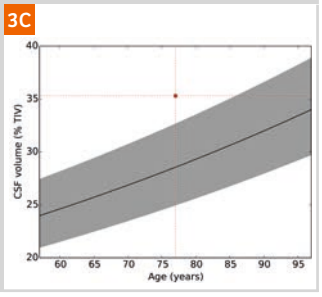


Figure 3: (3A) Axial slice of a 77-year-old woman with chronic vascular atrophy. Structures of interest segmented by MorphoBox and overlaid in color are the insula, putamen, pallidum, caudate nucleus, thalamus, lateral and third ventricles. In yellow are detected white matter lesions. **(3B–C)** Display of normative ranges for women as a function of age, respectively for the total normalized gray matter volume **(3B)** and the total normalized cerebrospinal fluid volume **(3C)**. The red dots indicate the volumes assessed by MorphoBox.





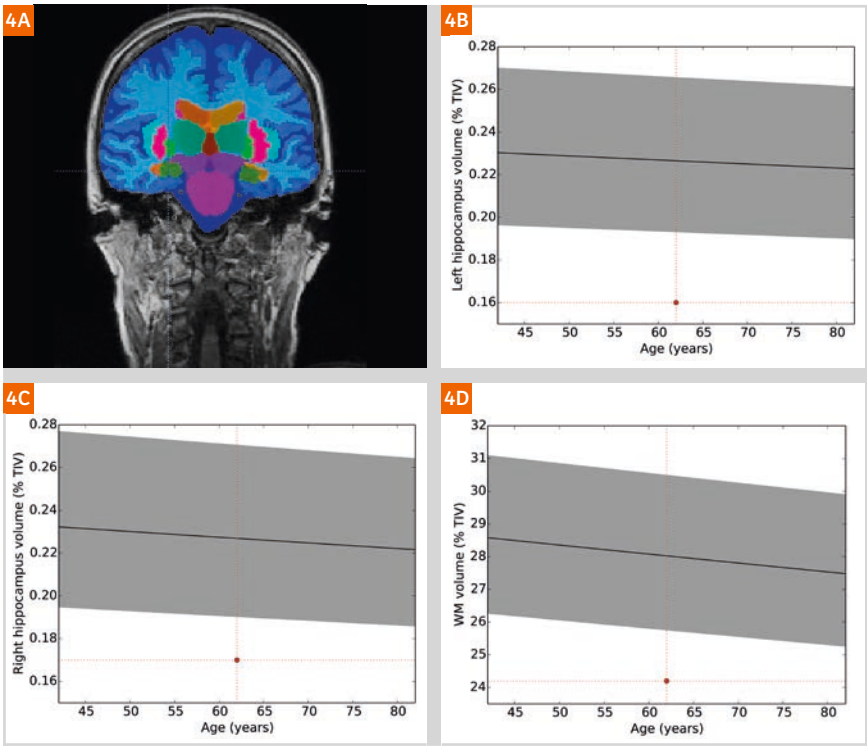


Figure 4: (4A) Coronal view of a 62-year-old woman with suspected Alzheimer's disease. The segmented hippocampi are shown in green. Other colored structures are the insula, putamen, pallidum, caudate nucleus, thalamus, lateral and third ventricles, mesencephalon, and pons. **(4B–D)** Display of normative ranges of TIV-normalized volumes for women as a function of age, **(4B)** for the left hippocampus, **(4C)** the right hippocampus and **(4D)** the total white matter, respectively.

Creation of report and deviation map
Finally, a report in form of a DICOM image is created containing patient identification, the result of the performed image quality assessment as well as a list of evaluated volumes, divided by hemispheres. Beside the absolute volumes, the TIV-normalized measures are reported and displayed in relation to the normative ranges. Detected deviations from the normative ranges are indicated with an asterisk (see Fig. 2). In addition, MorphoBox produces an image called "deviation map" displaying abnormal regions in hot colors (orange to red depending on the severity of deviation from normality). Since this information is stored as a DICOM image, it can be exported to the PACS like any other image and is available in other viewing software along with the imaging data.

