Barriers to brain volume measurement in the real world

M. Battaglini

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1240

Disclosure

Nothing to declare

Definition of measurement for a MR image.

Review of the most important barriers to the use of atrophy measurement in the real world: list and possible solutions

Normative rates of atrophy: a lack for the clinical use of brain volume measurement in the real world

Definition of measurement for a MR image.

Review of the most important barriers to the use of atrophy measurement in the real world: list and possible solutions

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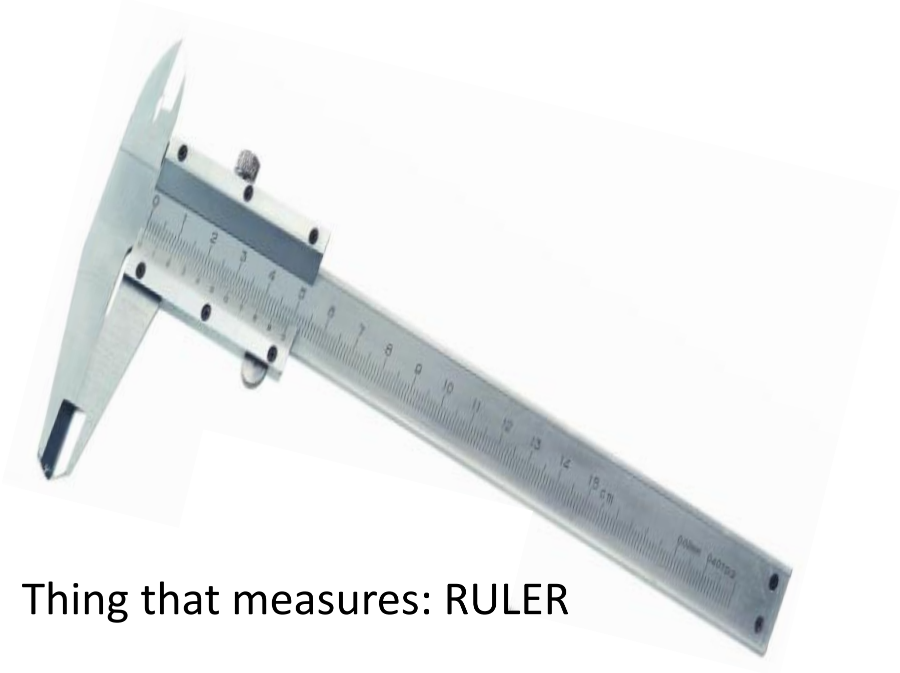
Quantification of a measure

Thing to be measured: TABLE



Thing that measures: RULER

Quantification of a measure

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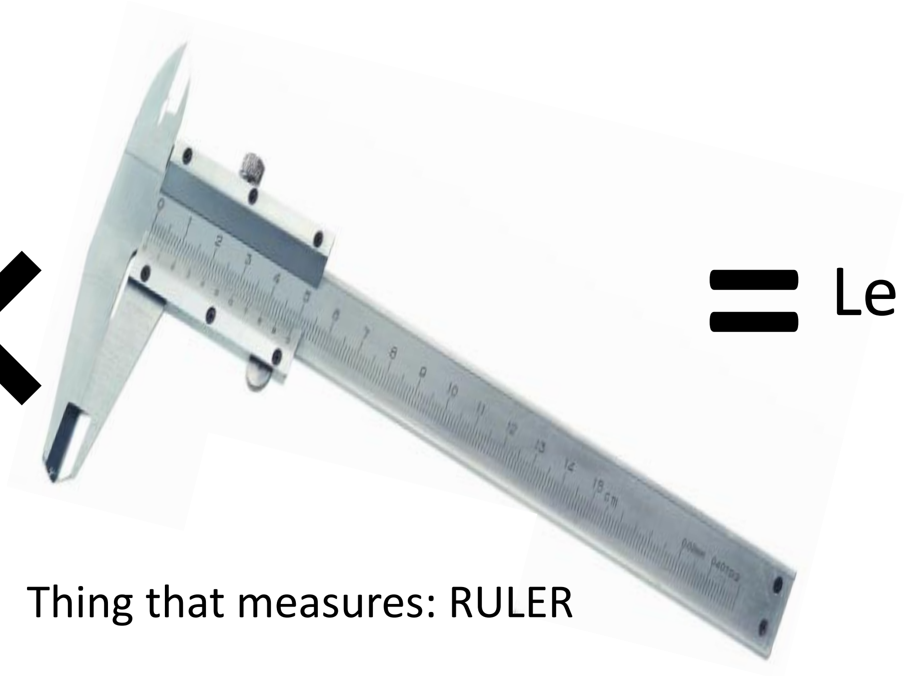

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= Length of the table

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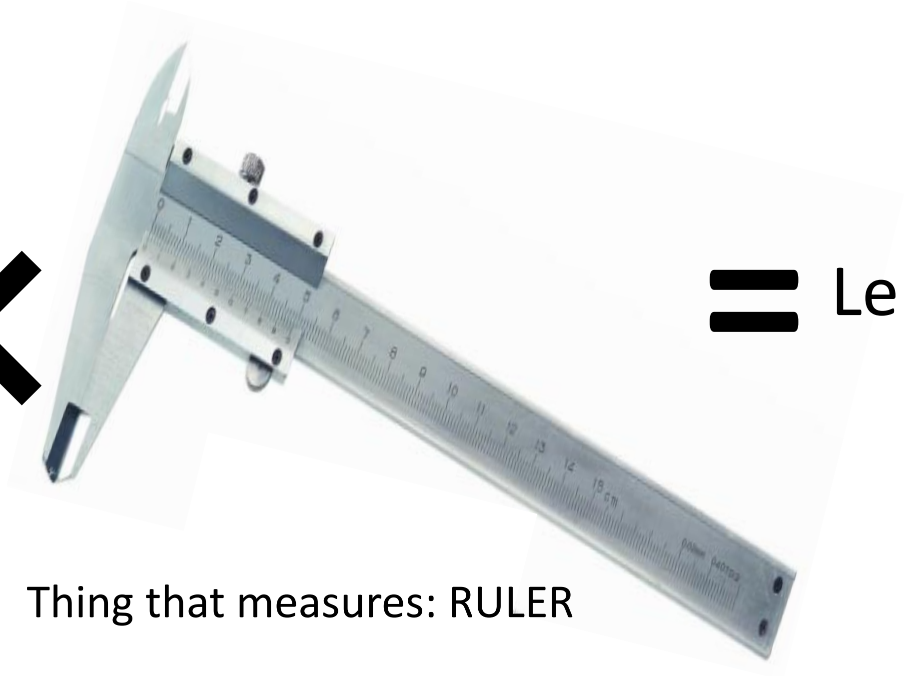

Thing that measures: RULER

= Length of the table

Changes in length if measured in summer (bigger) or in winter (smaller)

The length will have the error of the scale.
Example: If the scale is 10 cm long, you cannot say if the table is 204 or 196 cm but only 200 cm ± 5 cm

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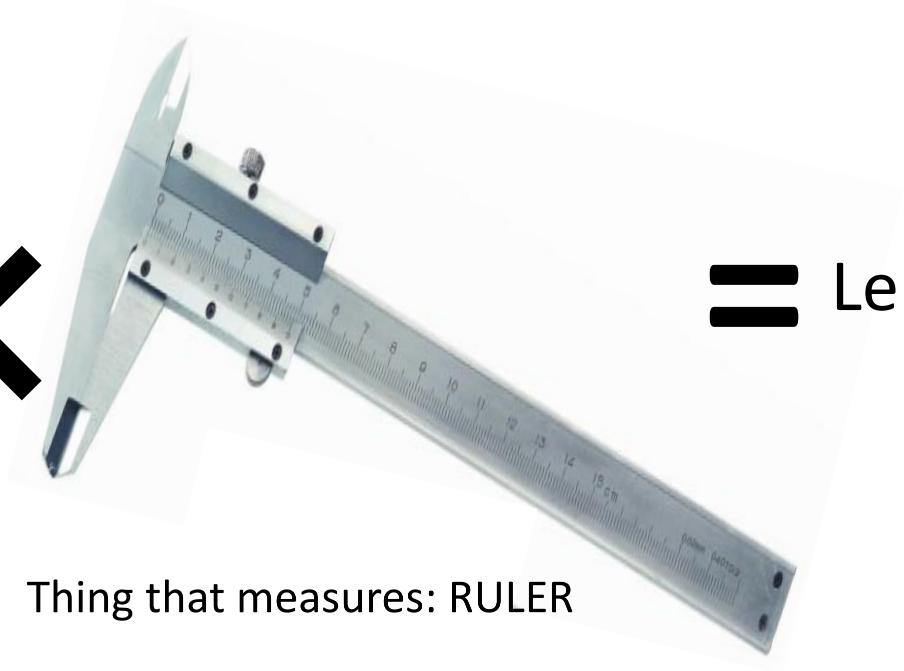

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Example: If the scale is 10 cm long, you cannot say if the table is 204 or 196 cm but only 200 cm ± 5 cm

Measure of the length of table= True length + “Physiological” variation + error of the Ruler

Quantification of a measure for MR images

×

is it correct?

Quantification of a measure for MR images

×

is it correct? NO

Quantification of a measure for MR images

Quantification of a measure for MR images

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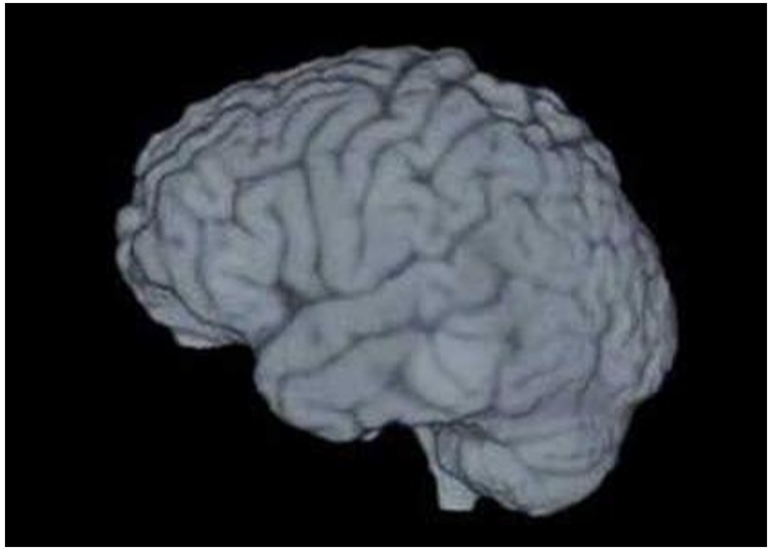

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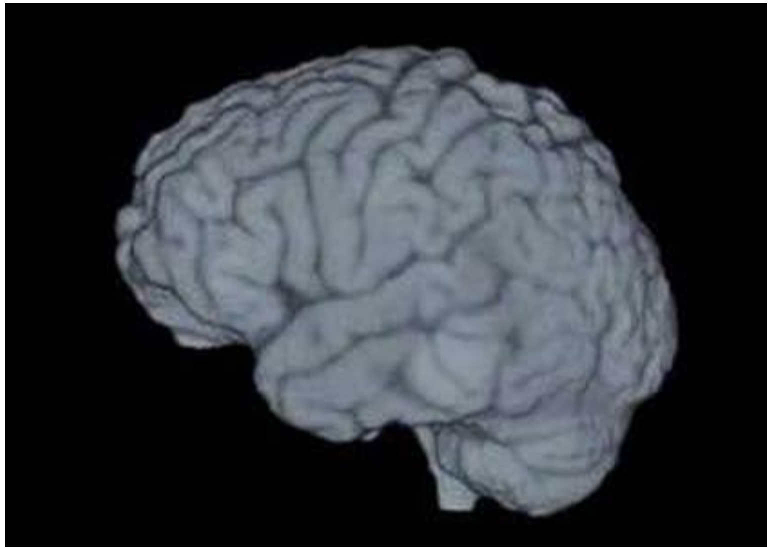

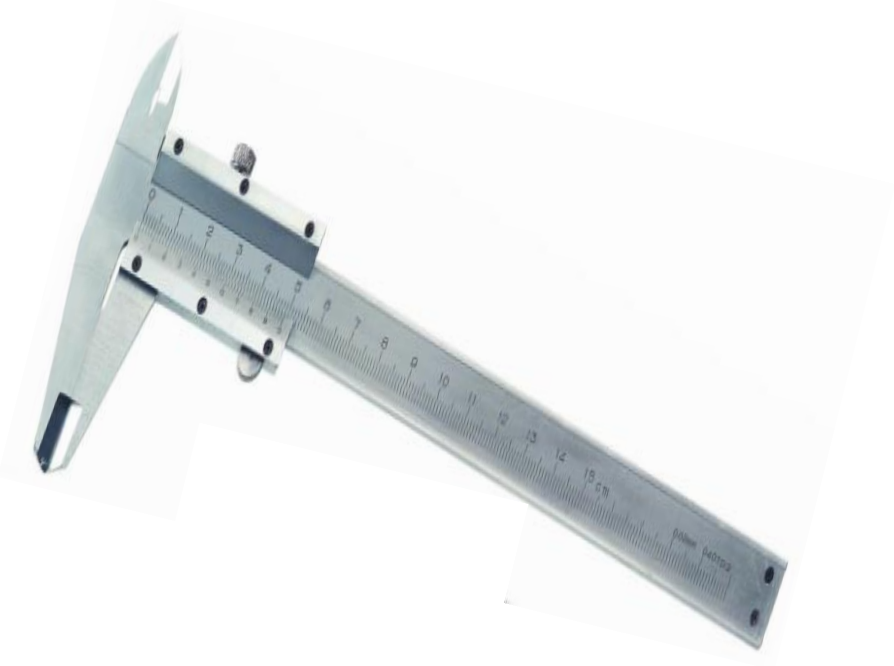

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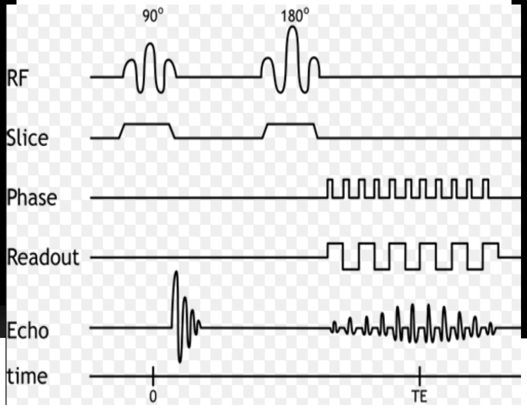

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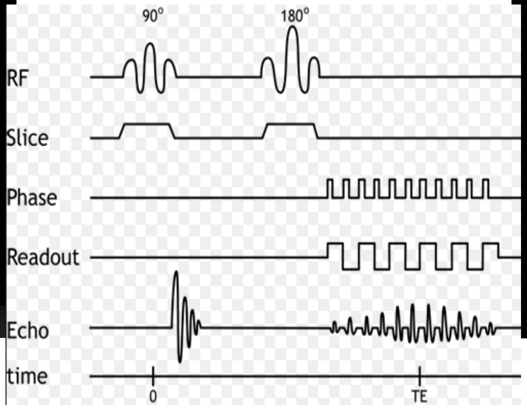
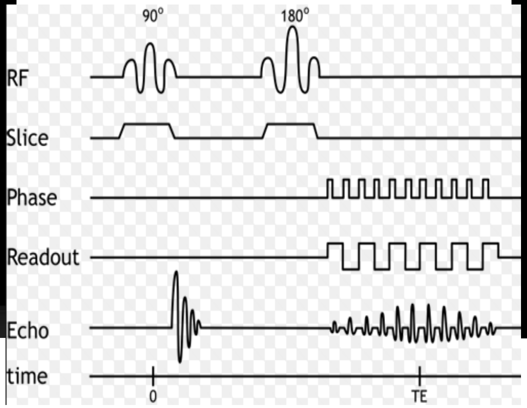


- Different field strength of the magnet

Quantification of a measure for MR images



- Different field strength of the magnet
- Different hardware architecture of the magnet

Quantification of a measure for MR images

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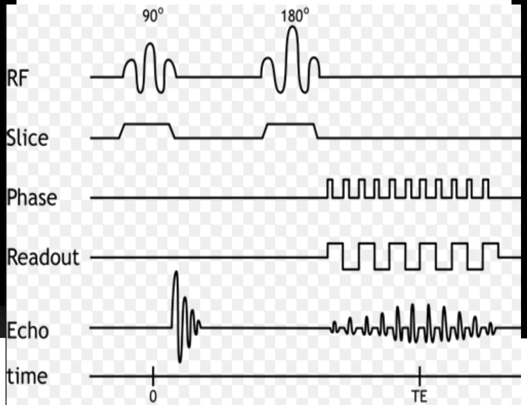

- Different field strength of the magnet
- Different hardware architecture of the magnet
- Different sequences

Quantification of a measure for MR images

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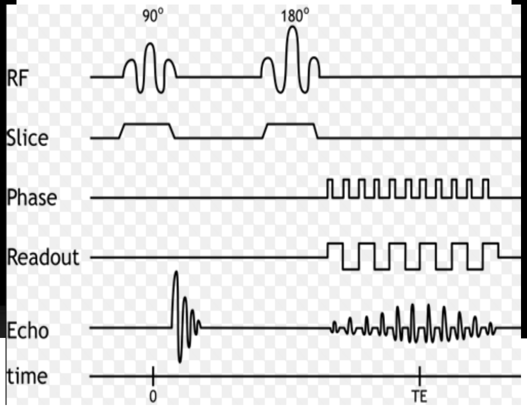

- Different field strength of the magnet
- Different hardware architecture of the magnet

- Different sequences
- Within the same sequence, different acquisition parameters

Quantification of a measure for MR images

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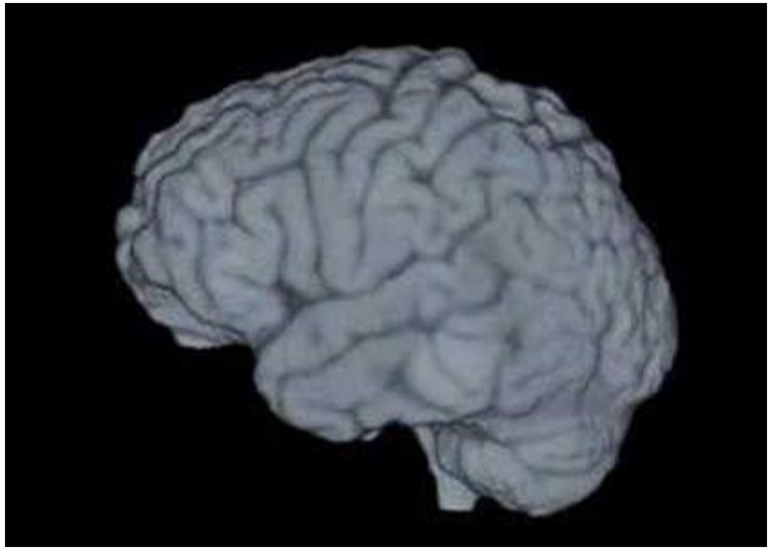

