



Transferring Multi-Parameter Mapping Into a Clinical Trial

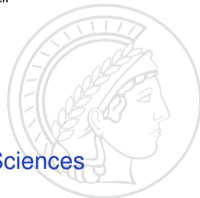
Advancements and Challenges



University of Zurich™

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15th January, 2018

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for Human Cognitive and Brain Sciences
Leipzig, Germany



Outline

The clinical trial NISCI

Multi-parameter mapping for use as a clinical biomarker

Data processing tools



The clinical trial NISCI

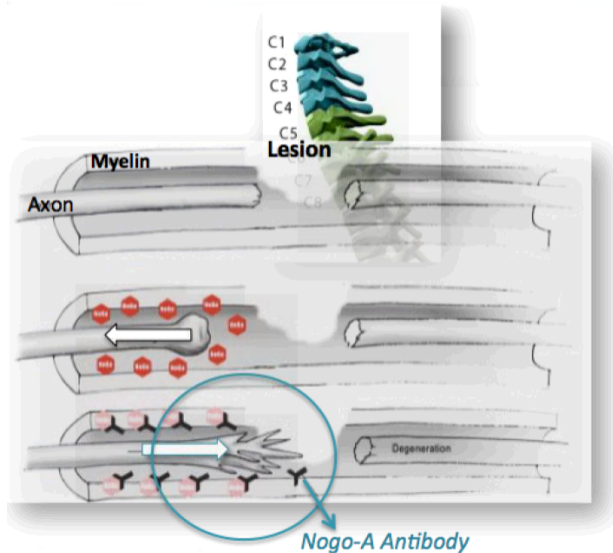
What does NISCI mean?

Nogo Inhibition in
Spinal Cord Injury

Therapy with
Nogo-A antibody



Regeneration of
nerves possible



The NISCI clinical trial within time and space

Multi-centre clinical proof of concept

- ▶ EU financed (Horizon 2020) for 5 years
- ▶ (>)7 clinical sites enrolling ≈ 150 patients



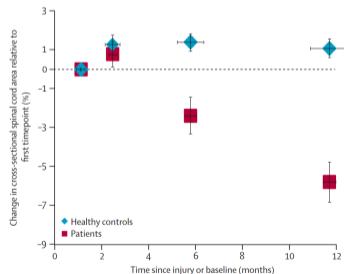
The NISCI clinical trial within time and space

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Longitudinal tracking of de- and regeneration of nerves

- ▶ neurological and functional tests
- ▶ biomarker development in addition:
 - ▶ biochemical (CSF and serum)
 - ▶ neuroimaging: cross-sectional cord area



P. Freund: Lancet Neurol 12 873–881, 2013.



The NISCI clinical trial within time and space

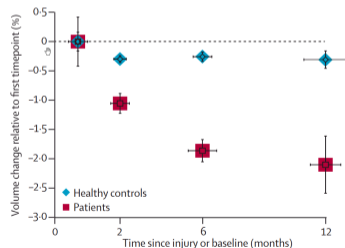
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Longitudinal tracking of de- and regeneration of nerves

- ▶ neurological and functional tests
- ▶ biomarker development in addition:
 - ▶ biochemical (CSF and serum)
 - ▶ neuroimaging: cross-sectional cord area, multi-parameter mapping at the brain



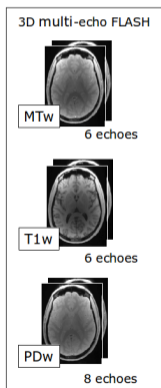
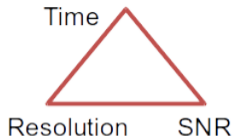
P. Freund: *Lancet Neurol* **12** 873–881, 2013.



Multi-parameter mapping for use as a clinical biomarker

Multi-parameter mapping in research

- ▶ high resolution (1 mm isotropic resolution within 26 min, whole brain)
- ▶ quantitative method for longitudinal and cross-sectional studies

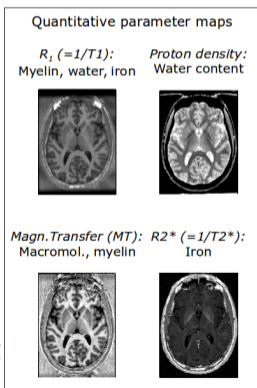


Physical models

$$S \propto A \alpha \frac{TR/T_1}{\alpha^2/2 + TR/T_1}$$

$$S_{MT} \propto A \alpha \frac{R_1 TR}{\alpha^2/2 + \delta + R_1 TR}$$

Helms et al., MRM 2008;
Helms et al., Neuroimage 2009;
Lutti et al., MRM 2010, PONE 2012
Weiskopf et al., Neuroimage 2011;
Weiskopf et al., FIBIM 2013