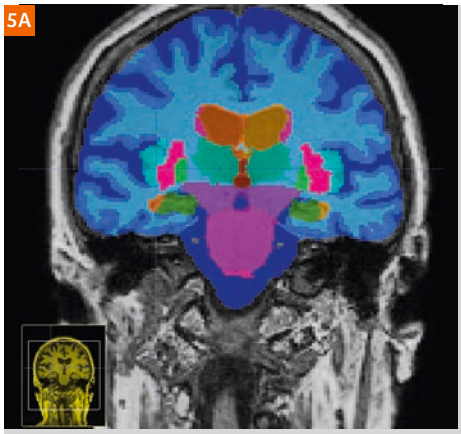
Clinical examples

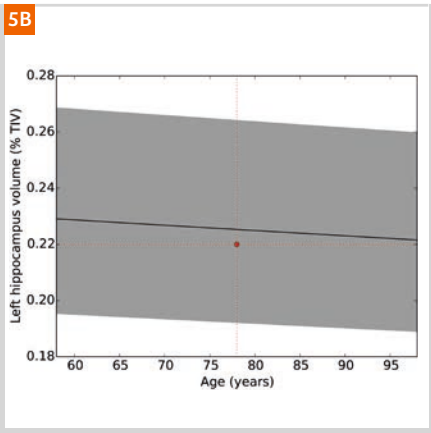
In the following examples, all brain MR slices are displayed in radiological convention (with the left hemisphere shown on the right of the image).

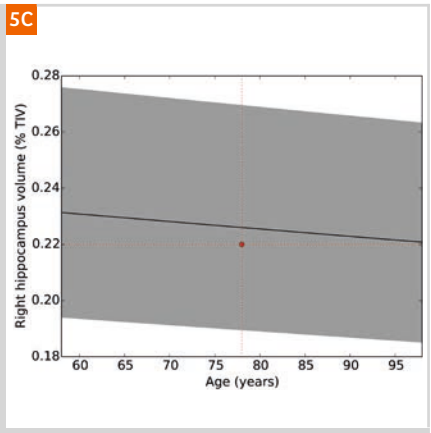
Results of applying MorphoBox on a 77-year-old female patient with chronic vascular atrophy are depicted in Figure 3A. Both global gray matter atrophy and global cerebrospinal fluid expansion, which are clearly visible in the MR scan, are appropriately detected by MorphoBox, as reflected in the normative range plots in Figure 3B. Other smaller structures are indicated as out-of-range in the MorphoBox report, including the ventricles, the frontal, temporal, parietal lobes, and the insula, in both hemispheres. Figure 4 shows the case of a 62-year-old woman with suspected Alzheimer's disease. Abnormal hippocampi are detected in both hemispheres, suggesting hippocampal atrophy. The total white matter volume is also flagged as abnormally low, which is common in early-age-of-onset Alzheimer's disease [10]. This case is in contrast with that of a 78-year-old woman with suspected early mild cognitive impairment, where the hippocampi like most brain structures are found normal, although insula atrophy is detected mainly on the left, see Figure 5.

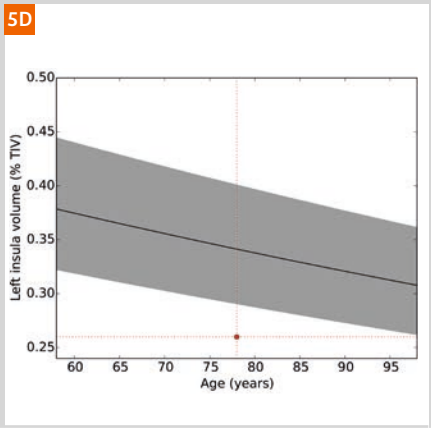
As another example, the case of an 88-year-old man with probable cognitive disorder is shown in Figure 6A, for which cortical atrophy can be suspected from visual inspection of the MR scan. Quantitative analysis using MorphoBox (Fig. 6B) reveals that both frontal lobes are small, yet within the bounds of normality, and that both temporal lobes are clearly out-of-range, although the right hippocampus is normal and the left hippocampus is only slightly below the 10th percentile.

MorphoBox can also provide clinically relevant quantitative information on young patients, such as the 20-year-old woman with brain stem disorder shown in Figure 7A. The pons and medulla oblongata are found abnormal by MorphoBox, while the mesencephalon is borderline within normal range, as illustrated in Figure 7B.