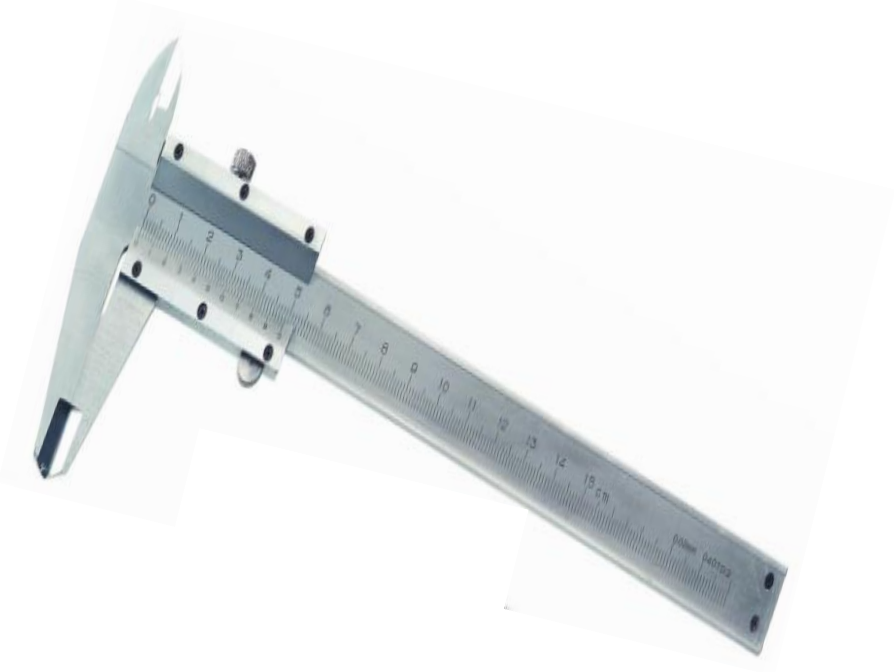

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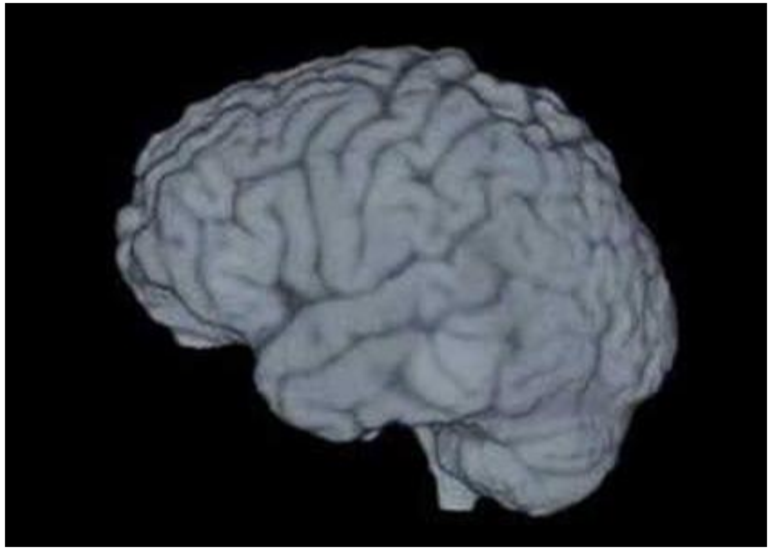

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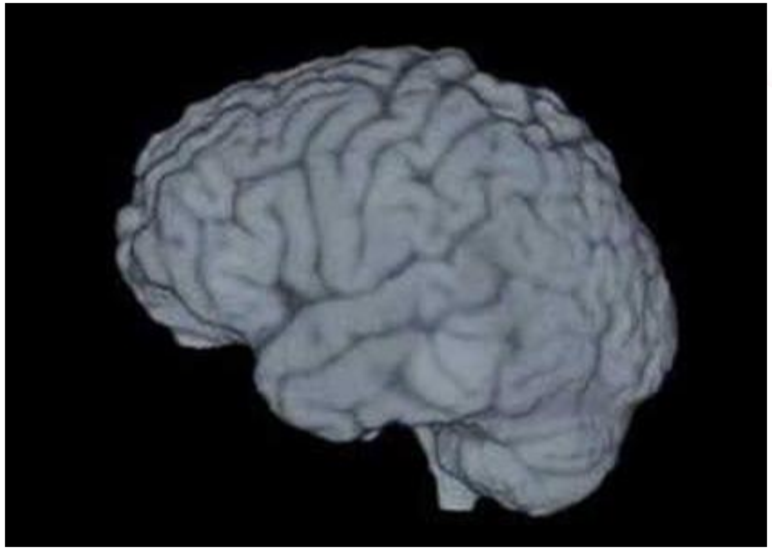

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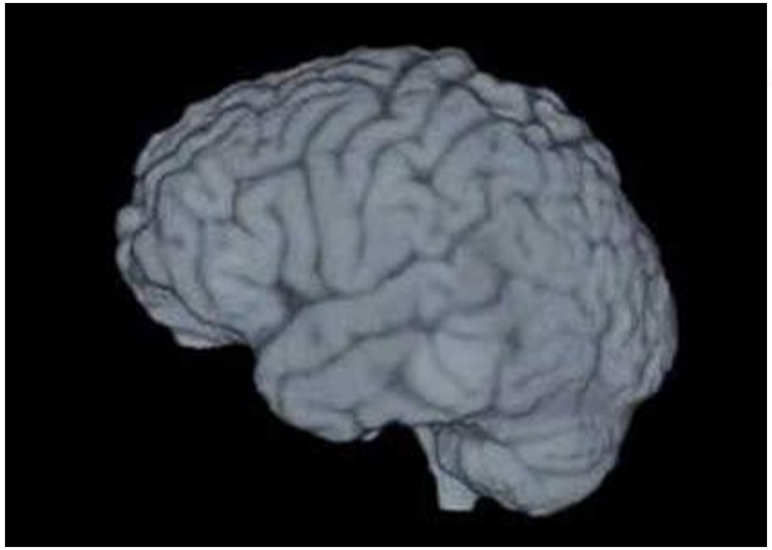
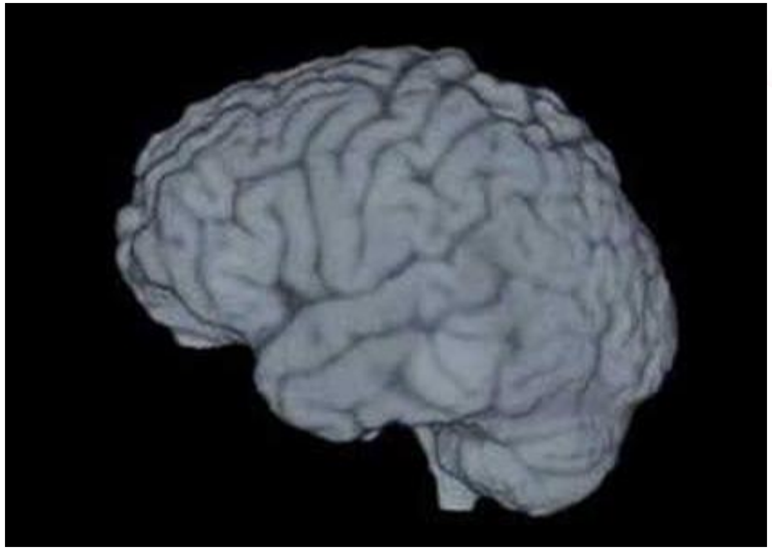


- There is not a gold standard algorithm to analyse 3D images

Quantification of a measure for MR images

 ~ 

- There is not a gold standard algorithm to analyse 3D images
- Different methods provide different measures for the same analysed image.

Definition of measurement for a MR image.

Key point: the measurement is not “objective” but depends on:

- the MR setting
- the software used to analyse the images

Definition of measurement for a MR image.

Review of the most important barriers to the use of atrophy measurement in the real world: list and possible solutions

Normative rates of atrophy: a lack for the clinical use of brain volume measurement in the real world

Barriers to the use of brain volume in real world

J Neurol (2013) 260:2458–2471
DOI 10.1007/s00415-012-6762-5

REVIEW

Recommendations to improve imaging and analysis of brain lesion load and atrophy in longitudinal studies of multiple sclerosis

H. Vrenken · M. Jenkinson · M. A. Horsfield · M. Battaglini · R. A. van Schijndel · E. Rostrup · J. J. G. Geurts · E. Fisher · A. Zijdenbos · J. Ashburner · D. H. Miller · M. Filippi · F. Fazekas · M. Rovaris · A. Rovira · F. Barkhof · N. de Stefano · MAGNIMS Study Group

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N. de Stefano · MAGNIMS Study Group**

Brain Atrophy in Multiple Sclerosis

Clinical Relevance and Technical Aspects

Jaume Sastre-Garriga, MD, PhD[a,*], Deborah Pareto, PhD[b,c],
Àlex Rovira, MD[b,c]

KEYWORDS

- Multiple sclerosis • MR imaging • Brain atrophy • Gray matter • Biological confounding factors
- Disability

Barriers to the use of brain volume in real world

Change of Volume= True atrophy + Physiological variation + Software error

Barriers to the use of brain volume in real world

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+

Variations due to the Image Acquisition

Barriers to the use of brain volume in real world

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Change of Volume= True atrophy + $\boldsymbol{\Sigma}$

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Change of Volume= True atrophy + $\boldsymbol{\Sigma}$

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Variations due to the Image Acquisition

+

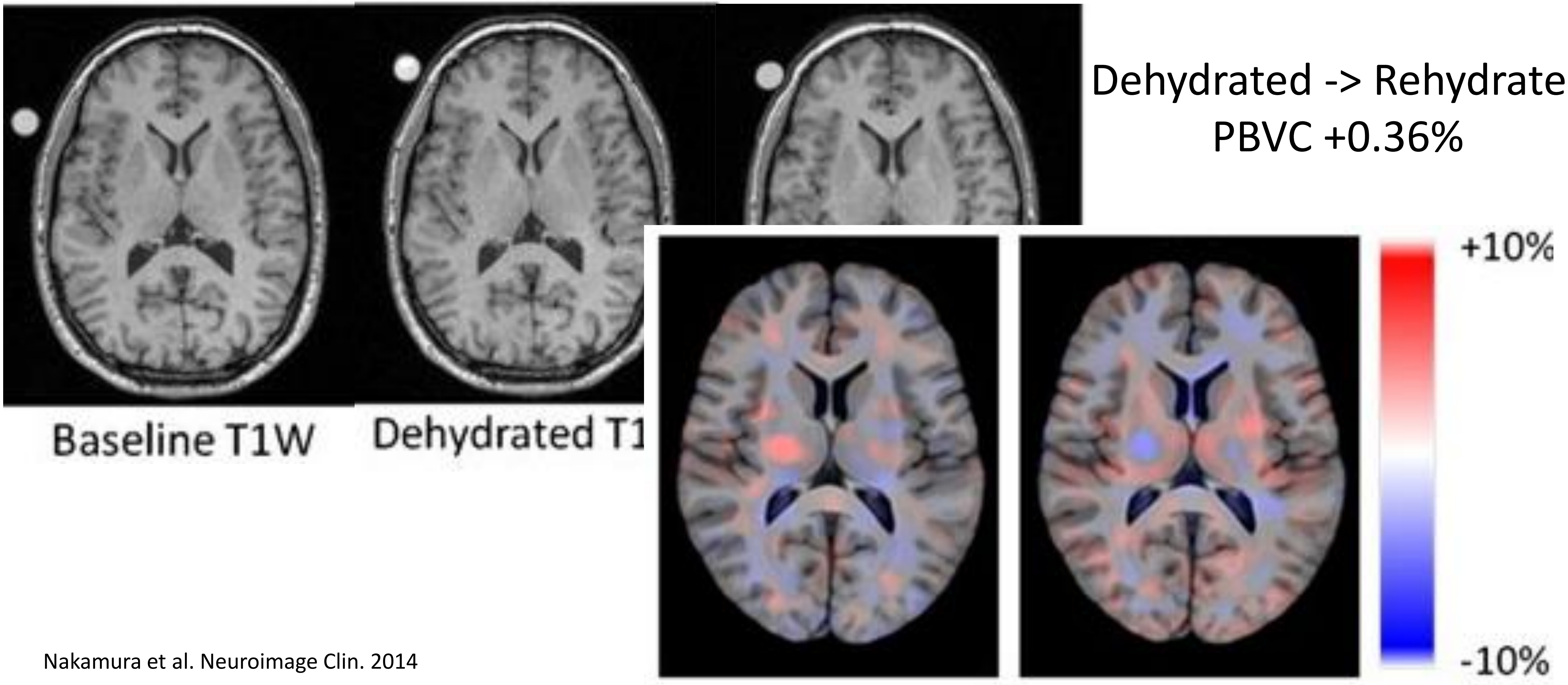
Errors due to the Image Acquisition

Physiological variation.

Category	Topic
Physiological factors [11, 57, 64, 66, 70, 74, 75]	Age
	Body mass index
	Diurnal variation
	Genotype (ApoE expression)
	Hydration state
	Menstrual cycle

De Stefano et al CNS Drugs 2017

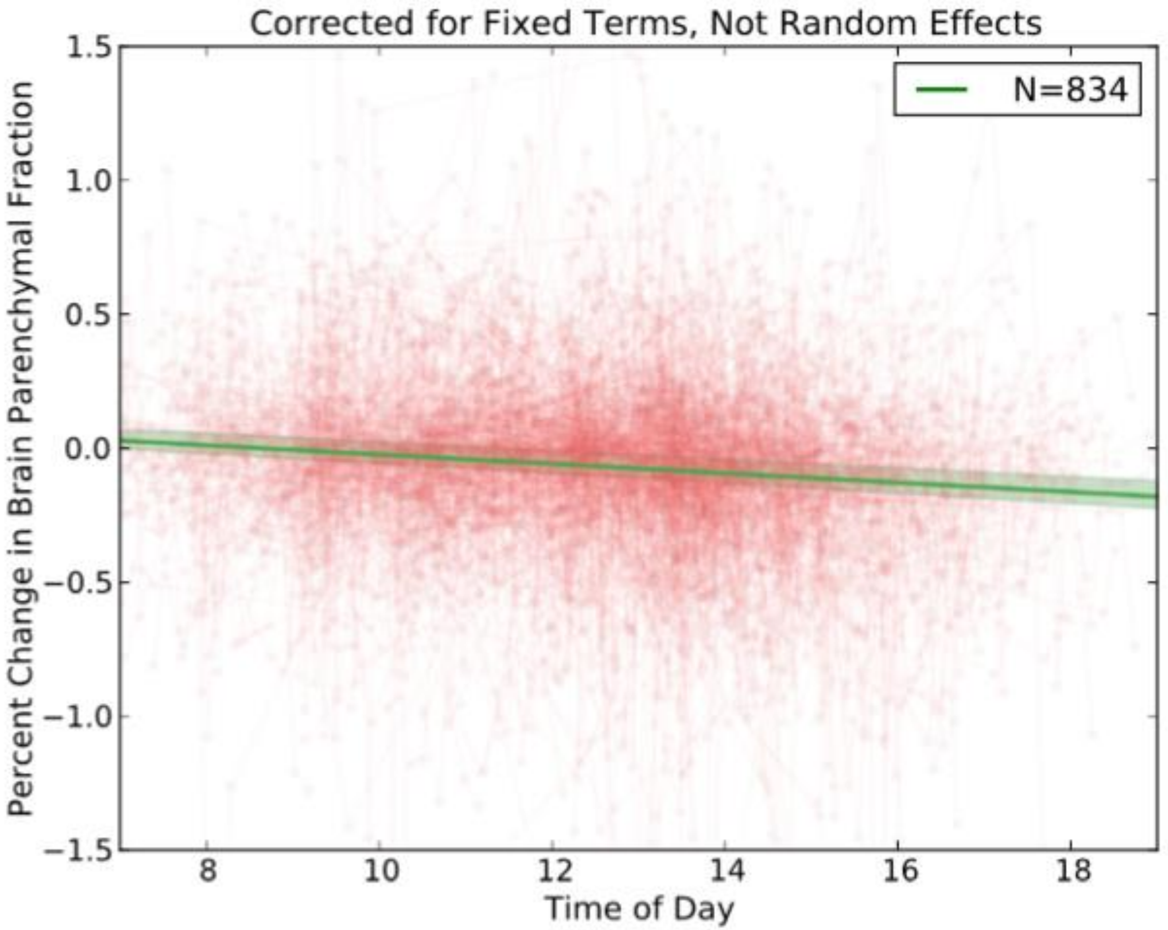
Physiological variation. Example 1 dehydration



Dehydrated -> Rehydrated
PBVC +0.36%

Nakamura et al. Neuroimage Clin. 2014

Physiological variation. Example 2 circadian rhythms



On 834 AD, the brain parenchyma fraction (BPF) decreased of -0.221% per 12 hours.

Nakamura et al. Neuroimage 2015

Review of the most important barriers to the use of atrophy measurement in the real world: list and possible solutions

- ❖ Physiological variation SOLUTION: to be included in the experimental design

Barriers to the use of brain volume in real world

$$\text{Change of Volume} = \text{True atrophy} + \Sigma$$

Change of Volume= True atrophy + Physiological variation + Software error

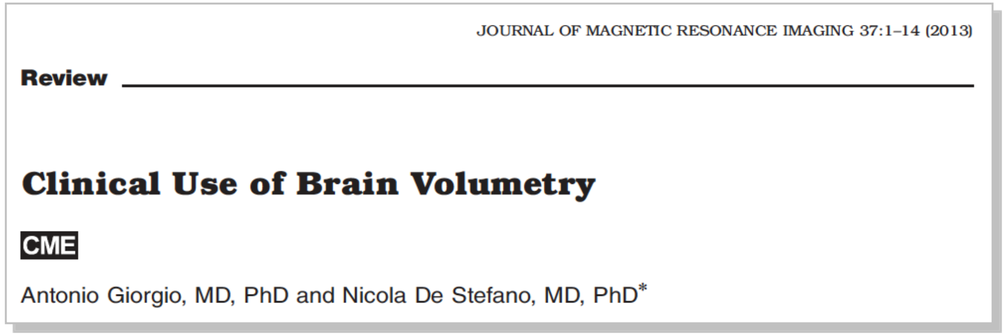
+

Variations due to the Acquisition

+

Errors due to the Image Acquisition

Error of Software


JOURNAL OF MAGNETIC RESONANCE IMAGING 37:1–14 (2013)

Review

Clinical Use of Brain Volumetry

CME

Antonio Giorgio, MD, PhD and Nicola De Stefano, MD, PhD*

Which software?

