



Success story of an MSCA ITN Alumnus

Nuno Pedrosa de Barros, PhD

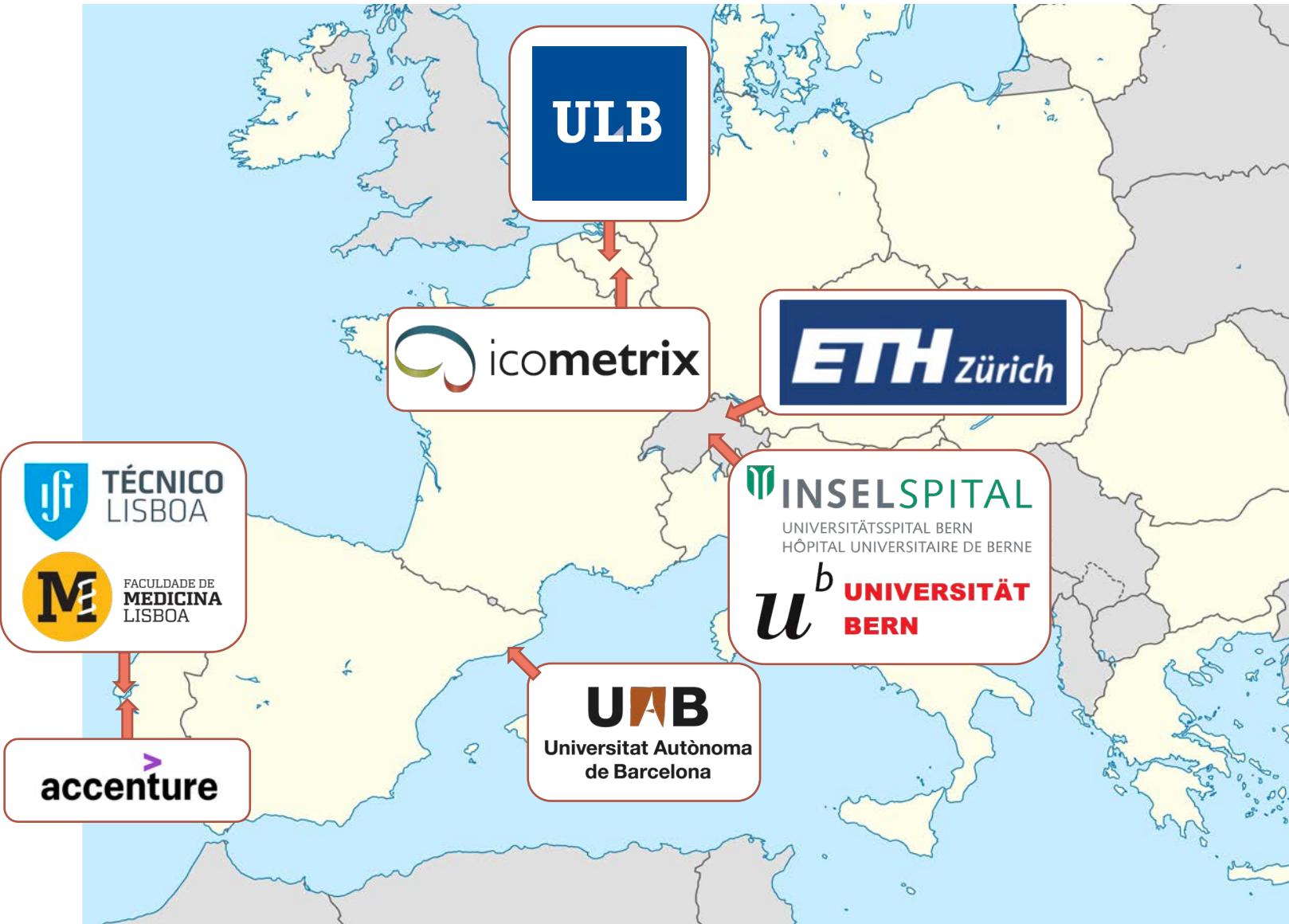
“Success”