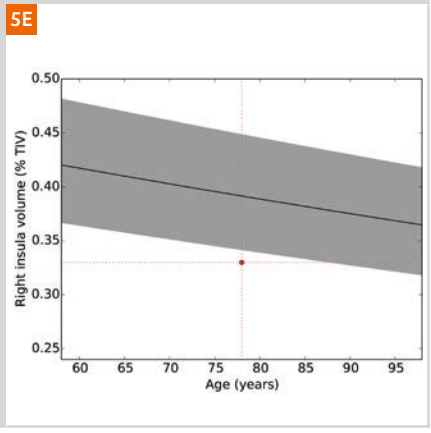
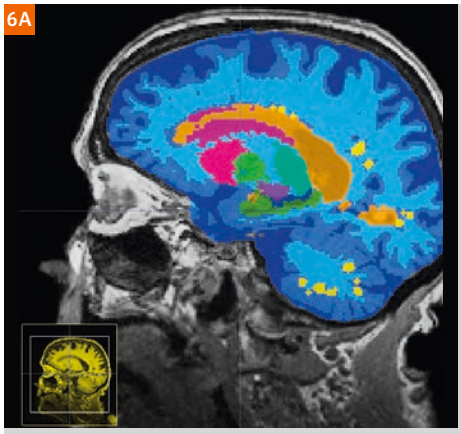
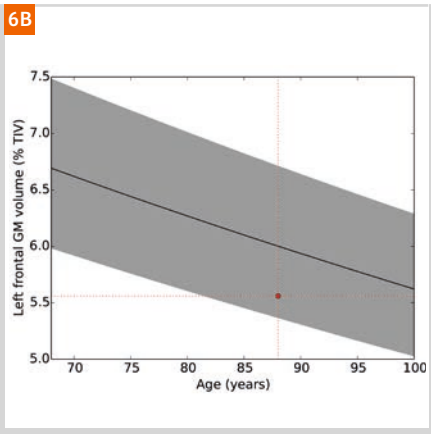
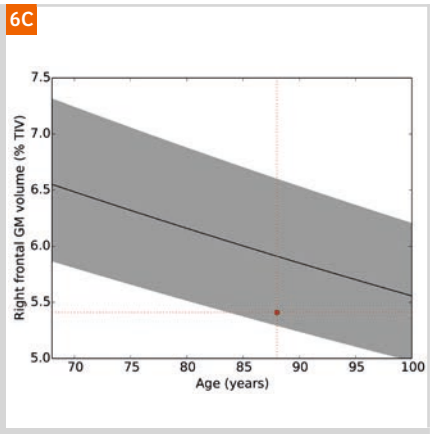
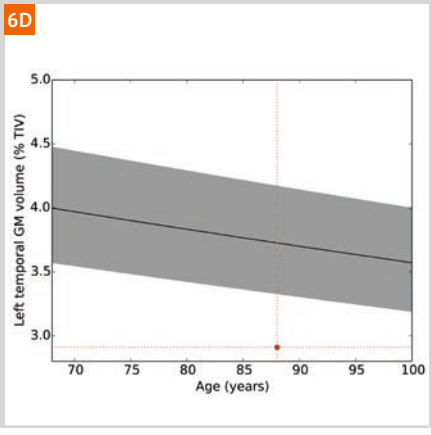


Figure 5: (5A) Coronal view of a 78-year-old woman with suspected MCI. The hippocampi (highlighted in green) are normal contrary to the left and right insulae (in light blue). Other structures shown in color (the central nuclei, ventricles, and brain stem) are normal. **(5B–E)** Display of normative ranges of TIV-normalized volumes for women as a function of age, **(5B)** for the left hippocampus, **(5C)** the right hippocampus, **(5D)** the left insula, and **(5E)** the right insula, respectively.









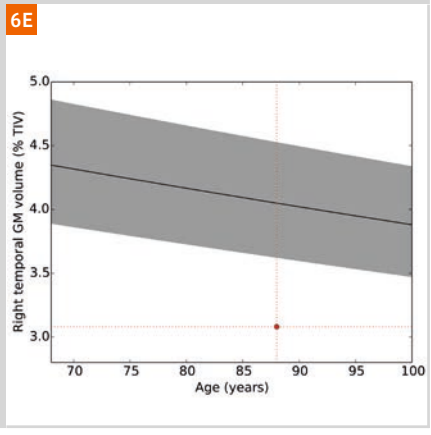


Figure 6: (6A) Sagittal view of an 88-year-old man with suspected cognitive disorder (left hemisphere). **(6B–E)** Display of normative ranges of TIV-normalized volumes for men as a function of age, **(6B)** for the left frontal lobe gray matter, **(6C)** the right frontal lobe gray matter, **(6D)** the left temporal lobe gray matter, and **(6E)** the right temporal lobe gray matter, respectively.