MRI-based methods for measuring brain volumes

	Features
Manual methods	
Bicaudate ratio	The minimum intercaudate distance divided by brain width along same line
Brain width	Distance between two points on the cortical surface, measured at the same level as lateral ventricle width on axial slides
Corpus callosum area	Measured on midsagital T1-weighted image
Training of the hippocampus, amygdata, entothinal cortex, paraippocampus, cholinergic nuclei of the basal forebrain	Several anatomical protocols available for delineation of these structures
M/P	Ratio of midbrain-to-pons areas measured on midsagital T1-weighted image
MCP width	Distance between the superior and inferior borders of the MCP, as delimited by the peripeduncular CSF spaces of the pontocerebellar cisterns
MRPI	Value obtained by multiplying the pons to midbrain areas by the MCP-to-SCP widths
Third and lateral ventricle width	Determined along a plane corresponding to the anteroposterior midpoint of the ventricle on axial slices
Semi automated methods	
Anatomatic	Segmentation algorithm for ventricles
Cavalieri method	Stereological method where brain volumes are obtained by the sum of the points counted on all the sections of the structure of interest multiplied by the sectioning intervals
Fuzzy connectedness	An operator identifies points of GM, WM and CSF, each of which is then automatically detected as a fuzzy connected object
ILAB4	Segmentation of thin-slice T1-weighted images based on a modifies watershed transform and an automatic histogram analysis
Losseff method	A large central volume of the brain is defined based on anatomical criteria
MIDAS	Thresholding technique for measurement of ventricle volumes
SABRE	Use of individualized Talairach brain maps for brain regions in each hemisphere
Seed growing technique	Intensity threshold-based algorithm propagating from a seed positioned in any part of the brain parenchyma
Automated methods	
Alfano method	Multispectral methods based on the relaxometric features of brain tissues
BBSI	Measurement of total volume difference between serial scans
BICCR	Digital morphometry for intracerial cavity classification and Bayesian tissue classification into GM, WM, lesions and CSF
BPF	Ratio of the volume of parenchymal brain tissue to the total volume within the outer surface of the brain
BICVR	Ratio of brain volume to intracranial volume
Central cerebral volume	Volume of four to seven (depending on the thickness) axial slices from the central portion of the brain
Chupin methos	Use of simultaneous region deformation driver by probabilistic and anatomical priors for hippocampus and amygdala segmentation
CIVET algorithm	Series of algorithms for corticomeatric analysis of MRI images including tissue classification and segmentation
Cortical pattern matching	Surface-based cortical modelling and 3D GM mapping
DBM	Variant of VBM in which brain volumes are compared on the basis of the deformation fields required to register them onto a common template
FIRST	Subcortical brain segmentation using Bayesian shape and appearance models
Freesurfer	Calculation of the cortical thickness after inflation of the folded cortical surface
HAMMER	High-dimensional warping of brain images producing gyral and subcortical brain structures and tissue density maps
Histogram segmentation	Brain extraction and segmentation technique optimised for 2D T1-weighted images
IBA	Percent ratio of the supratentorial brain parenchyma to supratentorial parenchyma and CSF
Localinfo	Entropy-based segmentation algorithm for subcortical brain structures
Segmentation propagation	Deformation field applied to the segmentation of the baseline brain and then automatically propagated through serial images to provide an estimate of volume change
SIENAx	Global and tissue-type volumes normalised for subject head size
SIENA, SIENAr	Percent brain volume change (PBVC) assessed by estimating the local shift in brain edges across the brain and its voxelwise extension for regional assessment
SPM-based segmentation	Prior spatial information are used to classify voxels according to their location and signal intensity features as GM, Wm and CSF
STAND score	Score based in the voxelwise degree and pattern of atrophy of a scan in comparison to the scans of a large database of well characterised AD and cognitively normal subjects
Support vector machines	Multidimensional classification of cerebral region (e.g. hippocampus) shape features
TDS	Brain tissues are identified by projecting anatomically labelled images of a template brain onto images of the patients brain
3DVIEWNIX	A data-, machine- and application-independent software system for the visualization and analysis of multidimensional images
VBM	Characterising regional volume and tissue 'concentration' differences throughout global brain
WBR	Ratio of the difference between intradural and CSF volumes to intradural volumes

Error of Software

1) CROSS-SECTIONAL ANALYSIS → SEGMENTATION METHOD

2) LONGITUDINAL ANALYSIS → SEGMENTATION METHOD

2) LONGITUDINAL ANALYSIS → REGISTRATION METHOD

Error of Software

1) CROSS-SECTIONAL ANALYSIS → SEGMENTATION METHOD

Error ~ 0.5-1%

2) LONGITUDINAL ANALYSIS → SEGMENTATION METHOD

2) LONGITUDINAL ANALYSIS → REGISTRATION METHOD

Error of Software

1) CROSS-SECTIONAL ANALYSIS → SEGMENTATION METHOD

2) LONGITUDINAL ANALYSIS → SEGMENTATION METHOD

2) LONGITUDINAL ANALYSIS → REGISTRATION METHOD   Error ~ 0.1-0.5%

Error of Software

Each software can be optimised depending on the studied population

Error of Software

Each software can be optimised depending on the the studied population

NeuroImage 61 (2012) 1484–1494

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Optimizing parameter choice for FSL-Brain Extraction Tool (BET) on 3D T1 images in multiple sclerosis

V. Popescu [a,*], M. Battaglini [b], W.S. Hoogstrate [a], S.C.J. Verfaillie [a], I.C. Sluimer [a], R.A. van Schijndel [a], B.W. van Dijk [c], K.S. Cover [c], D.L. Knol [d], M. Jenkinson [e], F. Barkhof [a], N. de Stefano [b], H. Vrenken [a,c] on behalf of the MAGNIMS Study Group[1]

[a] Department of Radiology, VU University Medical Center, Amsterdam, The Netherlands
[b] Department of Neurological and Behavioral Sciences, University of Siena, Siena, Italy
[c] Department of Physics and Medical Technology, VU University Medical Center, Amsterdam, The Netherlands
[d] Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands
[e] FMRIB Centre, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK

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Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

The SIENA/FSL whole brain atrophy algorithm is no more reproducible at 3 T than 1.5 T for Alzheimer's disease

Keith S. Cover [a,*], Ronald A. van Schijndel [b], Veronica Popescu [b], Bob W. van Dijk [a],
Alberto Redolfi [c], Dirk L. Knol [d], Giovanni B. Frisoni [c], Frederik Barkhof [b,e],
Hugo Vrenken [a,b,e], neuGRID[1], the Alzheimer's Disease Neuroimaging Initiative[2]

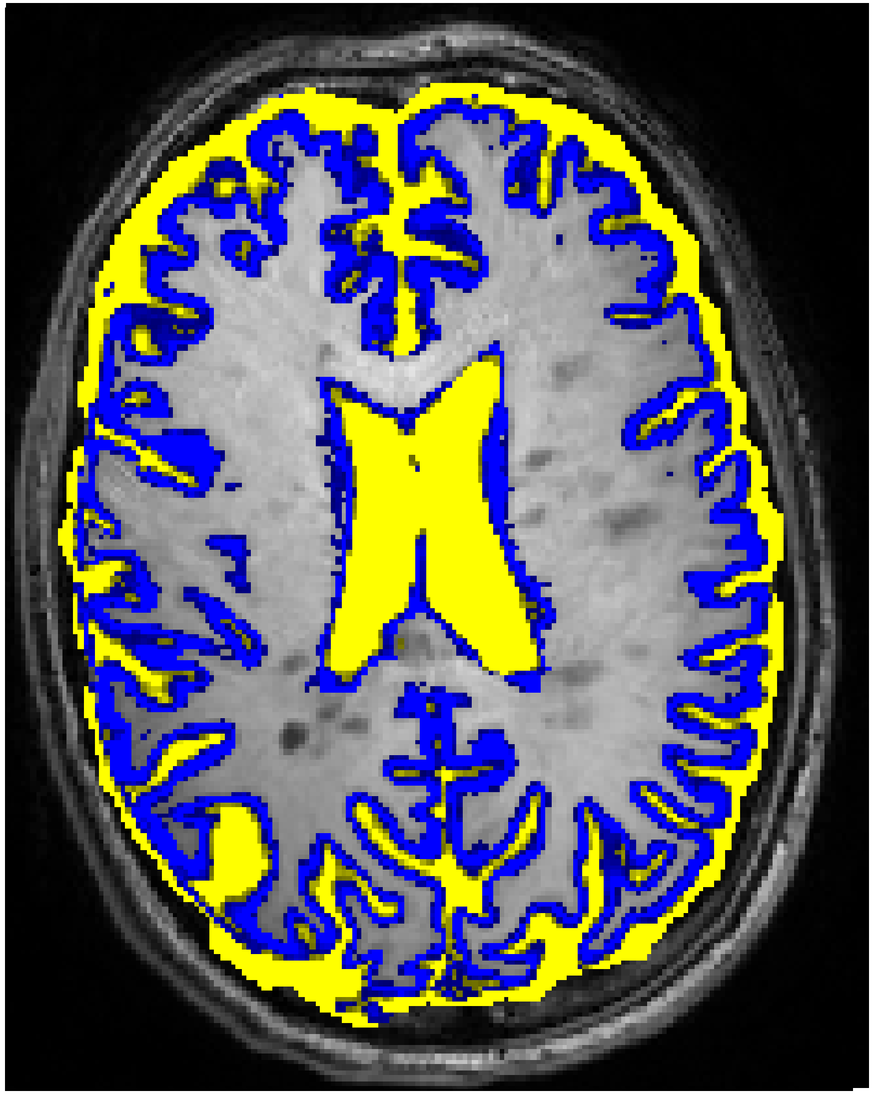
[a] Department of Physics and Medical Technology, VU University medical center, Amsterdam, The Netherlands
[b] Department of Radiology, VU University medical center, Amsterdam, The Netherlands
[c] Laboratory of Epidemiology & Neuroimaging, IRCCS San Giovanni di Dio Fatebenefratelli, Via Pilastroni 4, 25125 Brescia, Italy
[d] Department of Epidemiology and Biostatistics, VU University medical center, Amsterdam, The Netherlands
[e] MS Center Amsterdam and Alzheimer Center, VU University medical center, Amsterdam, The Netherlands

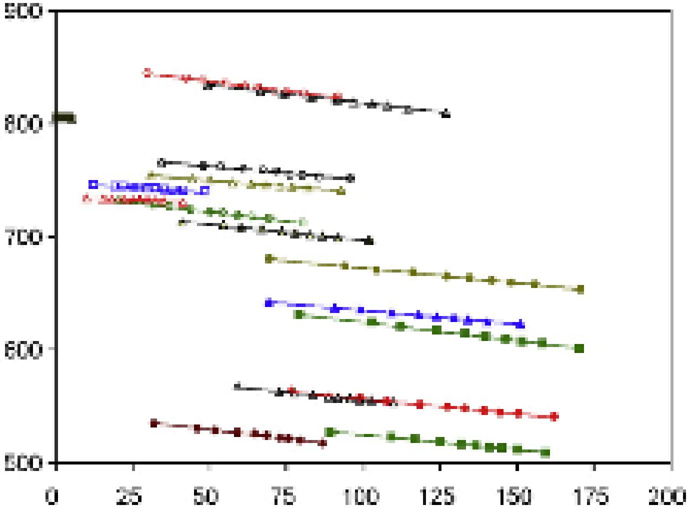
Error of Software

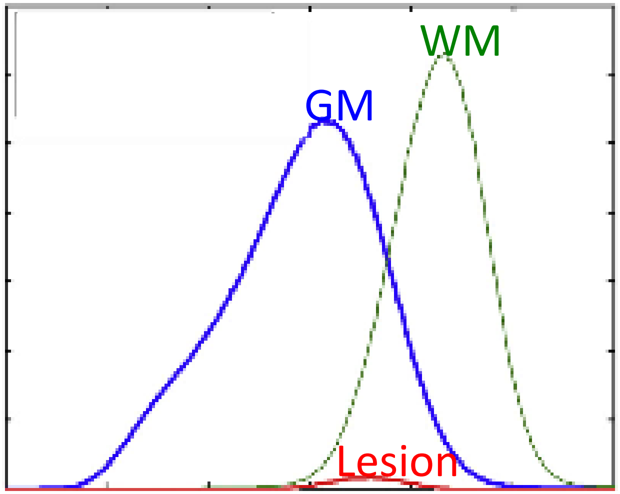
Each software can be optimised depending on the studied population

Each software can be improved in order to address the peculiar MRI features of patients

Error of Software: MRI of MS patients

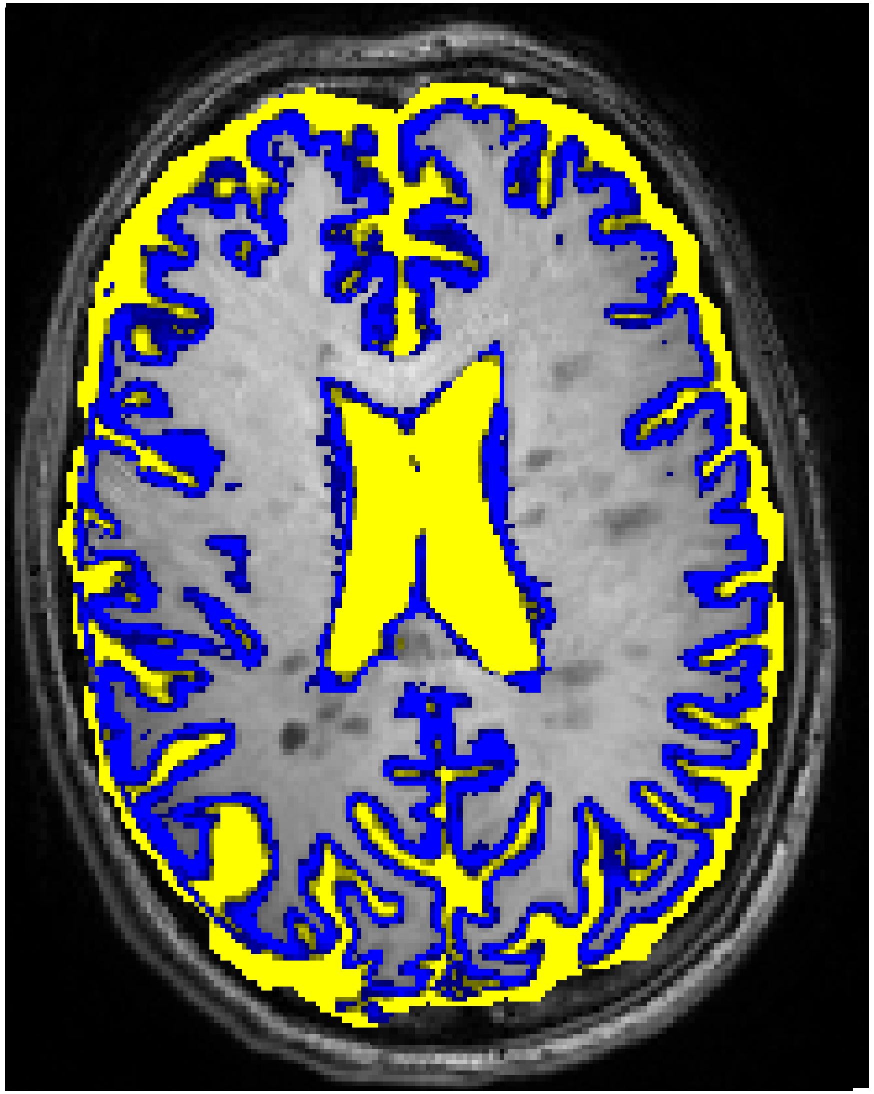


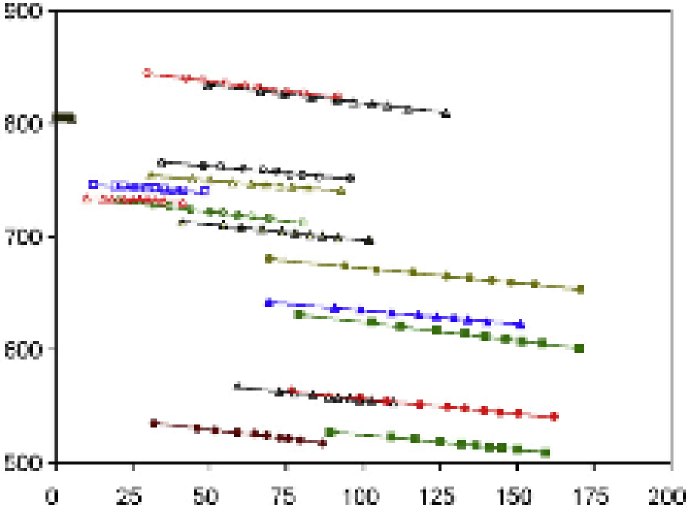


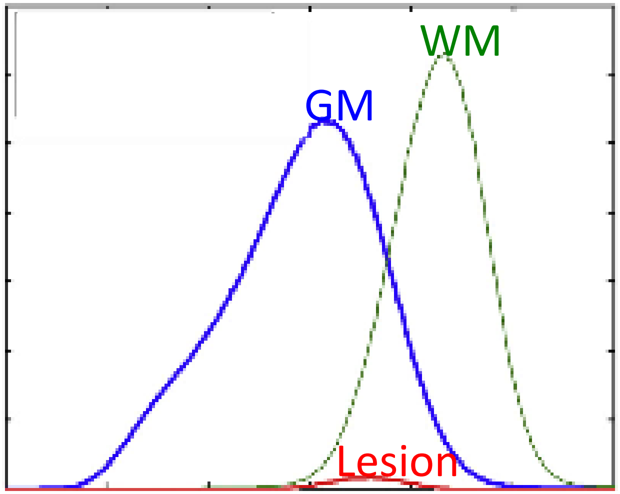


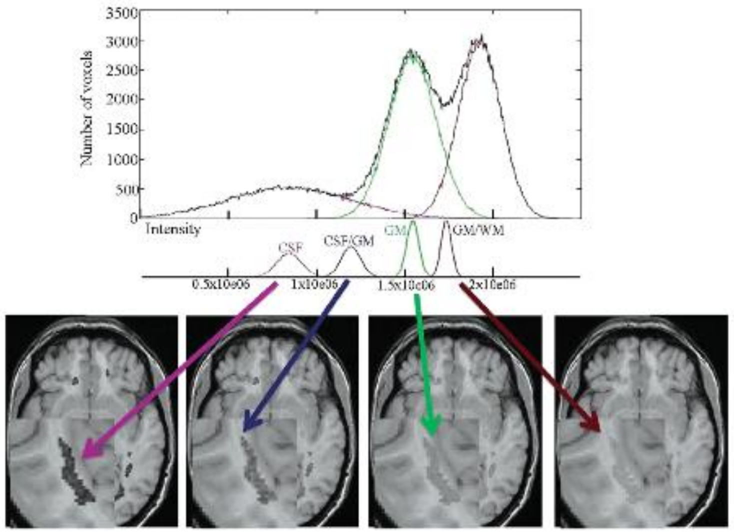
Nakamura et al. Neuroimage 2009

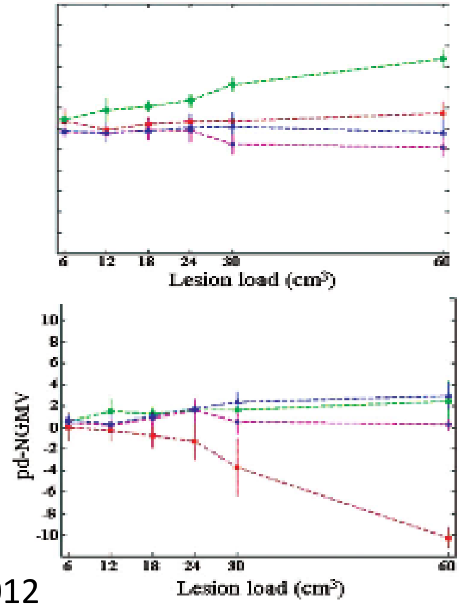
Error of Software: MRI of MS patients











Nakamura et al. Neuroimage 2009, Battaglini et al. HBM 2012

Error of Software: MRI of MS patients

Methods	Global WM intensity distribution	Local WM intensity distribution
Gaussian Kernel Based	Chard et al (J Mag Res Imaging, 2010)	Sdika et al (Human Brain Mapping 2009)
Non parametric		Battaglini et al (Human Brain Mapping 2012)

Review of the most important barriers to the use of atrophy measurement in the real world: list and possible solutions

- ❖ Physiological variation SOLUTION: to be included in the experimental design
- ❖ Error of the software SOLUTION:
  - ✓ optimise the software parameters for the specific analysis
  - ✓ Do not change version of the software during the experiment

Quantification of a measure for MR images

Change of Volume= True atrophy + $\boldsymbol{\Sigma}$

Change of Volume= True atrophy + Physiological variation + Software error

+

Variations due to the Image Acquisition

+

Errors due to the Image Acquisition

Variations due to the acquisition

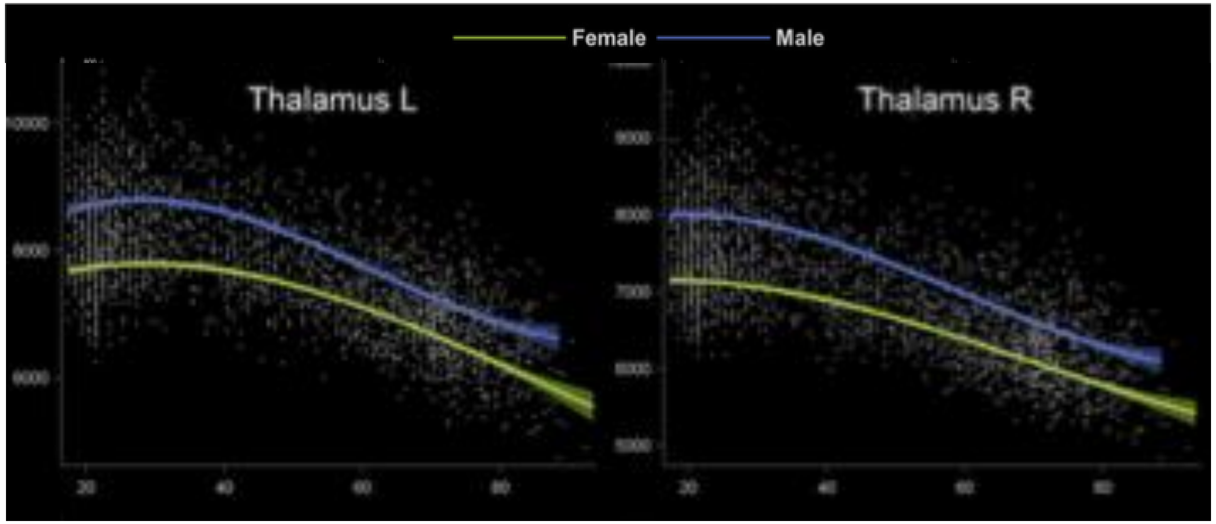
- Can the atrophy measurement be affected by:

1) Different vendor
2) Different Magnetic Strength
3) Different acquisition parameters

Variations due to the acquisition

- Can the atrophy measurement be affected by:

1) Different vendor?
2) Different Magnetic Strength
3) Different acquisition parameters



Thalamus L: Not significant
Thalamus R: -250 mm^3
(Philips Vs Siemens)

Potvin et al, NeuroImage 2016

Variations due to the acquisition

- Can the atrophy measurement be affected by:

1) Different vendor? YES (due to different coil, changing SNR)
2) Different Magnetic Strength
3) Different acquisition parameters

Variations due to the acquisition

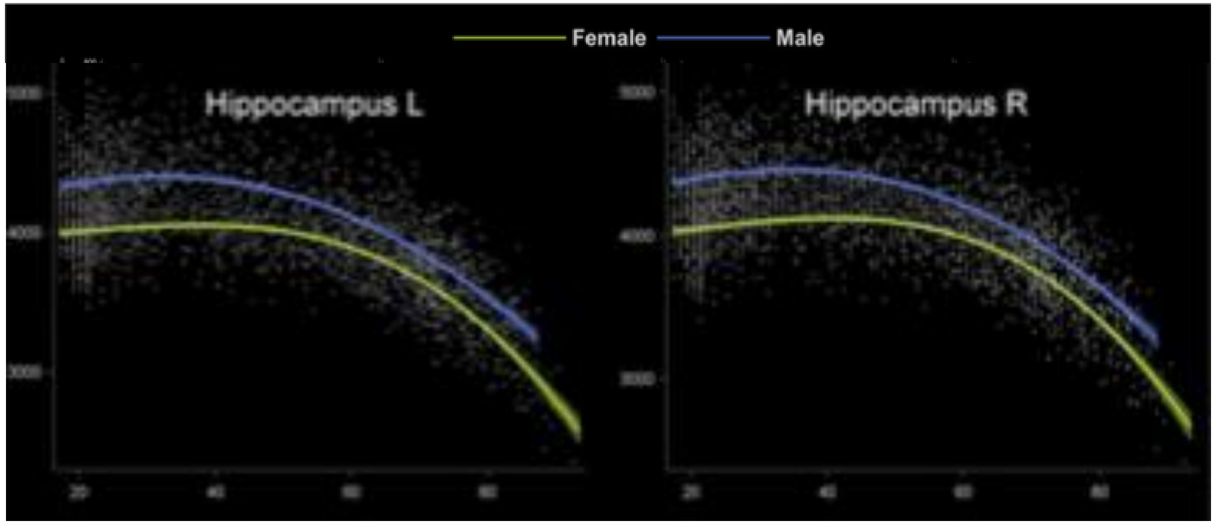
- Can the atrophy measurement be affected by:

1) Different vendor
2) Different Magnetic Strength?
3) Different acquisition parameters

Variations due to the acquisition

- Can the atrophy measurement be affected by:

1) Different vendor
2) Different Magnetic Strength?
3) Different acquisition parameters



Hippocampus L: -234 mm^3
Hippocampus R: -298 mm^3

Potvin et al, NeuroImage 2016

Variations due to the acquisition

- Can the atrophy measurement be affected by:

1) Different vendor
2) Different Magnetic Strength? YES (due to improved tissue contrast in 3T)
3) Different acquisition parameters

Variations due to the acquisition

- Can the atrophy measurement be affected by:

1) Different vendor
2) Different Magnetic Strength
3) Different acquisition parameters?

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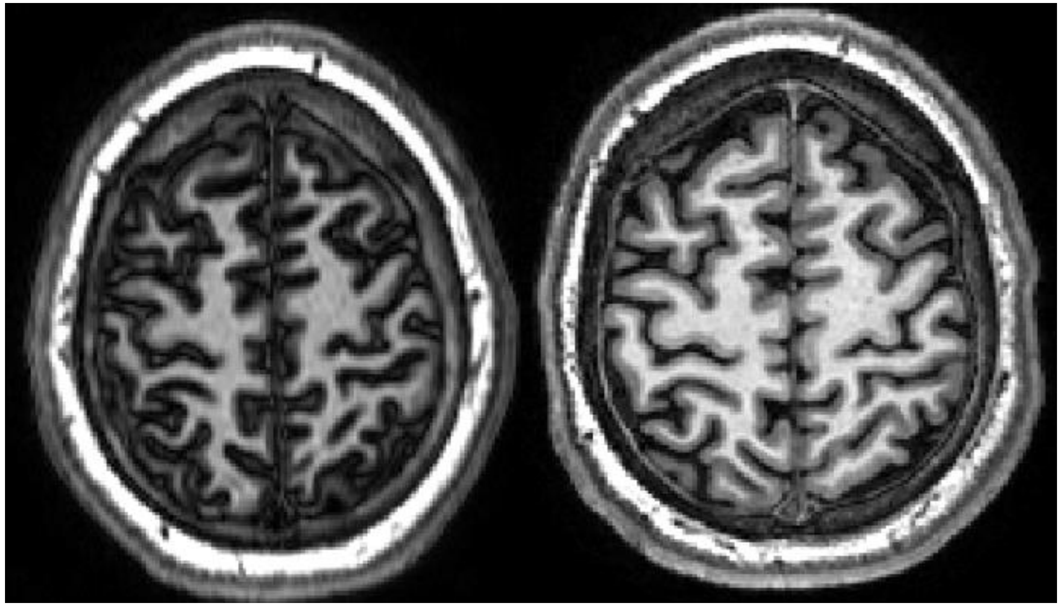

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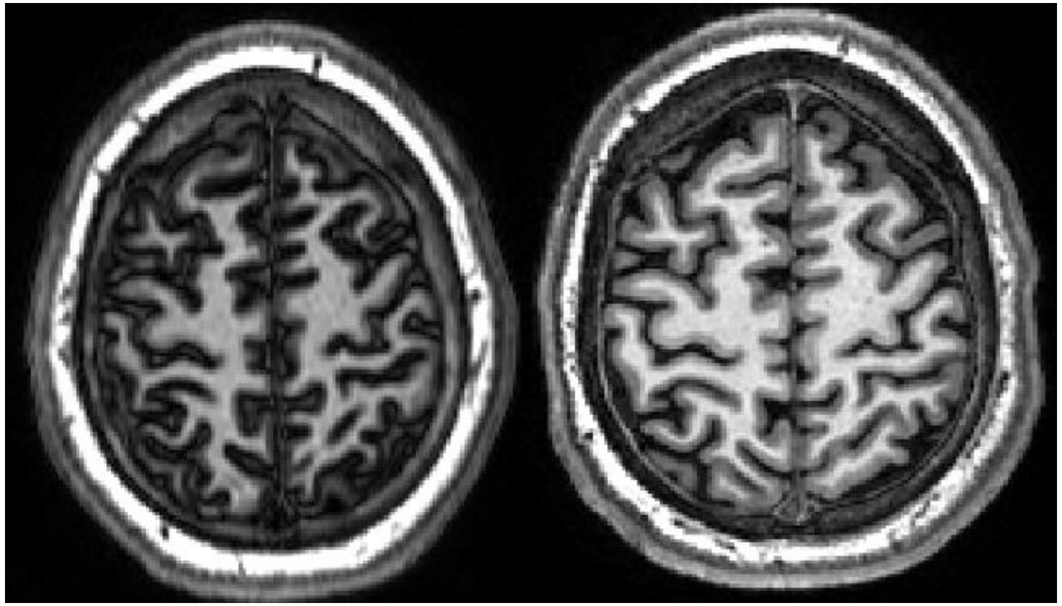

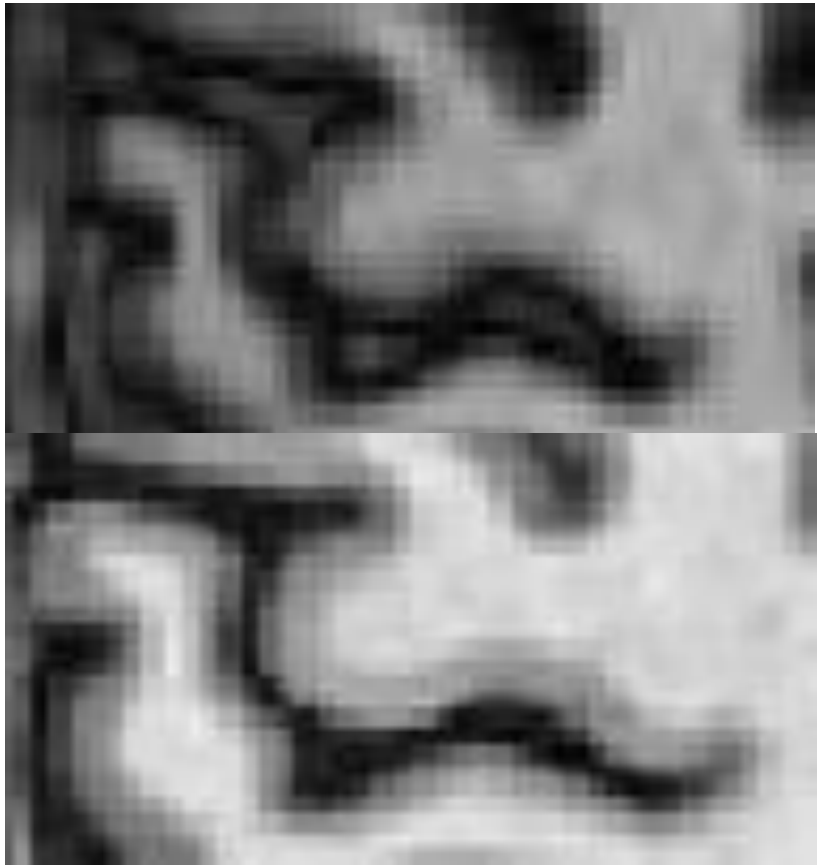

Variations due to the acquisition

- Can the atrophy measurement be affected by:

1) Different vendor
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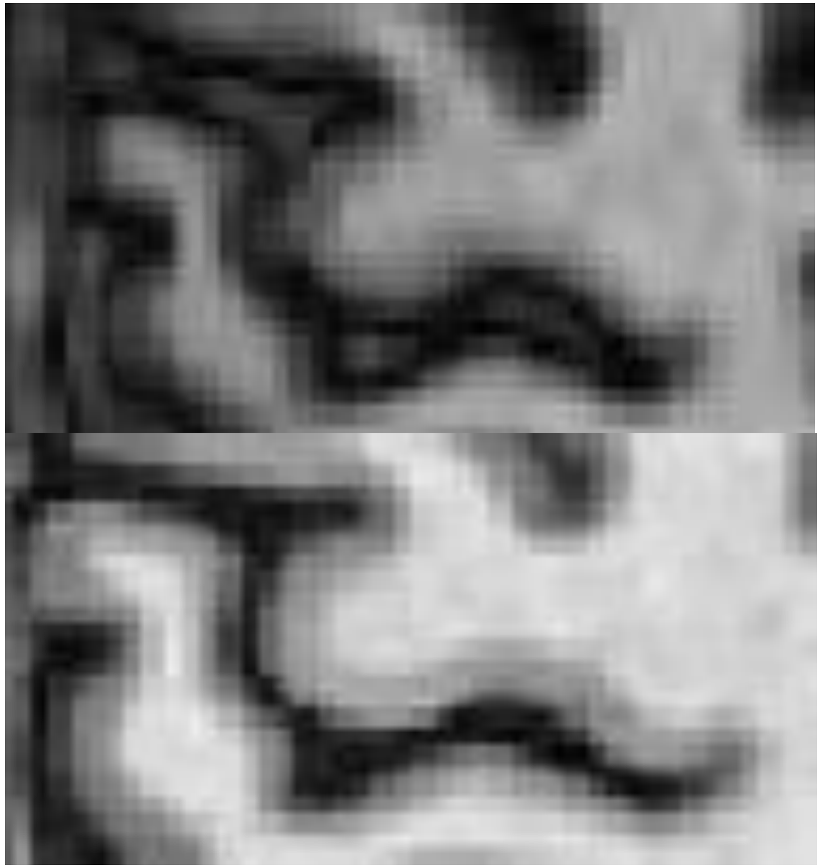
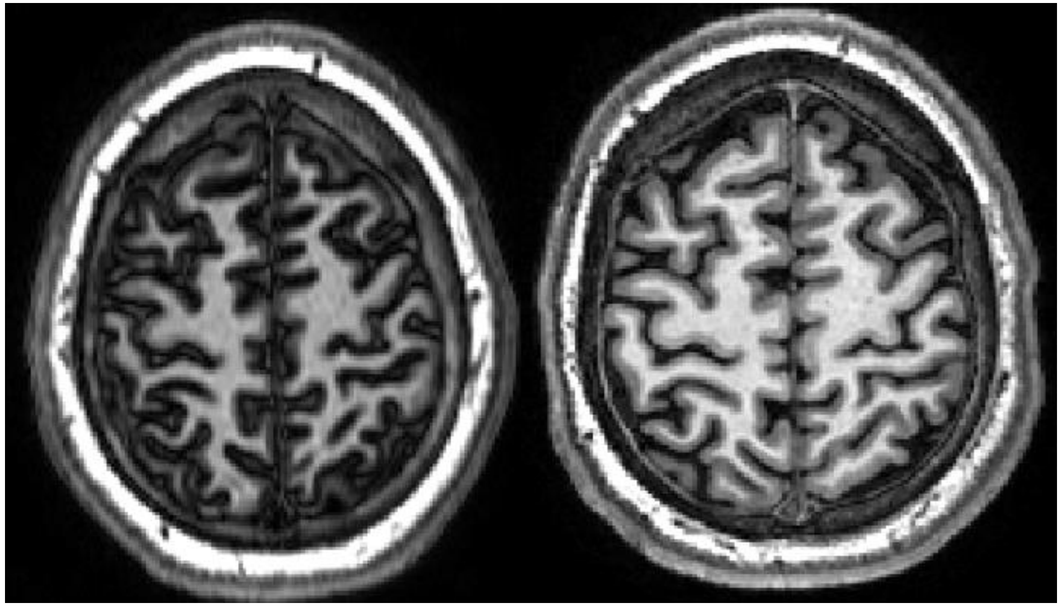
3) Different acquisition parameters?

PBVC= -10%





Variations due to the acquisition

- Can the atrophy measurement be affected by:

1) Different vendor

2) Different Magnetic Strength

3) Different acquisition parameters? YES (Different TR and TE, with the same vendor and magnetic strength, give different tissue contrast!)

Review of the most important barriers to the use of atrophy measurement in the real world: list and possible solutions

- Physiological variation SOLUTION: to be included in the experimental design
- Error of the software SOLUTION:
  - ✓ optimise the software parameters for the specific analysis
  - ✓ Do not change version of the software during the experiment
- Variation due to the image acquisition: SOLUTION:
  - ✓ do not change hardware and software MRI equipment over time;
  - ✓ set the best parameters to obtain high SNR and CNR.

Quantification of a measure for MR images

Change of Volume= True atrophy + Σ

Change of Volume= True atrophy + Physiological variation + Software error

+

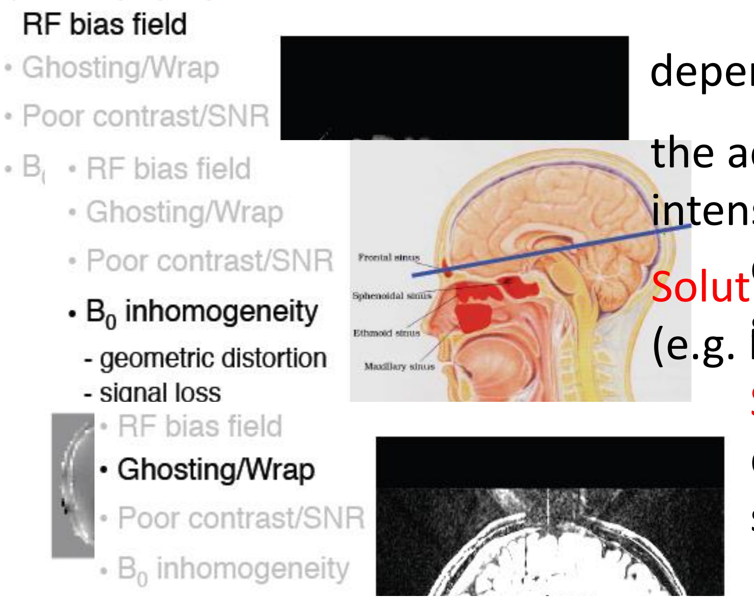
Variations due to the Image Acquisition

+

Errors due to the Image Acquisition

Errors due to the image acquisition

artifacts



depends on coil architecture

the acquired image has strong intensity inhomogeneities

Solutions: post-processing software (e.g. N3, FAST, SPM)

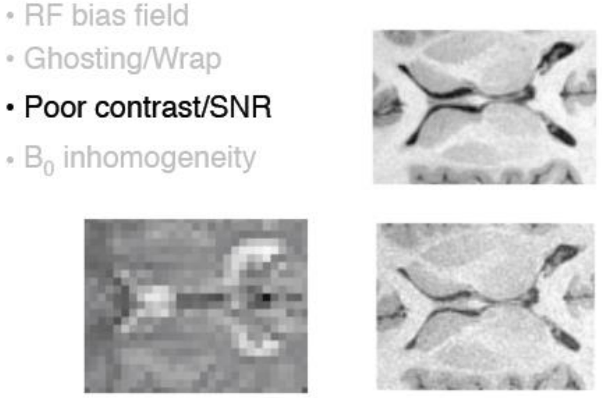
due to magnetic susceptibility differences