⇒ markers of

- ▶ iron
- ▶ myelin
- ▶ water
- ▶ macromolecule content

[K. Pine, 03.04.2017
Institute Colloquium]

Challenges of the clinical trial



*“Forty minutes at three hundred and fifty degrees should do it,
Miriam, but don't neglect to baste continuously.”*

Challenges of the clinical trial

Clinical sites require

- ▶ short measurement time (22 min)
- ▶ use of product sequences

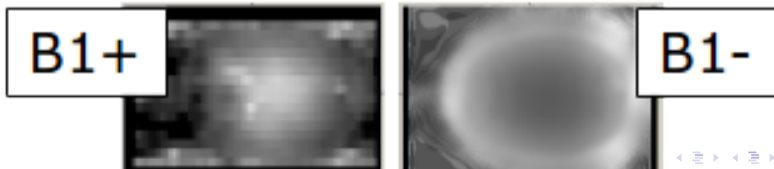
Challenges of the clinical trial

Clinical sites require

- ▶ short measurement time (22 min)
- ▶ use of product sequences

Multi-centre & long-time study requires

- ▶ harmonization of different HW/SW versions
- ▶ quantitative methods \Rightarrow reduced instrumental bias
- ▶ minimize instrumental bias by mapping of RF transmit and receive field inhomogenieties

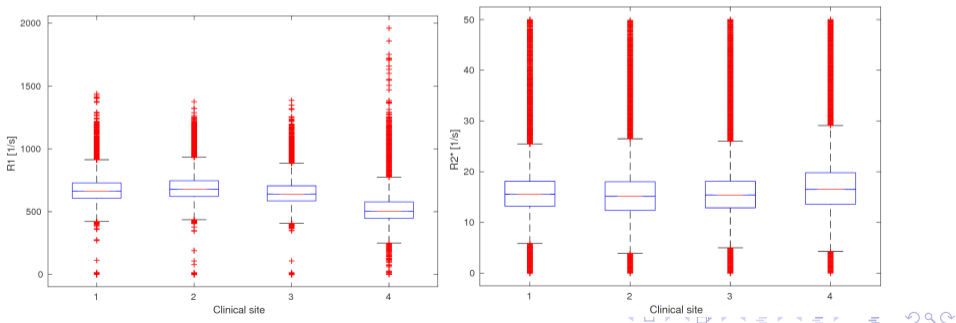


Traveling heads study

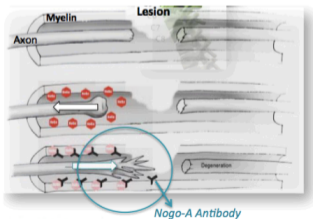
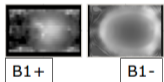
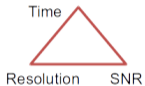
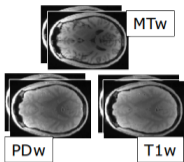
- ▶ test-retest measurements
- ▶ 5 healthy subjects visting 4 clinical sites
- ▶ 3 different Siemens scanners, 1 Philips scanner

Traveling heads study

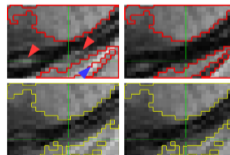
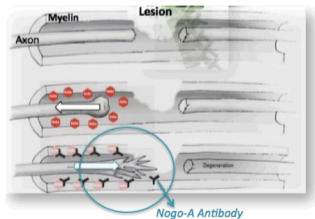
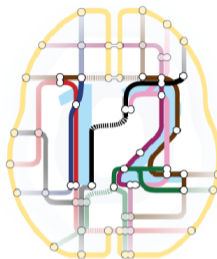
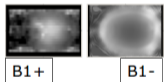
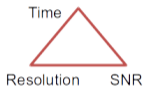
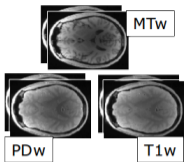
- ▶ test-retest measurements
 - ▶ 5 healthy subjects visiting 4 clinical sites
 - ▶ 3 different Siemens scanners, 1 Philips scanner
- ⇒ high repeatability (<7%) and inter-site comparability (<5%)
– for now only for Siemens scanners