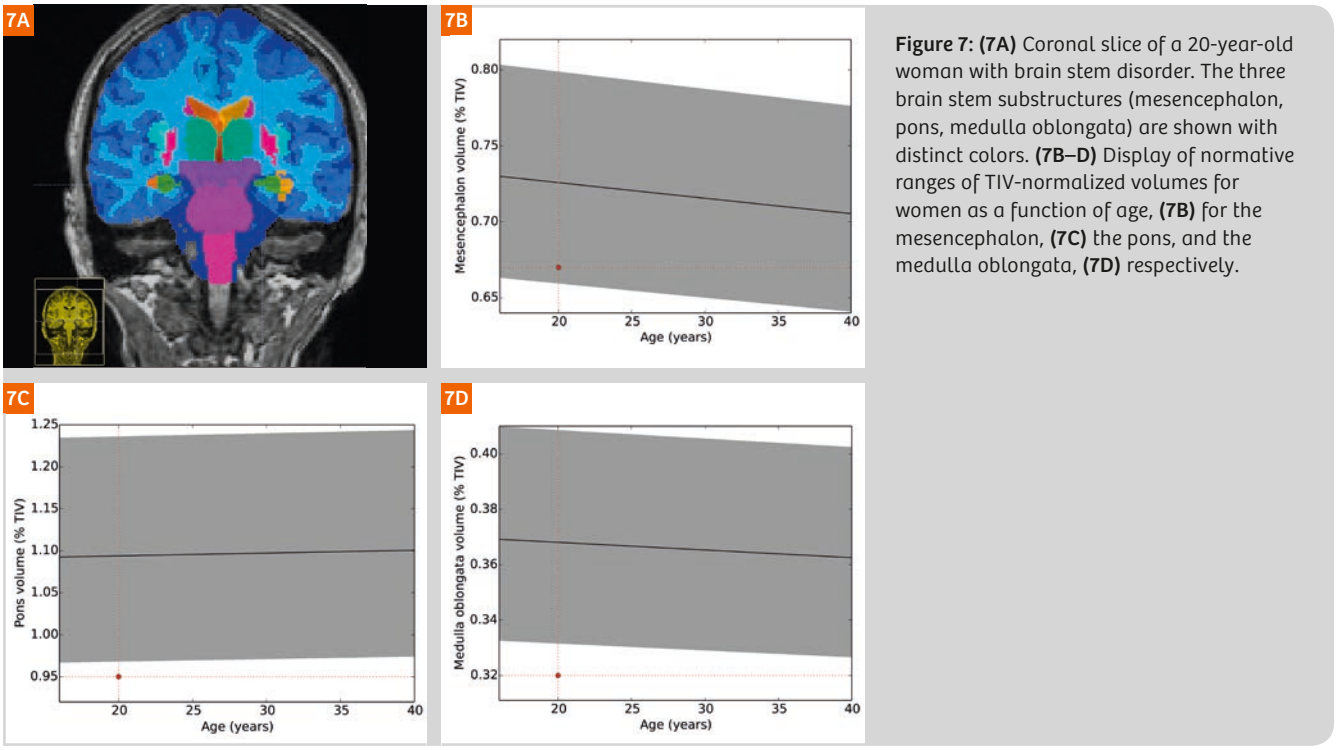


Figure 7: (7A) Coronal slice of a 20-year-old woman with brain stem disorder. The three brain stem substructures (mesencephalon, pons, medulla oblongata) are shown with distinct colors. **(7B–D)** Display of normative ranges of TIV-normalized volumes for women as a function of age, **(7B)** for the mesencephalon, **(7C)** the pons, and the medulla oblongata, **(7D)** respectively.

Conclusion

MorphoBox is a user-friendly brain volumetry prototype software compatible with clinical workflow constraints and intended for routine use. It provides quantitative information that can help radiological reading for patients with suspected neurodegeneration, as briefly exemplified in this article, and it is fully integrated in a clinical workflow. Our current objective is to further develop MorphoBox as a decision support tool for differential diagnosis of brain diseases.

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