Solution: gradient correction during the acquisition, post-pr software (FAST)

poor shimming, gradient coil

patient motion, reconstructio

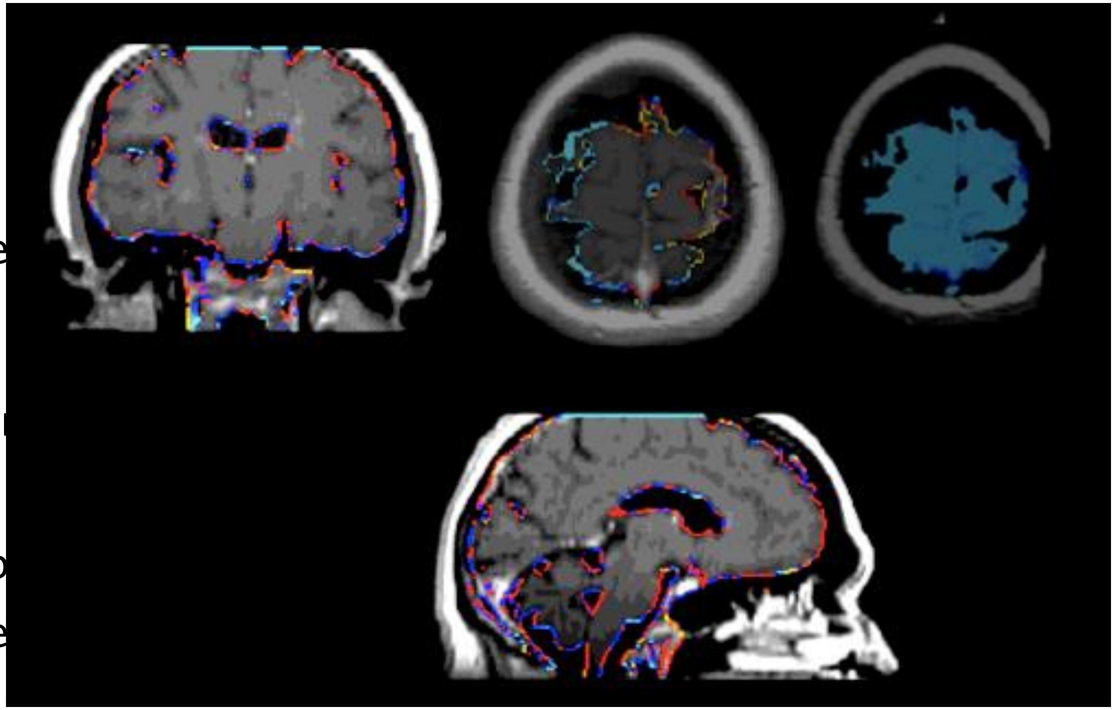
Solution: to acquire again the



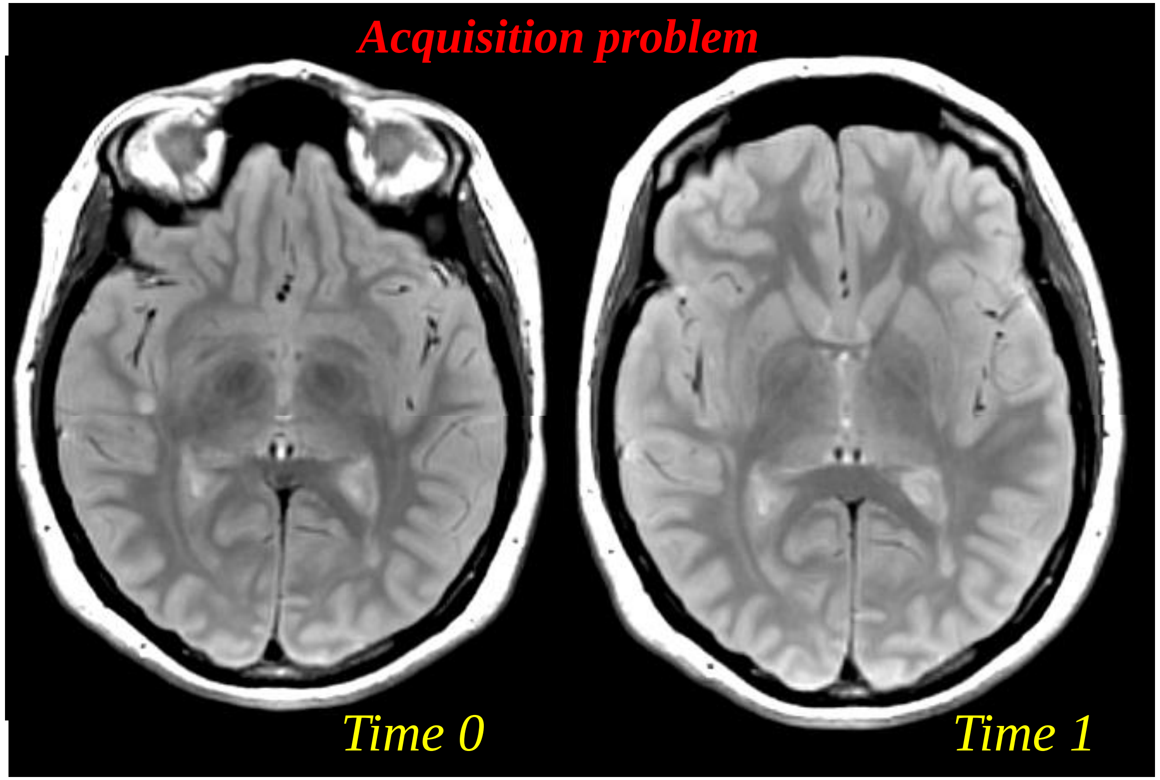
MR field strength, type of coil, parameter acquisitions (TR and TE)

Solution: to use MR scanner with higher field, to set carefully parameters of your acquisition (TR, TE)

Partial head



Errors due to the acquisition



Bad repositioning can bias atrophy measurement

Review of the most important barriers to the use of atrophy measurement in the real world: list and possible solutions

- Physiological variation   SOLUTION: to be included in the experimental design
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- Variation due to the image acquisition: SOLUTION:
  - ✓ do not change hardware and software MRI equipment over time;
  - ✓ set the best parameters to obtain high SNR and CNR.
- Errors due to the acquisition   SOLUTION:
  - ✓ Use the gradient correction option during the MR acquisitions
  - ✓ Perform quality control (check for movement artifact, bad repositioning)
  - ✓ Perform appropriate post-processing for improving MRI quality

Definition of measurement for a MR image.

Review of the most important barriers to the use of atrophy measurement in the real world: list and possible solutions

Normative rates of atrophy: a lack for the clinical use of brain volume measurement in the real world

Normative rates of atrophy

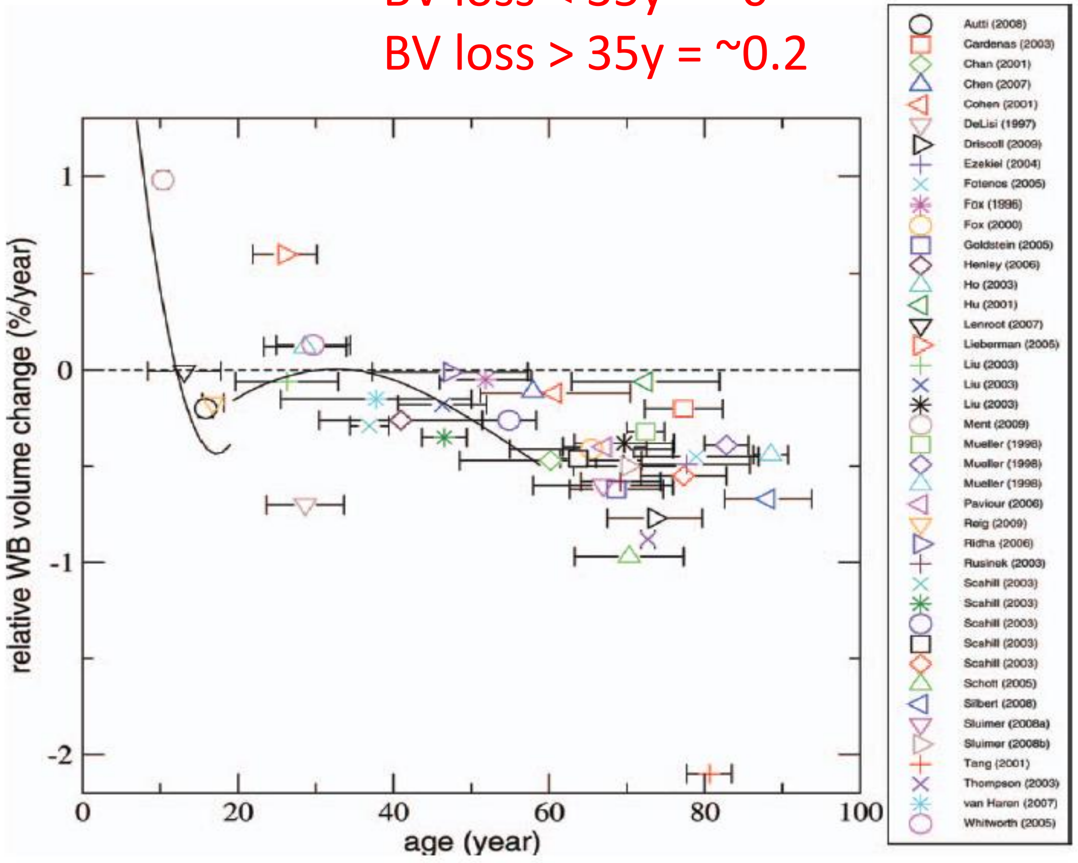
BV loss < 35y = ~0
BV loss > 35y = ~0.2

◆ Human Brain Mapping 33:1987–2002 (2012) ◆

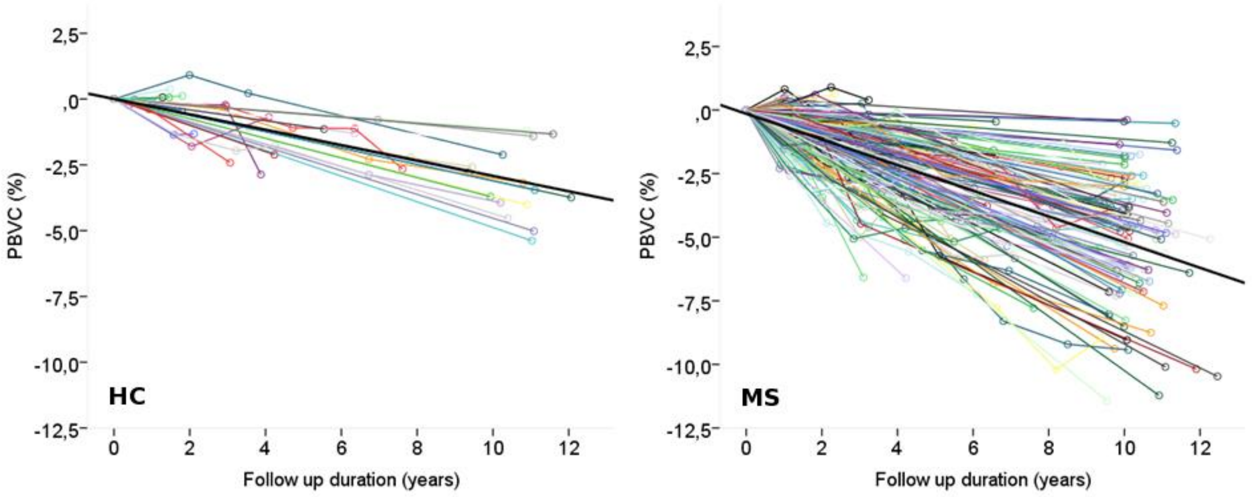
Human Brain Changes Across the Life Span: A Review of 56 Longitudinal Magnetic Resonance Imaging Studies

Anna M. Hedman*, **Neeltje E.M. van Haren, Hugo G. Schnack, René S. Kahn, and Hilleke E. Hulshoff Pol**

Rudolf Magnus Institute of Neuroscience, Department of Psychiatry, University Medical Centre Utrecht, The Netherlands

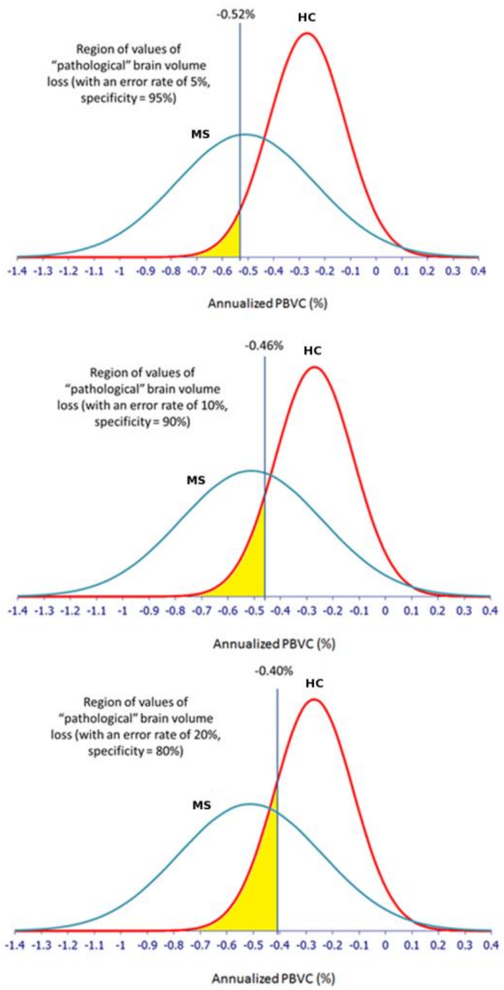


Normative rates of atrophy



PBVC cutoffs	Specificity	Sensitivity
-0.52%	95% (observed 97%)	49% (observed 44%)
-0.46%	90% (observed 91%)	56% (observed 48%)
-0.40%	80% (observed 86%)	65% (observed 61%)

Specificity= probability of being below the cutoff for an HC
Sensitivity= probability of being above the cutoff for a MS patient



MS patients: 206
Healthy Control: 35

Long follow-up > 6 years

Same scanner: Philips 1.5T

De Stefano et al JNNP 2016

Normative rates of atrophy

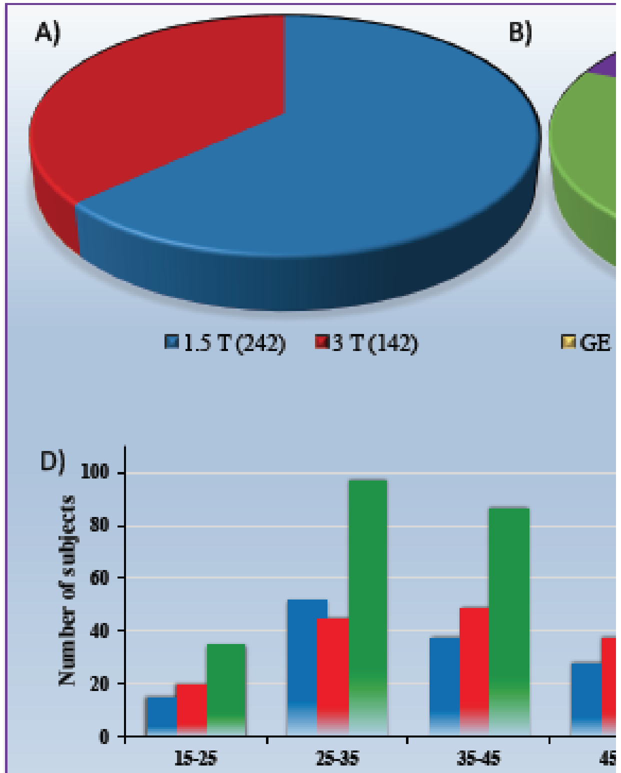


Fig. 1 Stratification of the population by magnetic strength (A), s

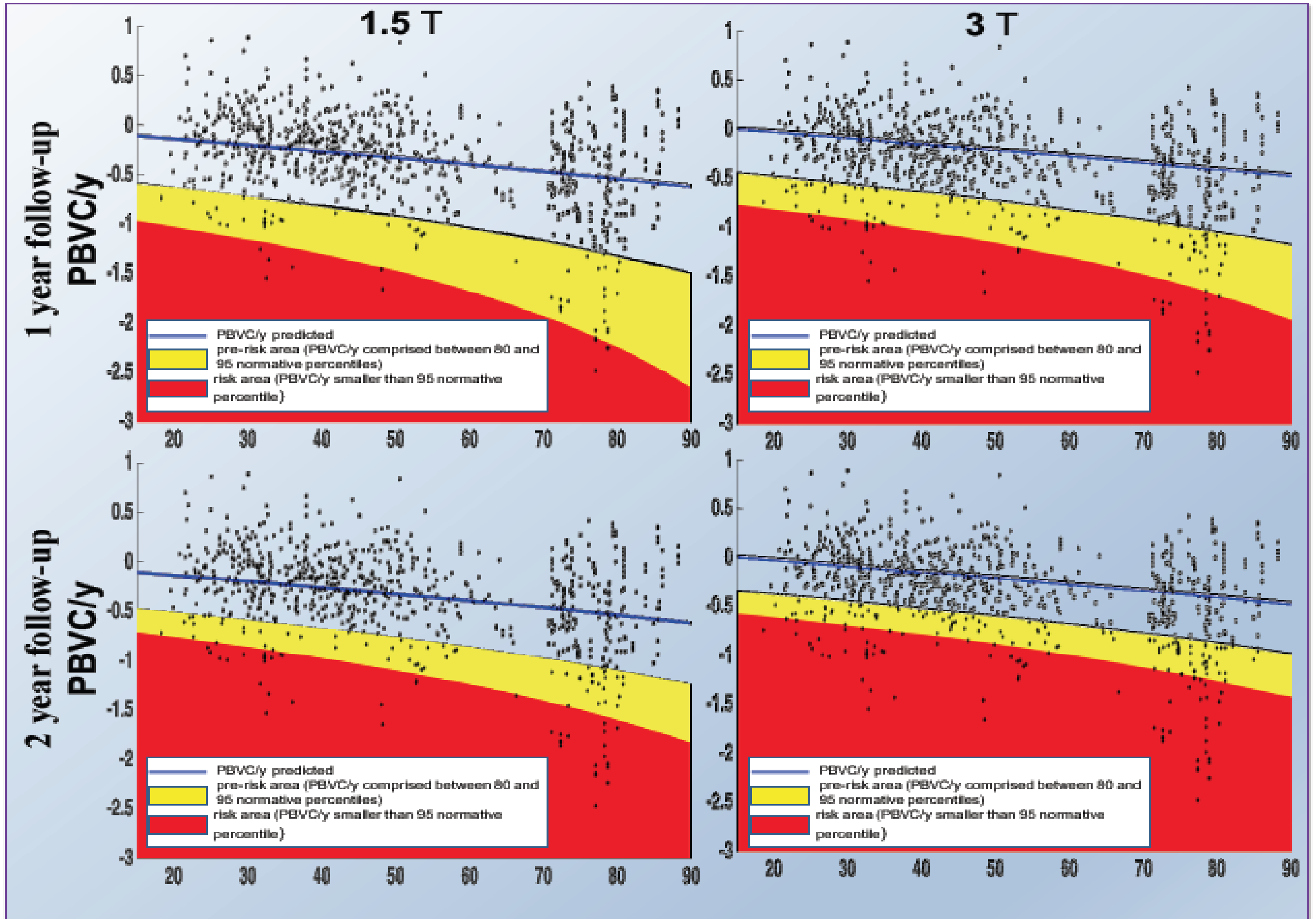


Fig.2 Normative values at 1.5 T (left side) and 3 T (right side) for 1 year (top) and 2 years (bottom) follow-up. Predicted values resulted from the model are shown (blue line). In each panel, note the PBVC/y of 80-95 (yellow areas) and higher than 95 (red areas) normative percentiles.

Healthy Controls: n=386

Variable follow-up:
median 1.1 y; (0.5y – 12y)

Different MR setting

Battaglini et al, P529

Normative rates of atrophy: a lack for the clinical use of brain volume measurement in the real world

- Multicentre data from HC at different age and magnetic field strength show significant variability, explaining the difficulties in using atrophy rate for single patient assessment.
- Statistical models can provide normative data that take into account all these variables.
- For atrophy rates, the variability decreases with increases of follow-up length. Data at 3T seem to be less variable than data at 1.5T

.

Take home message:

The impact of the barriers to brain volume measurement in the real world can be drastically reduced by:

❖carefully designing the experiment

❖carefully setting the MR scan and sequences

❖using dedicated, optimised software

Normative data are essential for better characterizing the individual course of the atrophy

Work in progress

Group analysis

Single subject analysis

MCQ-1 Quantification of atrophy in longitudinal setting.

Which is the most precise and robust method for evaluating whole brain volume changes over time on MRI?