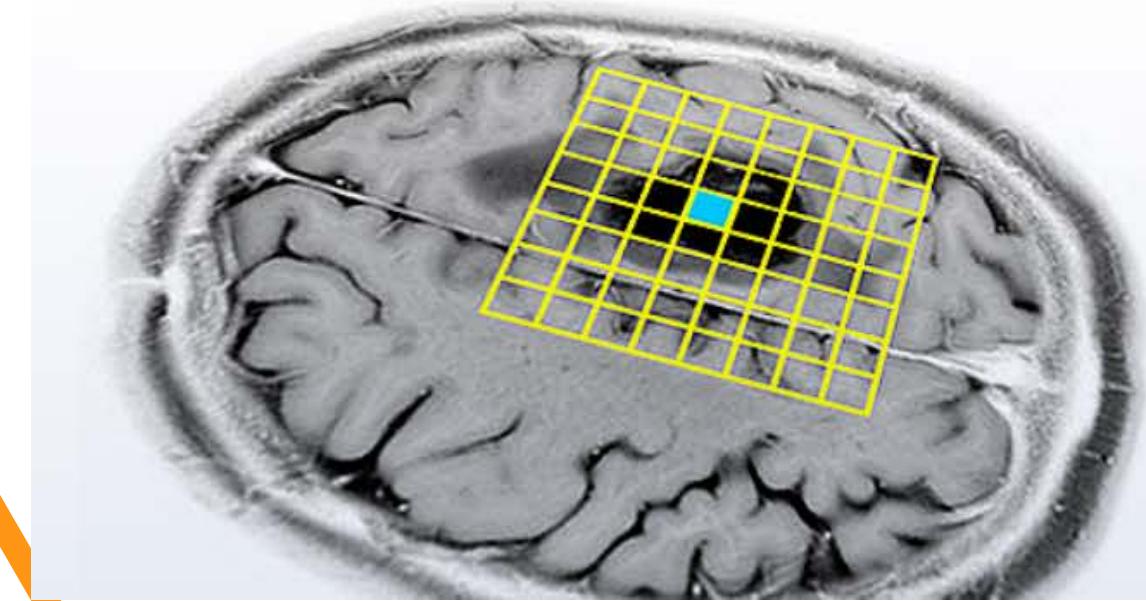
- What does a “Successful” PhD mean for **you**?
- What are **main goals** that you want to achieve during **your PhD**?
- What is the career path that **you** desire?





My story





Welcome to Transact!

Transforming Magnetic Resonance
Spectroscopy into a Clinical Tool



[FIND OUT MORE](#)

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TRANSACT

- Aim of the ITN: Improve clinical use of MRS
- 10 full partners
- Coordinator: KU Leuven ESAT (Prof. Sabine Van Huffel, Prof. Uwe Himmelreich, Dr. Diana Sima)
- 13 ESRs
- My role:
 - ESR 8 - Develop a software tool for the clinical use of MRS

TRANSACT

TRANSforming
Magnetic Resonance Spectroscopy
into **A**
Clinical Tool

ACRONYMFY!

Transforming Magnetic Resonance Spectroscopy into a clinical tool

Example Search

Found 1585 acronyms in 18.10 seconds.

Showing acronyms spanning at least 4 words: 