Intermediate graphical summary



Intermediate graphical summary

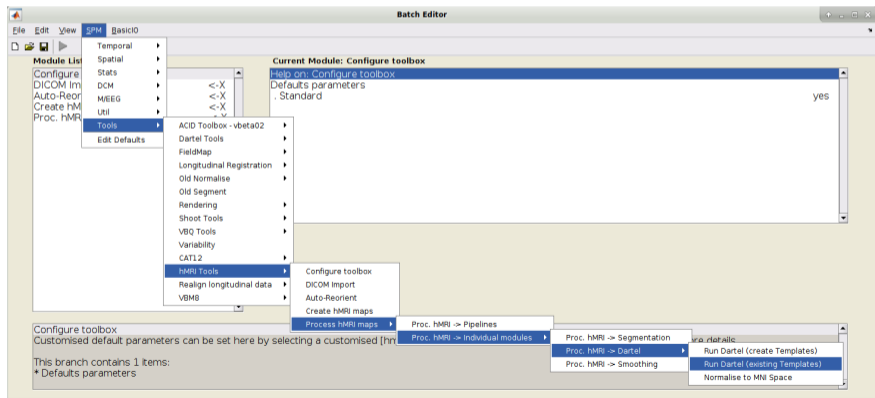


Data processing tools

hMRI-Toolbox

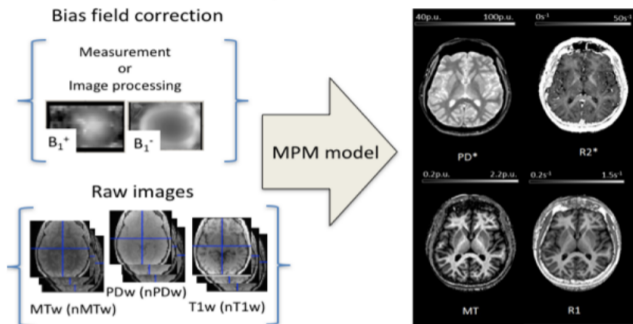
What is the hMRI-Toolbox?

- ▶ SPM toolbox for quantitative MRI and *in vivo* histology
- ▶ formerly known as VBQ-Toolbox (Voxel Based Quantification)



Basic functionality of the hMRI-Toolbox

Map Creation



[E. Balteau: ISMRM 2018 abstract #6545]

- ▶ input of PD-, T1- and MT-weighted multi-echo data
- ▶ output of quantitative maps ($R1$, $R2^*$, MT , PD) with meta-data
- ▶ value preservation by tissue specific normalisation

hMRI-Toolbox developments (I/II)

Main changes

- ▶ standardised, clear structure and pipeline for qMRI-data
- ▶ RF transmit and receive field methods refined and extended for multi-vendor support
- ▶ include meta-data (BIDS, JSON)

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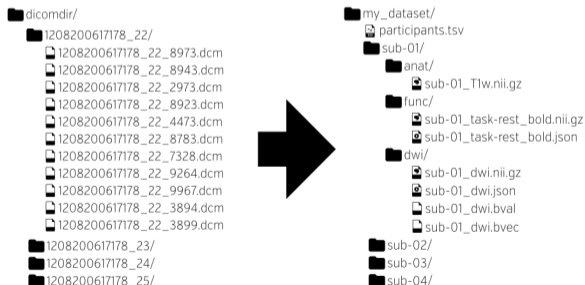
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  1208200617178_22/  
    1208200617178_22_8973.dcm  
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    1208200617178_22_4473.dcm  
    1208200617178_22_8783.dcm  
    1208200617178_22_7328.dcm  
    1208200617178_22_9264.dcm  
    1208200617178_22_9967.dcm  
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  1208200617178_23/  
  1208200617178_24/  
  1208200617178_25/
```

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Brain
Imaging
Data
Structure

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```
s2017-08-12_09-56-1022D...00176-1_R1_UNICORT.json
1  {
2    "history": {
3      "procstep": {
4        "descrip": "UNICORT",
5        "version": "v0.1.0-338-g465f1c3\n",
6        "procpars": {
7          "reg": 0.001,
8          "pmm": 60,
9          "thr": 2
10       }
11     },
12     "input": {
13       "filename": "\\data\\pt_phy048\\SD\\HD\\THIS\\maps\\502\\M01\\iPAT2\\UNICORT\\Results\\Supplementary\\s2017-08-12_09-56-102202-00001-00176-1_PDw.nii",
14       "history": {
15         "procstep": {
16           "descrip": "MPM calculation",
17           "version": "v0.1.0-338-g465f1c3\n",
18           "procpars": {
19             "json": {
20               "extended": false,
21               "separate": true,
22               "anonym": "none",
23               "overwrite": true,
24               "indent": "\\t"
25             }
26           }
27         }
28       }
29     }
30   }
31 }
```