1. Segmentation method
2. Registration method
3. None of them, all the methods have the same magnitude of error.

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MCQ-2 Error of segmentation on MRI of MS patients

Does the lesion filling permit a better evaluation of

1. CSF?
2. Whole brain?
3. GM and WM separately?
4. optic nerve?

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MCQ-3 Reduction of source of variability

A more robust quantification of atrophy can be obtained by:

1. an accurate repositioning of the subject in the scan
2. an accurate post-processing to remove Magnetic field inhomogeneity
3. strictly keeping the same sequences during different MRI sessions
4. All of them

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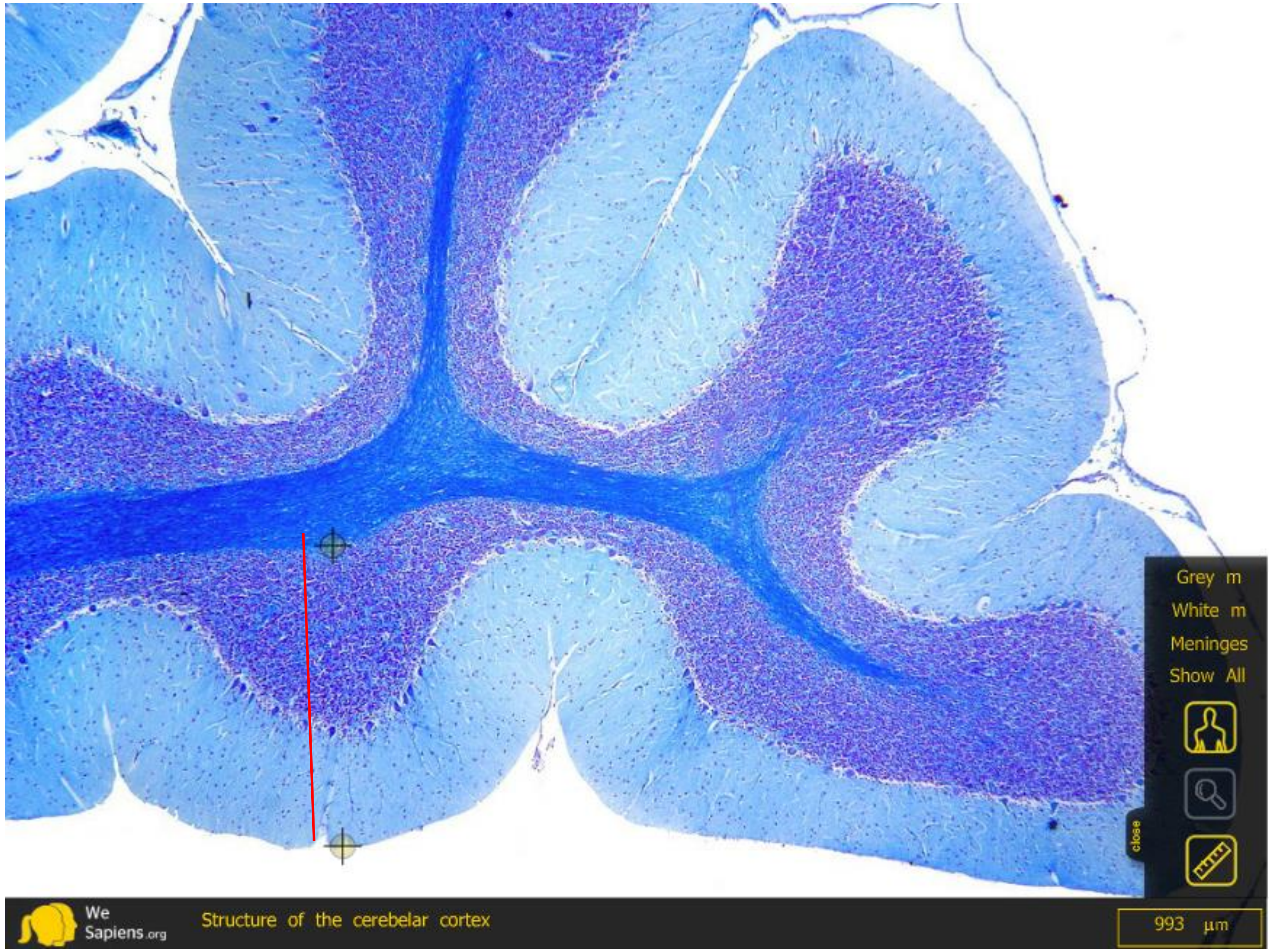
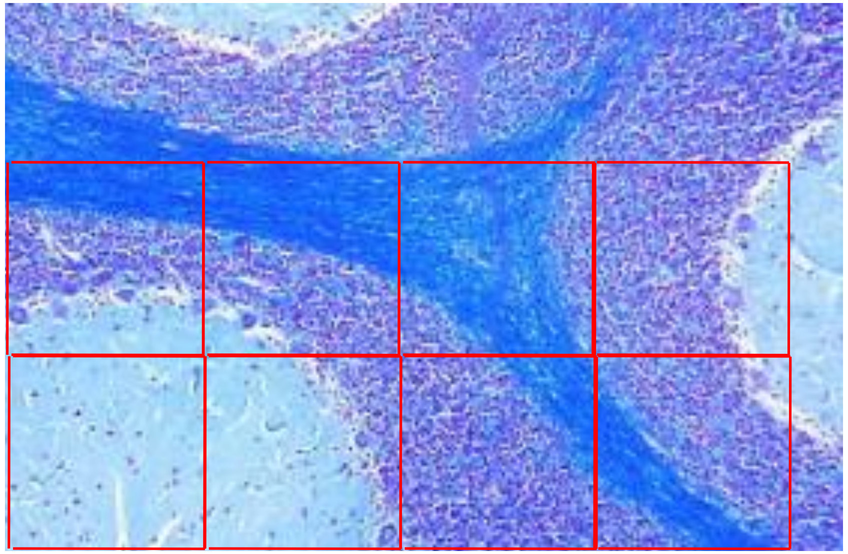
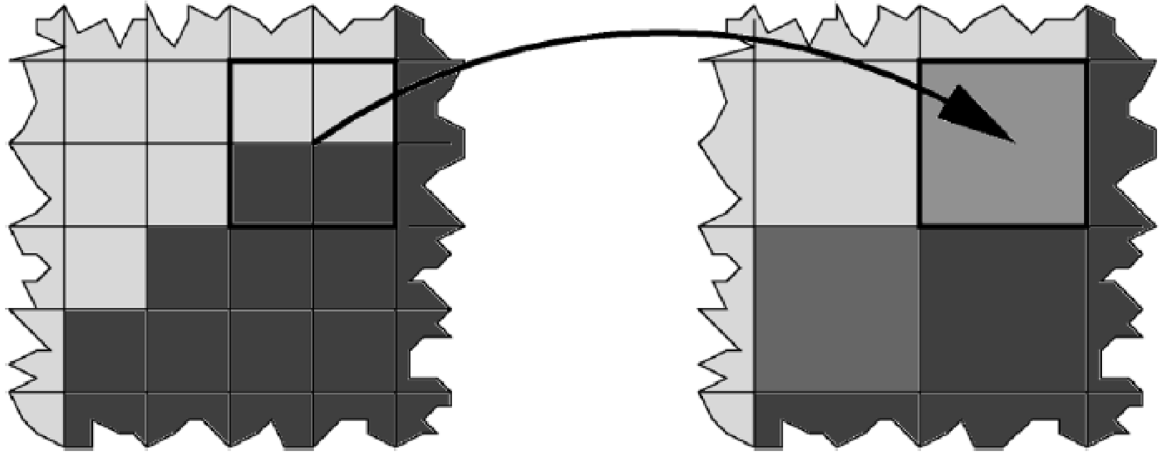
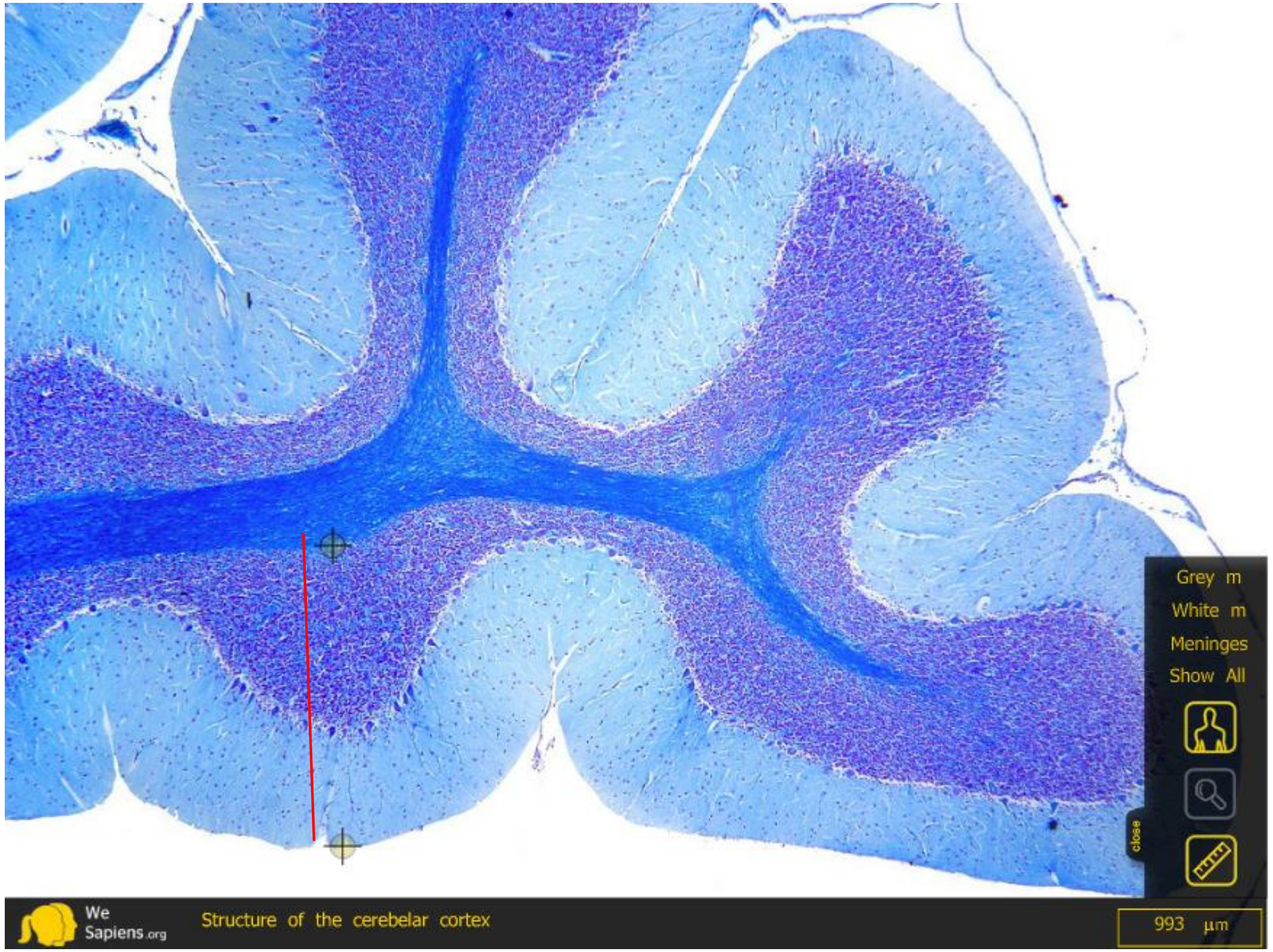
Error of Software   Segmentation methods



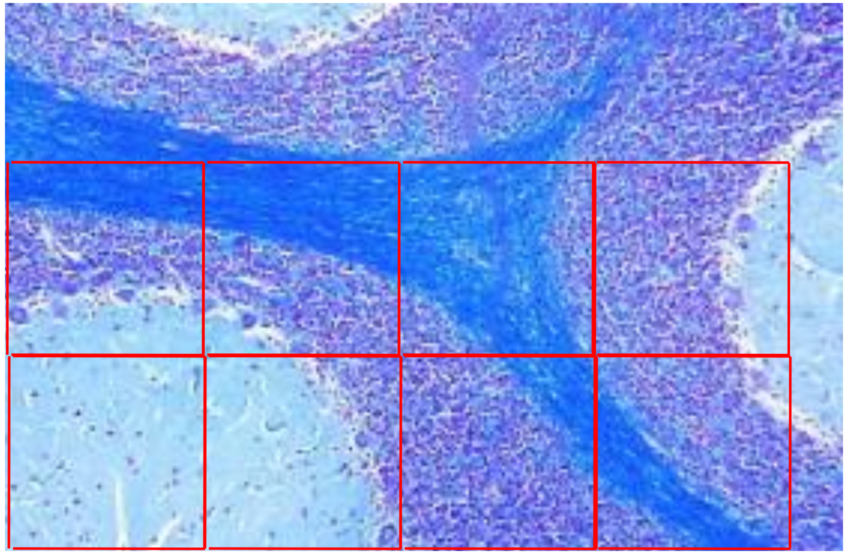


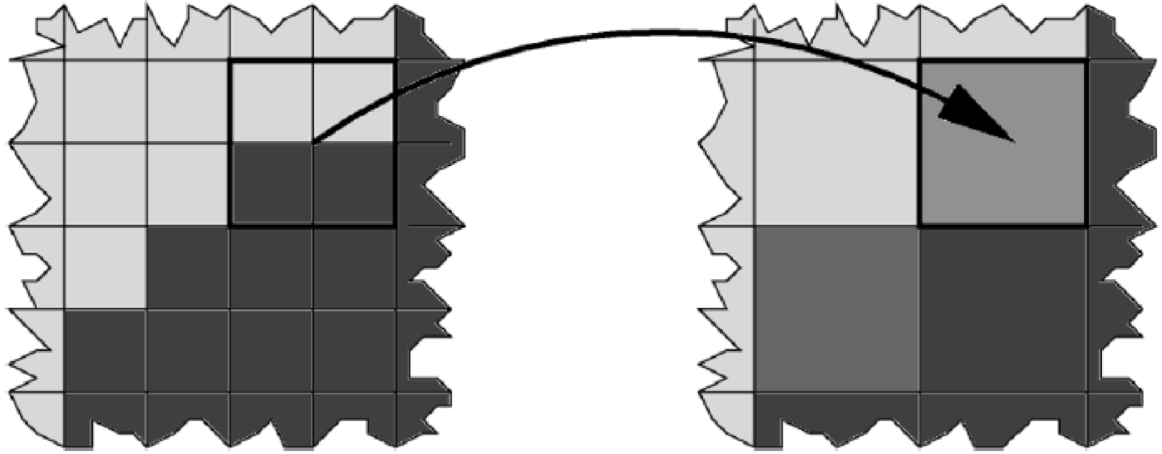


Error of Software Segmentation methods



ERROR ~0.5-1%





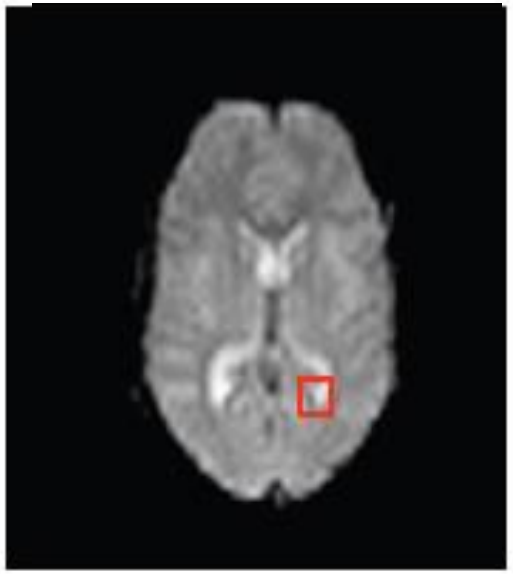
Error of Software

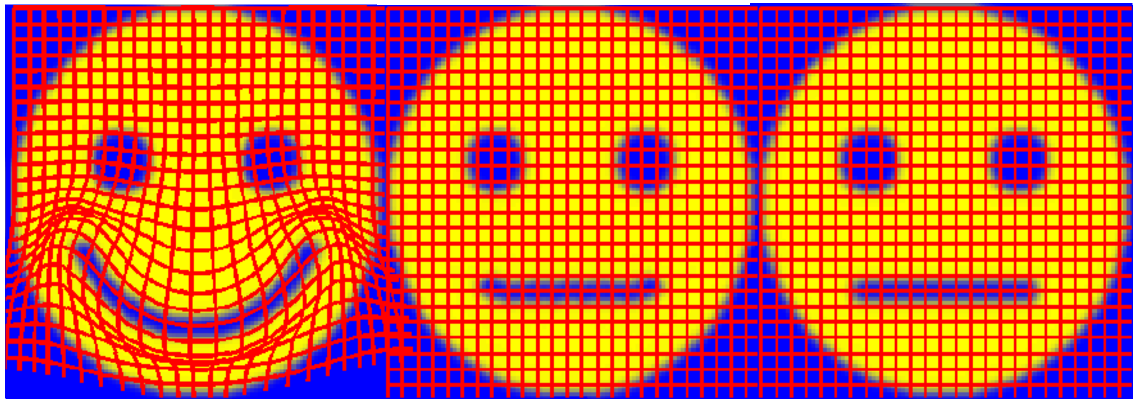
1) CROSS-SECTIONAL ANALYSIS → SEGMENTATION METHOD

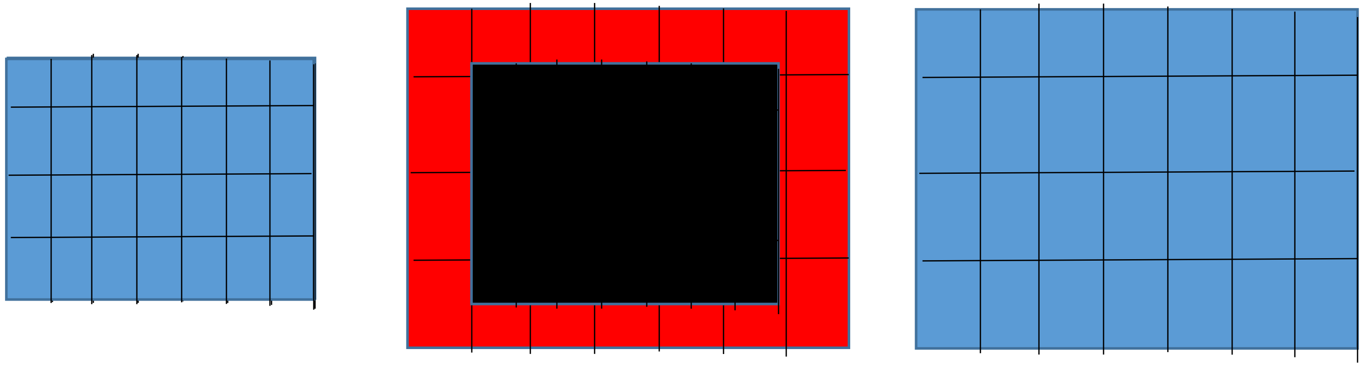
2) LONGITUDINAL ANALYSIS → SEGMENTATION METHOD