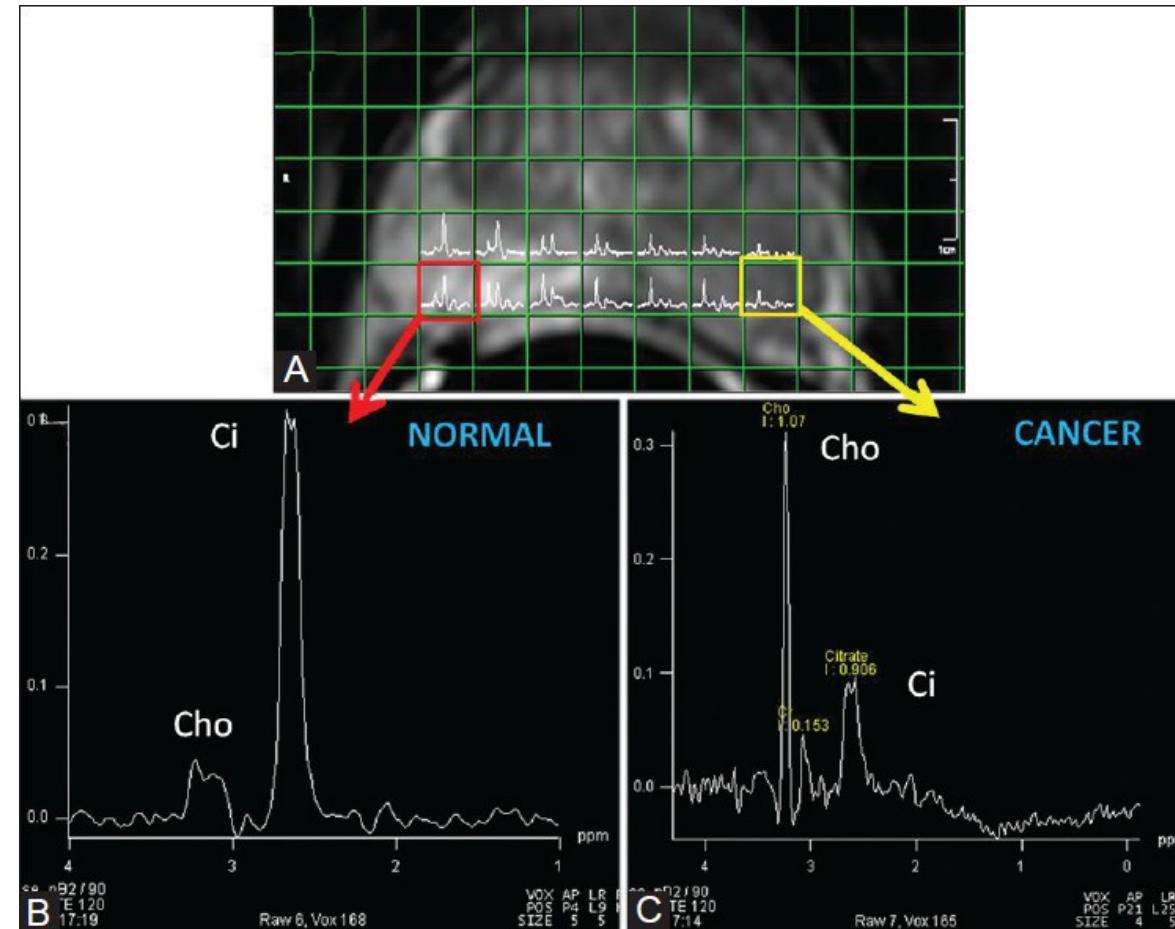
Acronym	Expanded	Score
INTACT	INTo A Clinical Tool	2.00
TRANSACT	TRANSforming A Clinical Tool	2.00
TRACT	TRansforming A Clinical Tool	2.00
TACT	Transforming A Clinical Tool	2.00
TACIT	Transforming A Clinical Tool	2.00

Magnetic Resonance Spectroscopy

- MR Spectroscopy is a method that allows to evaluate the chemical composition of a given tissue, **non-invasively**;
- Requires the same hardware as MRI