Java
Script
Object
Notation

hMRI-Toolbox developments (II/II)

Newly integrated

- ▶ AC-PC realignment script improves segmentation
- ▶ enhanced TPMs from Lausanne based on MPMs
- ▶ TE=0 approximation to minimize R2* bias
- ▶ quality control measures included (R2* std, realign parameters)
- ▶ process datasets without MTw images
- ▶ publicly available at www.hmri.info

hMRI-Toolbox developments (II/II)

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Enterprise This repository Search Explore Sign in

hMRI-group / **Toolbox**
forked from VBO-toolbox-group/hMRI-Toolbox-public

Watch 1 Star 0 Fork 4

Code Pull requests 2 Projects 0 **Wiki** Pulse Graphs

No description, website, or topics provided.

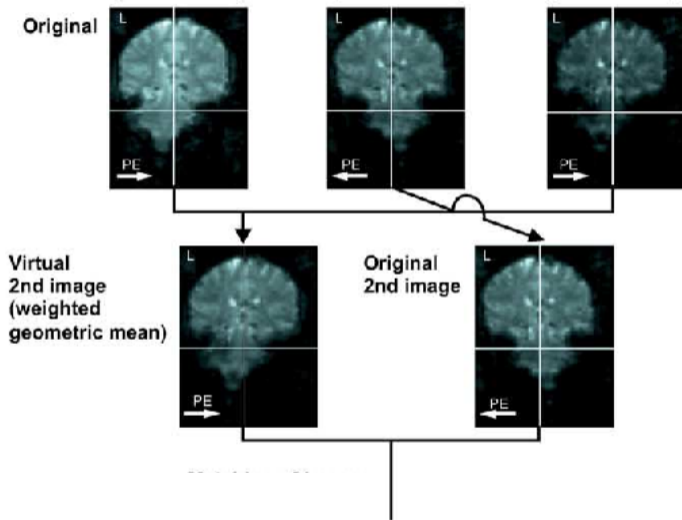
427 commits 1 branch 2 releases 7 contributors

Branch: master New pull request Find file Clone & download

scroll down for README

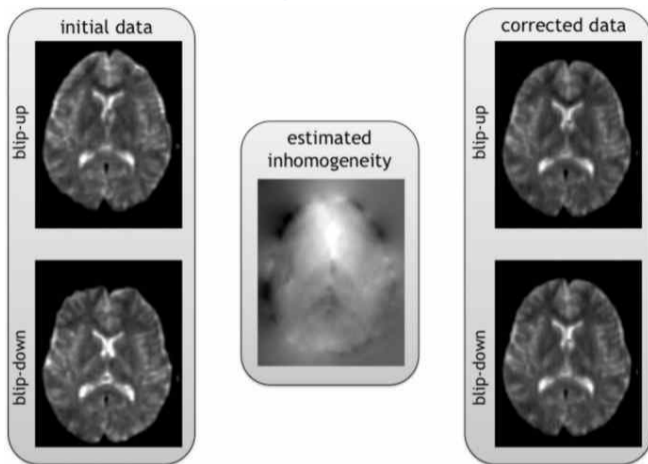
Distortions from bipolar readout...

... undistortion without any additional measurement (I/II)



N. Weiskopf: NeuroImage **24** 1068 – 1079, 2005.

... undistortion without any additional measurement (II/II)



HySCO - Hyperelastic Susceptibility Artefact Correction
L. Ruthotto: Phys Med Biol **57**(18) 5715 – 5731, 2012.

Undistorted multi-echo data

Undistorted multi-echo data

Summary

Quantitative MRI biomarkers

- ▶ multi-parameter mapping (MPM) offers measures for iron, myelin, water & macromolecule content
- ▶ longitudinal and cross-sectional studies
- ▶ investigation of structural *in vivo* changes (hMRI)

hMRI-toolbox

- ▶ MPM data \Rightarrow quantitative maps of R1, R2*, MT and PD
- ▶ spatial normalisation preserves quantitative values, taking tissue classes into account
- ▶ MPM data and maps accompanied with JSON meta-data and BIDS compatible data structure



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Bogdan Draganski (LREN)	Karsten Tabelow (WIAA)
Lars Ruthotto (Emory)	Gunther Helms (Lund)
Gabriel Ziegler (DZNE)	Enrico Reimer
Siawoosh Mohammadi (UKE)	Kerrin Pine
	Nikolaus Weiskopf

Thank **you** for your attention!



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