2) LONGITUDINAL ANALYSIS → REGISTRATION METHOD

Error of Software Registration methods

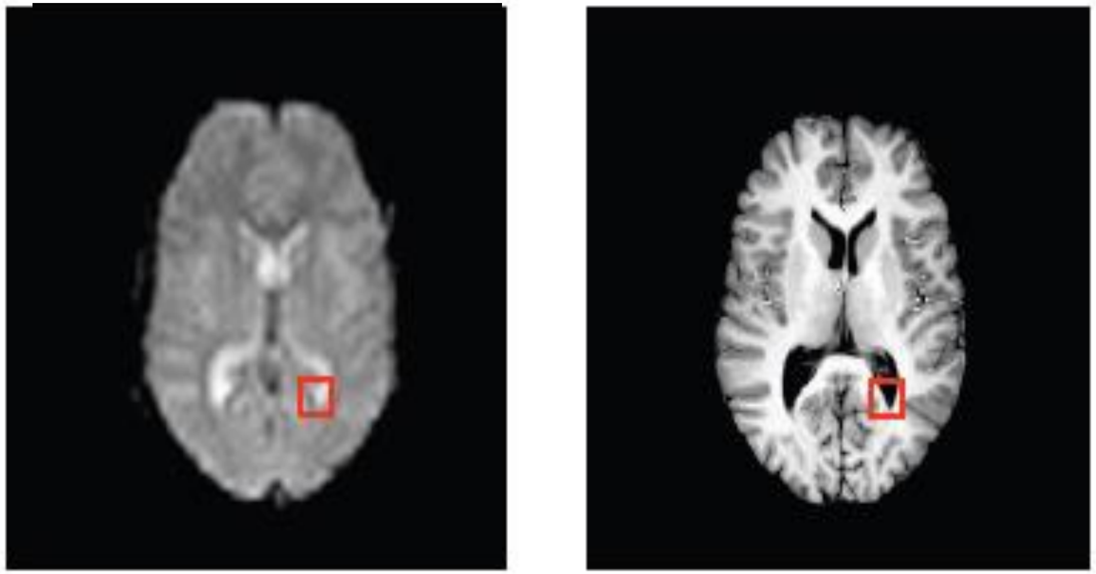


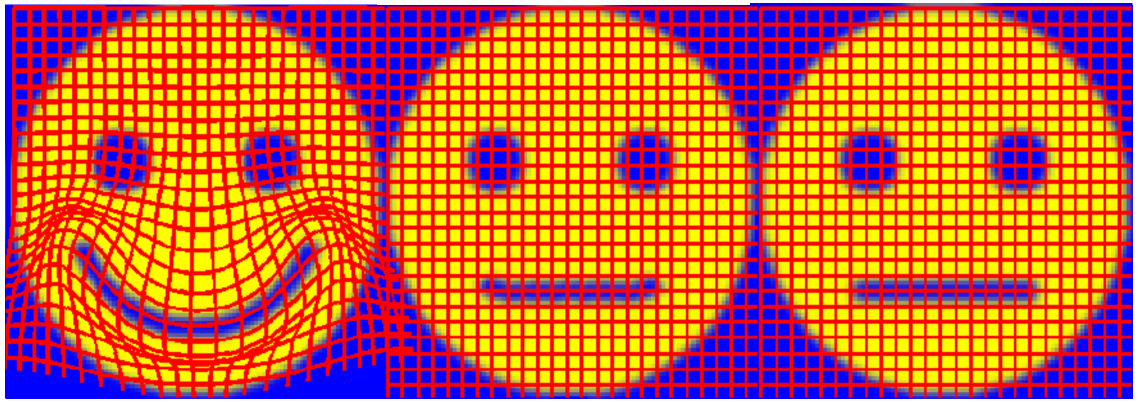




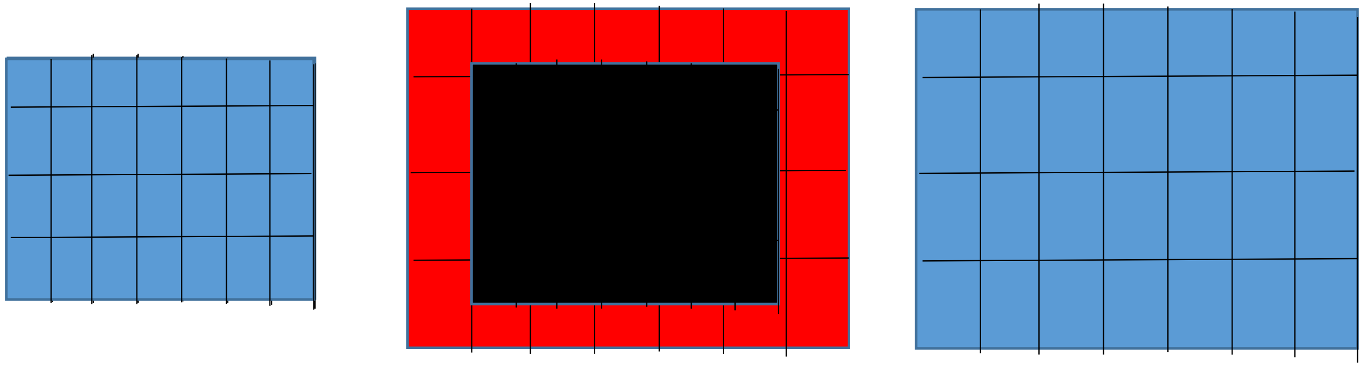
Error of Software

Registration methods



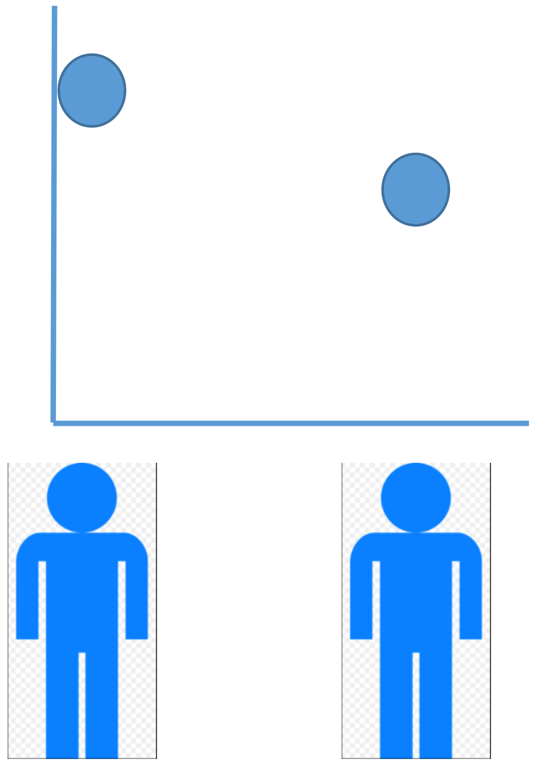


ERROR ~0.1-0.5%



Quantification of a measure for MR images

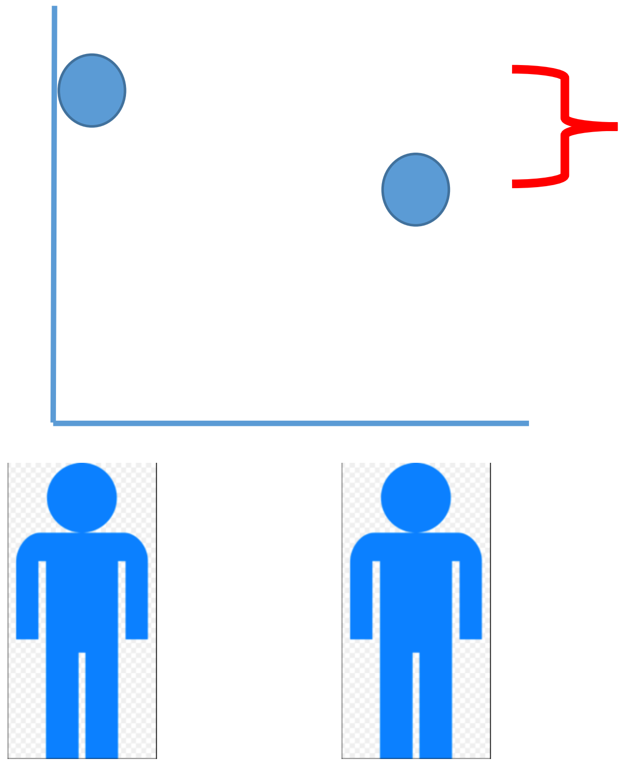
Change of Volume= True atrophy + $\boldsymbol{\Sigma}$



Quantification of a measure for MR images

Change of Volume= True atrophy + Σ

Vol time 1 Vol time 2



Change of Volume= 100*(Vol2 –Vol1)/Vol1

Quantification of a measure for MR images

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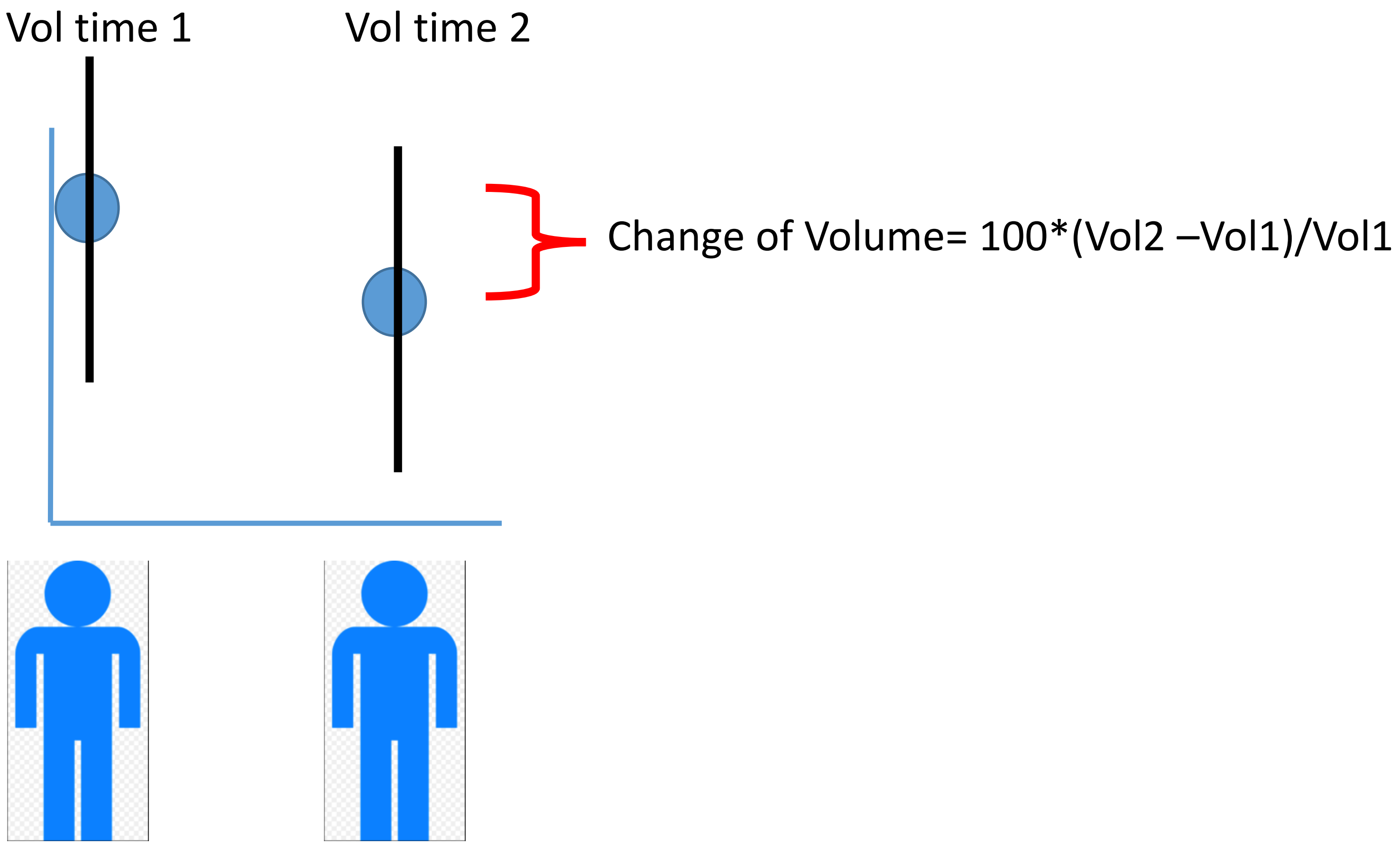

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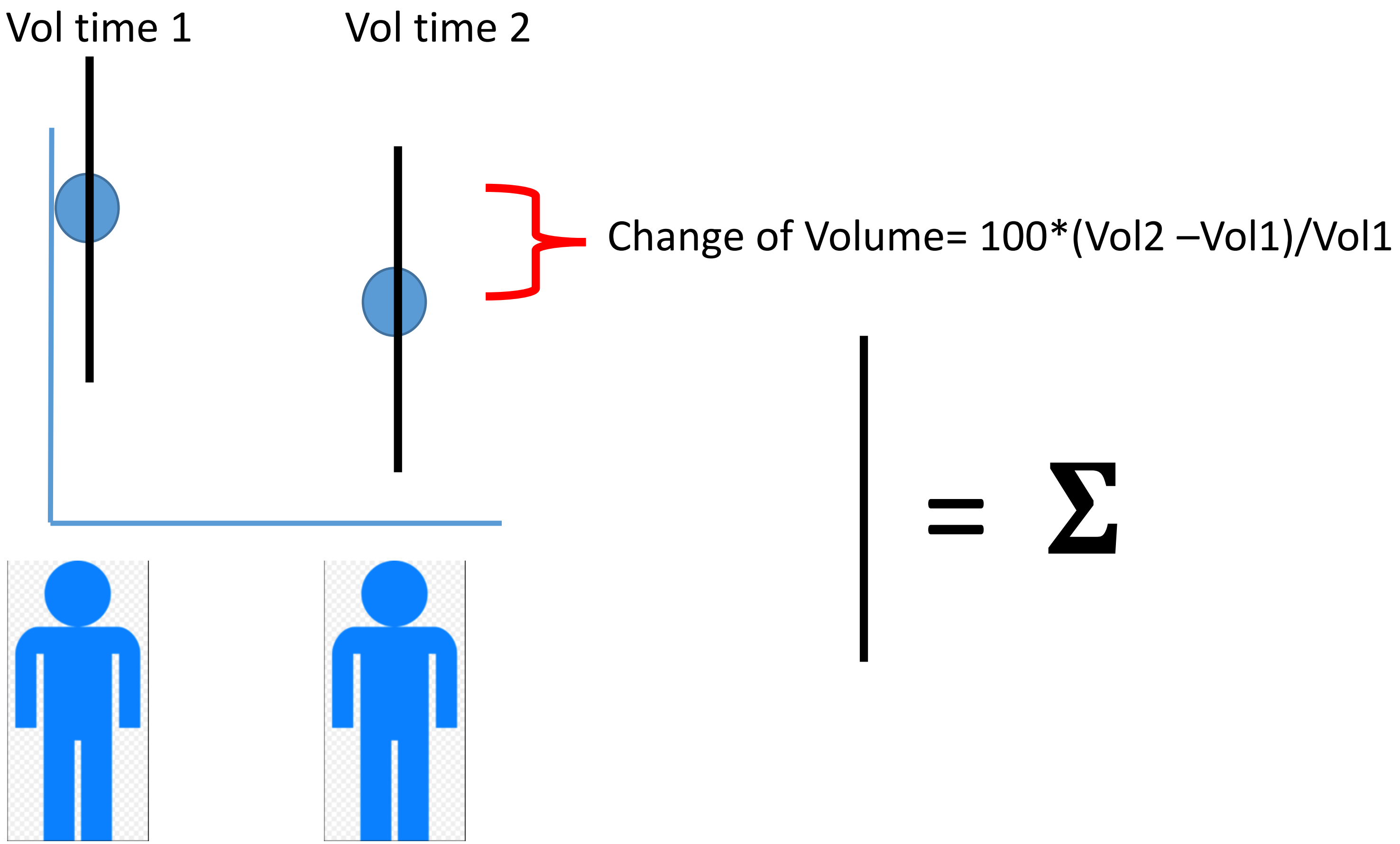

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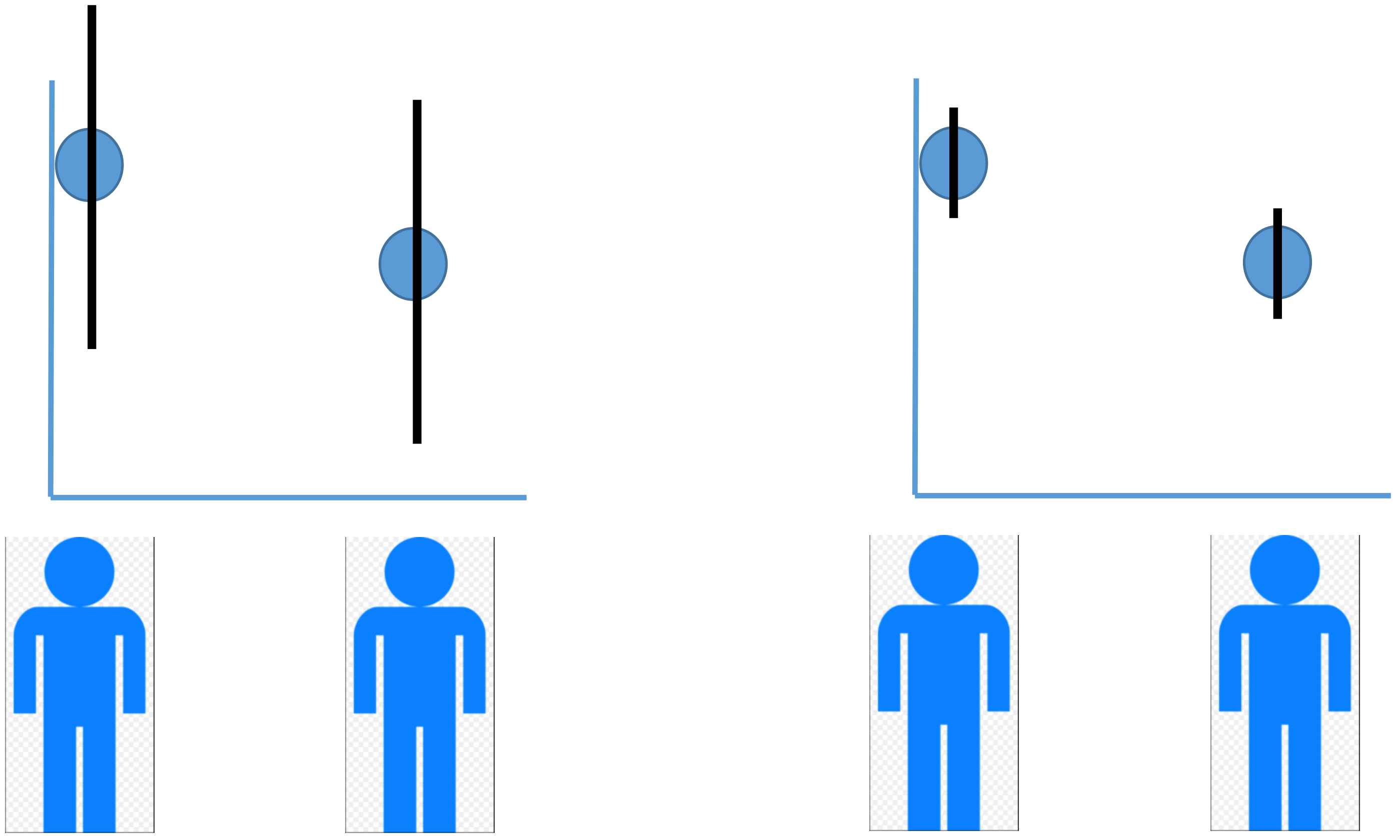

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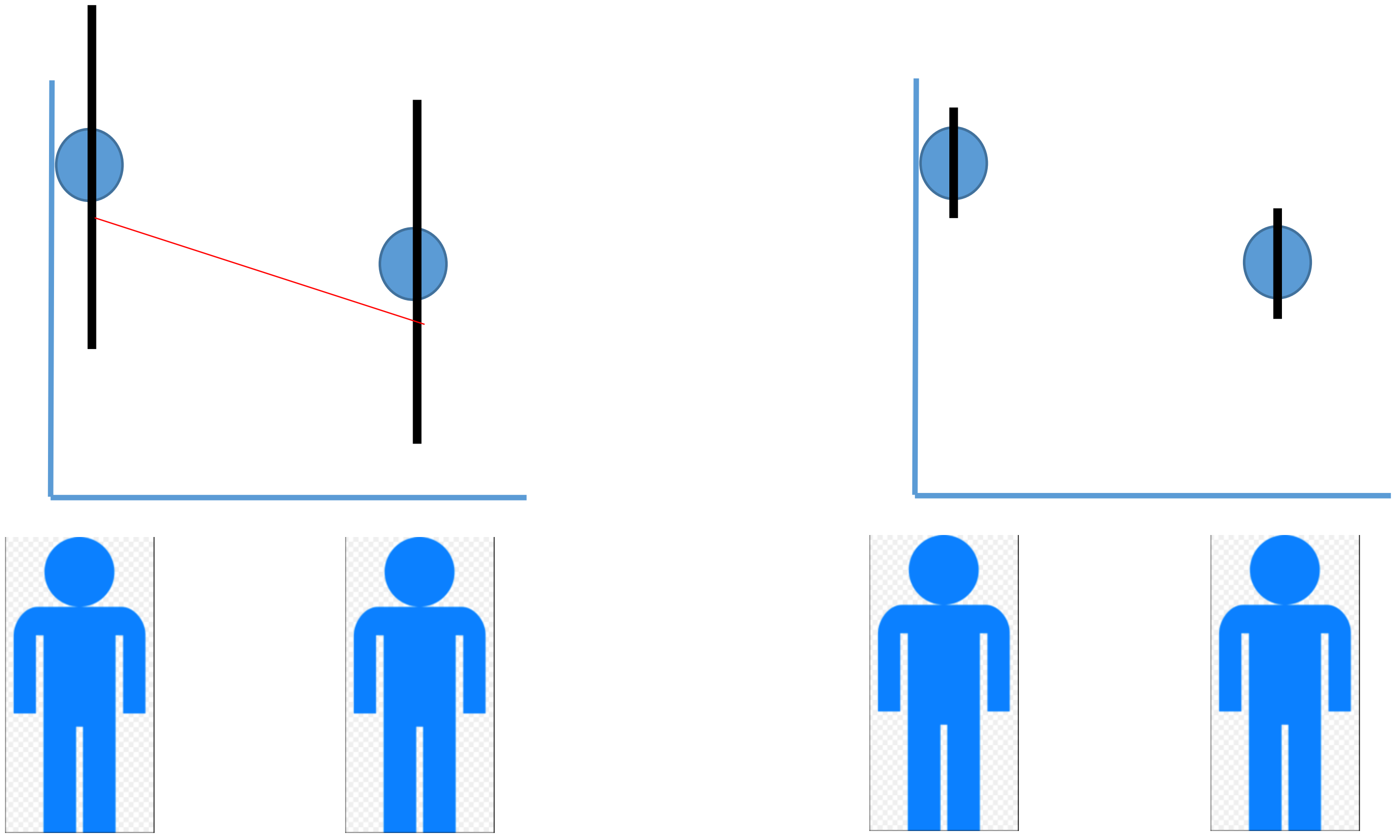

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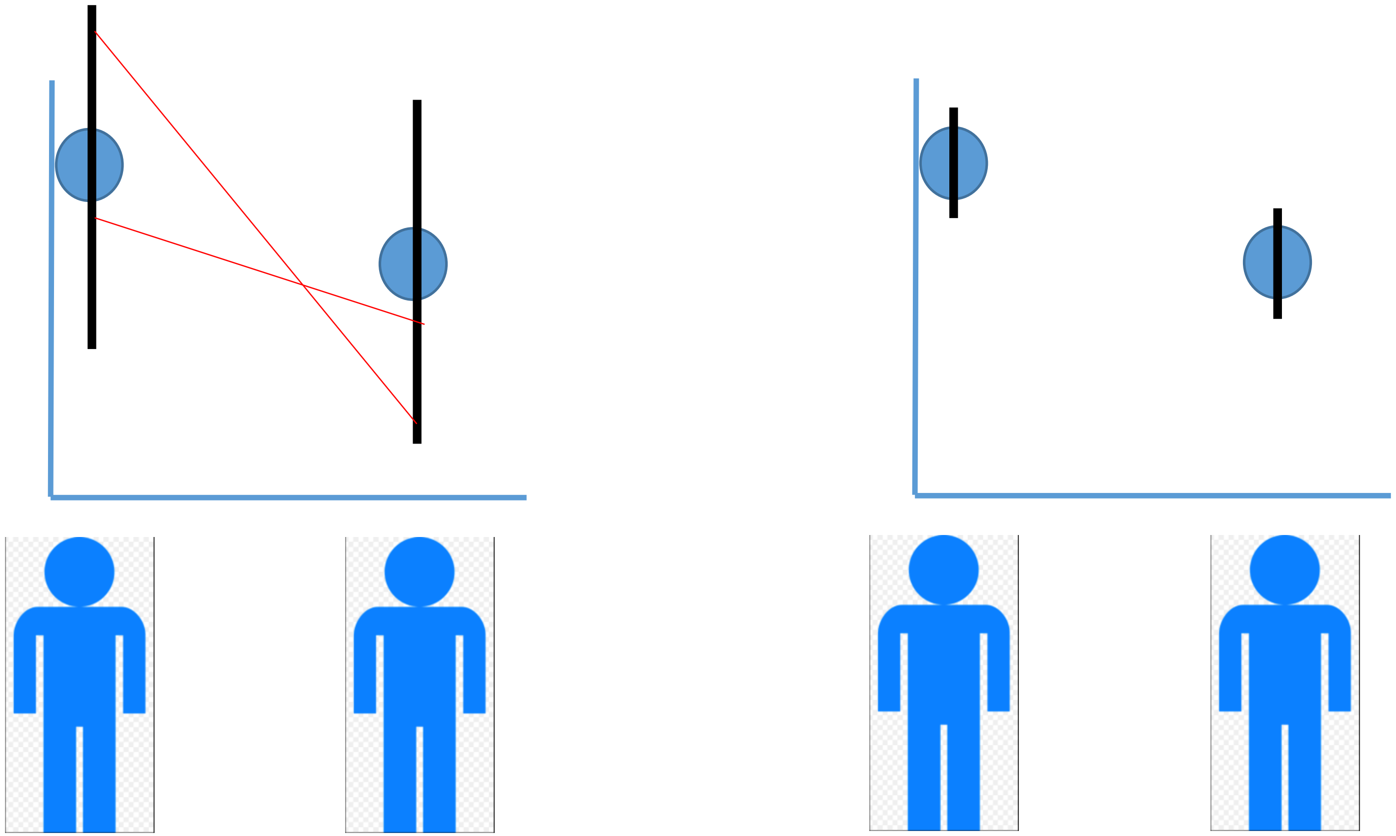

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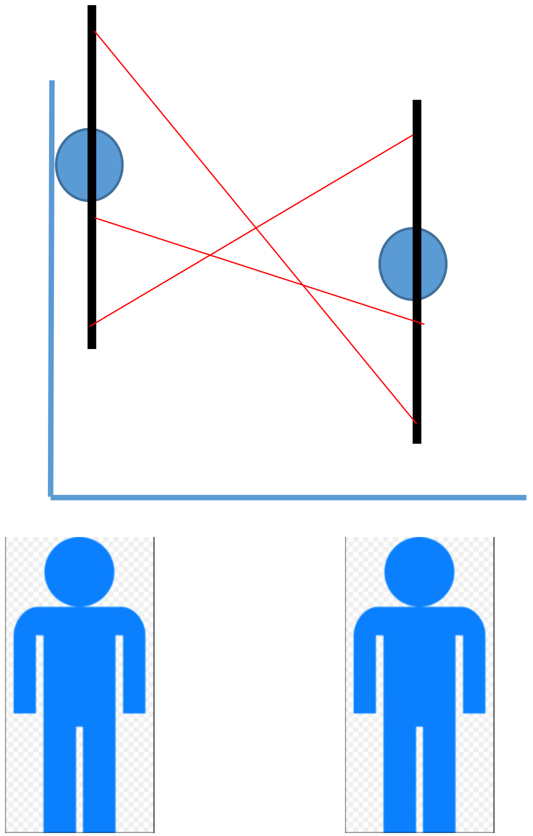

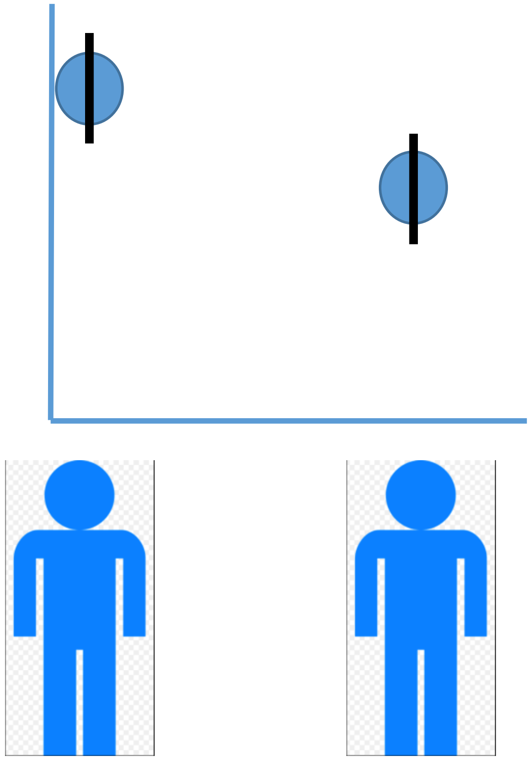

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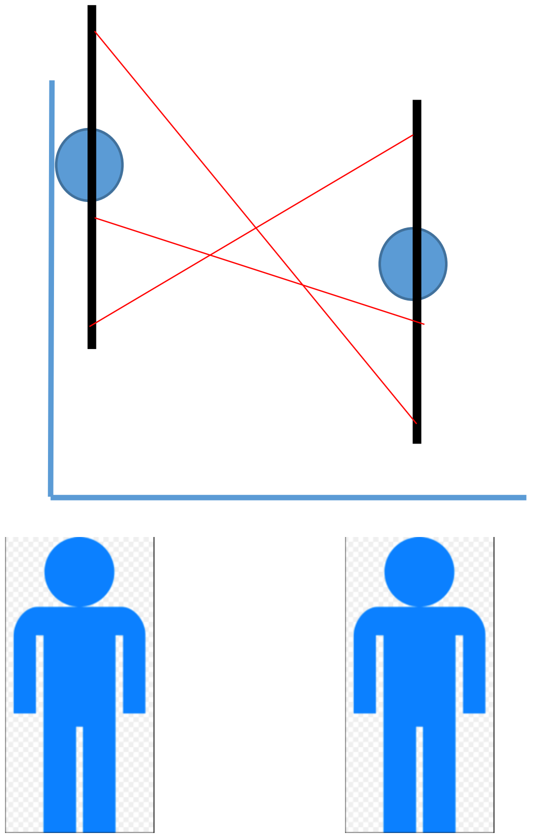

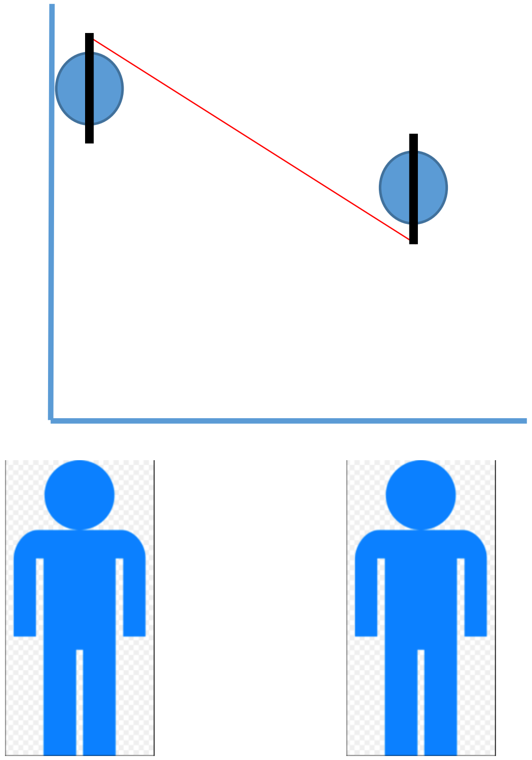

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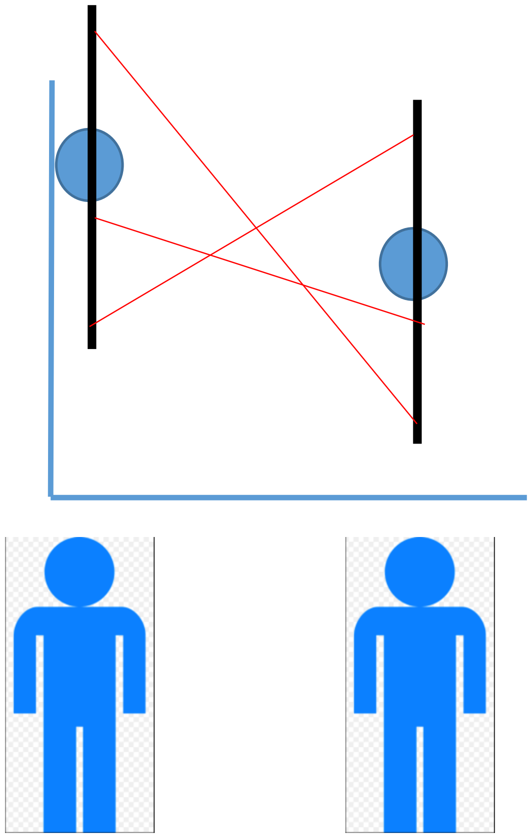

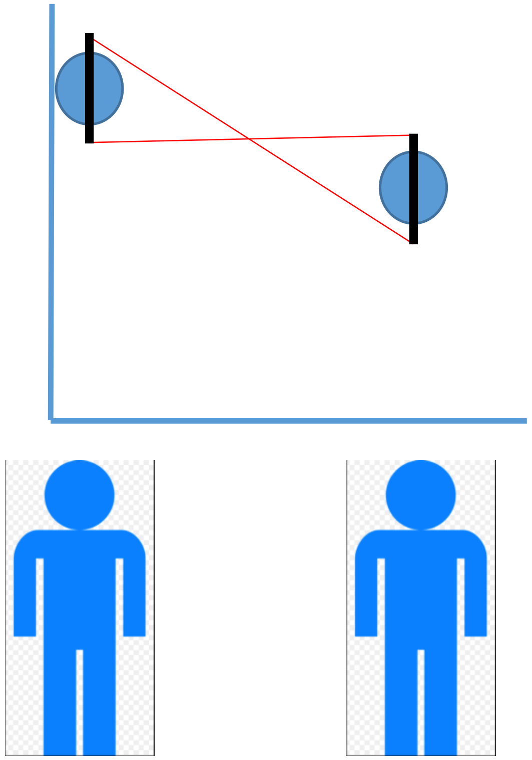

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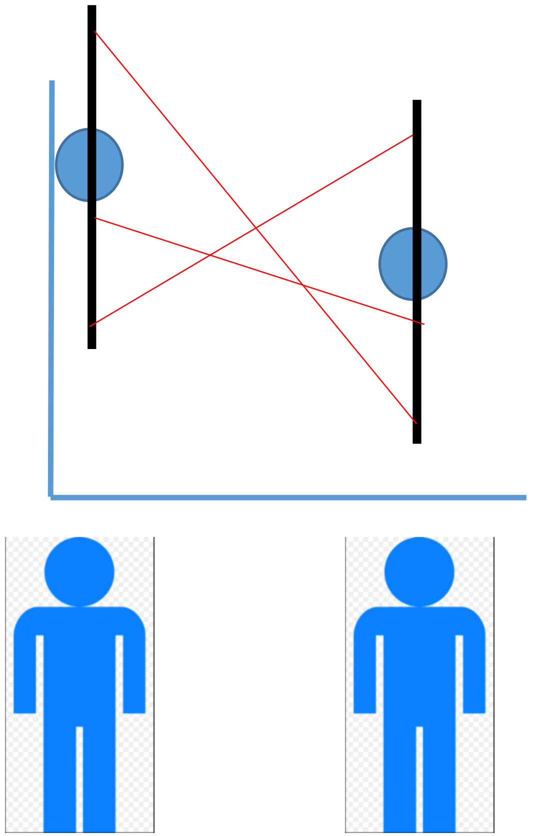

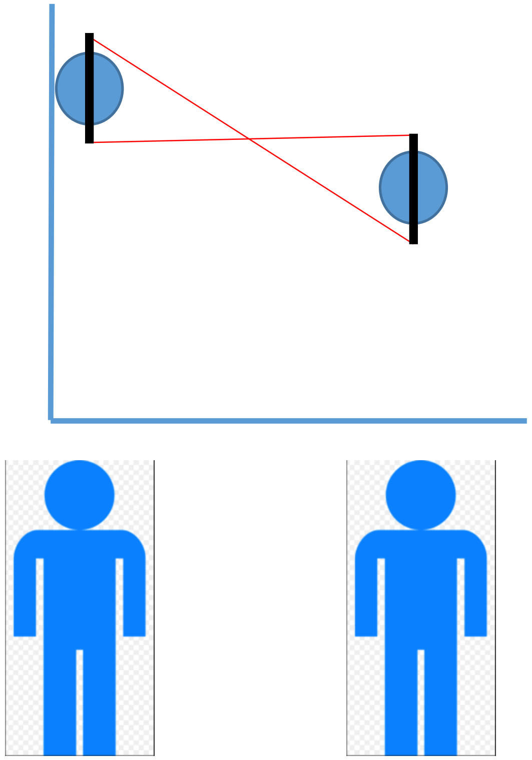

$$\frac{\text{Change of Volume}}{\boldsymbol{\Sigma}}$$

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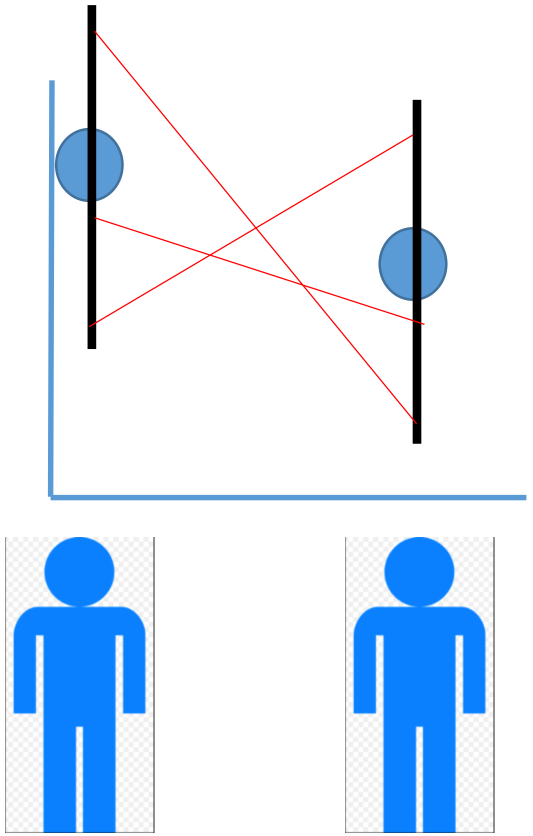

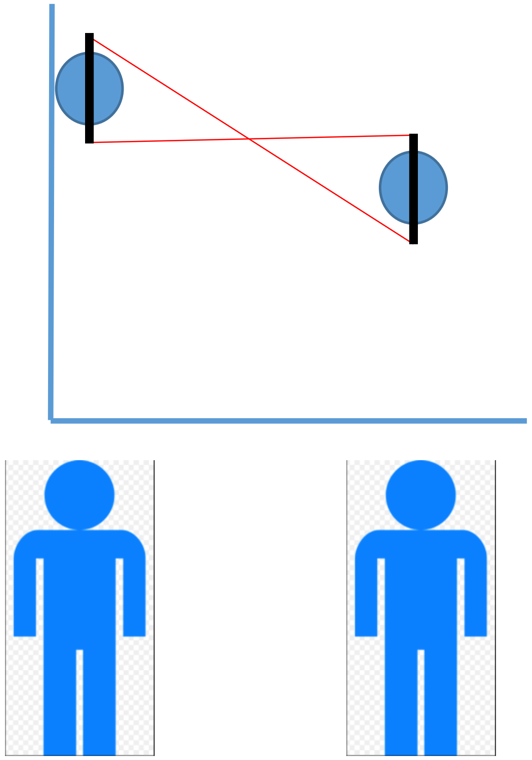

$$\frac{\text{Change of Volume}\uparrow}{\boldsymbol{\Sigma}\downarrow}$$

Quantification of a measure for MR images

Change of Volume= True atrophy + Σ

Change of Volume $\uparrow$ Increase the length of Follow-up