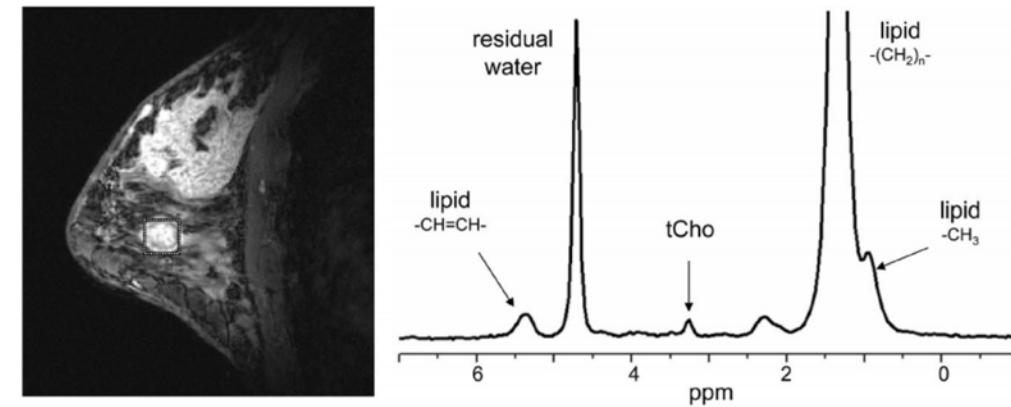
MR Spectroscopy in different organs

- Prostate



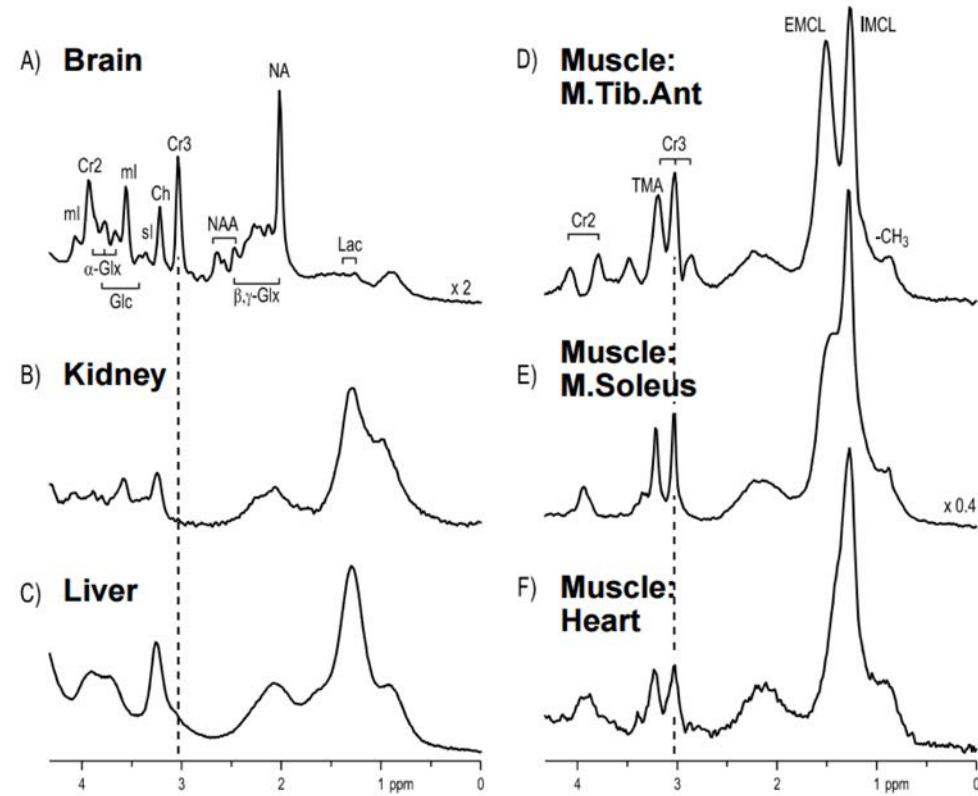
MR Spectroscopy in different organs

- Prostate
- Breast



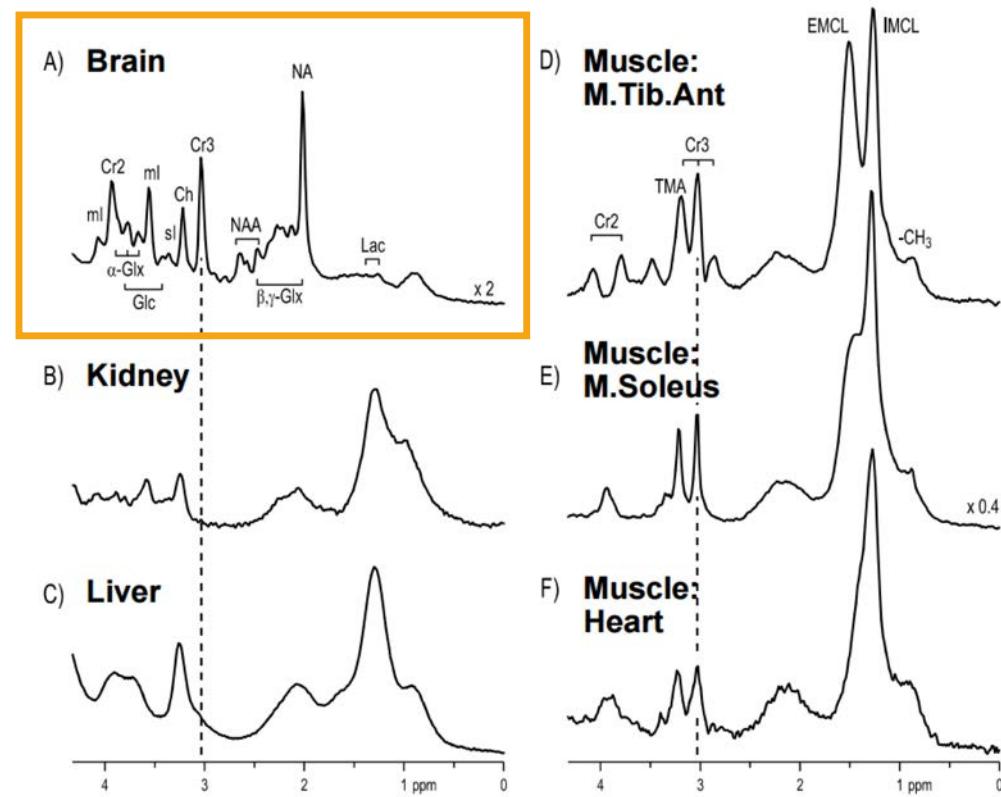
MR Spectroscopy in different organs

- Prostate
- Breast
- Brain
- Kidney
- Liver
- Heart
- Skeletal muscle



MR Spectroscopy in different organs

- Prostate
- Breast
- Brain
- Kidney
- Liver
- Heart
- Skeletal muscle

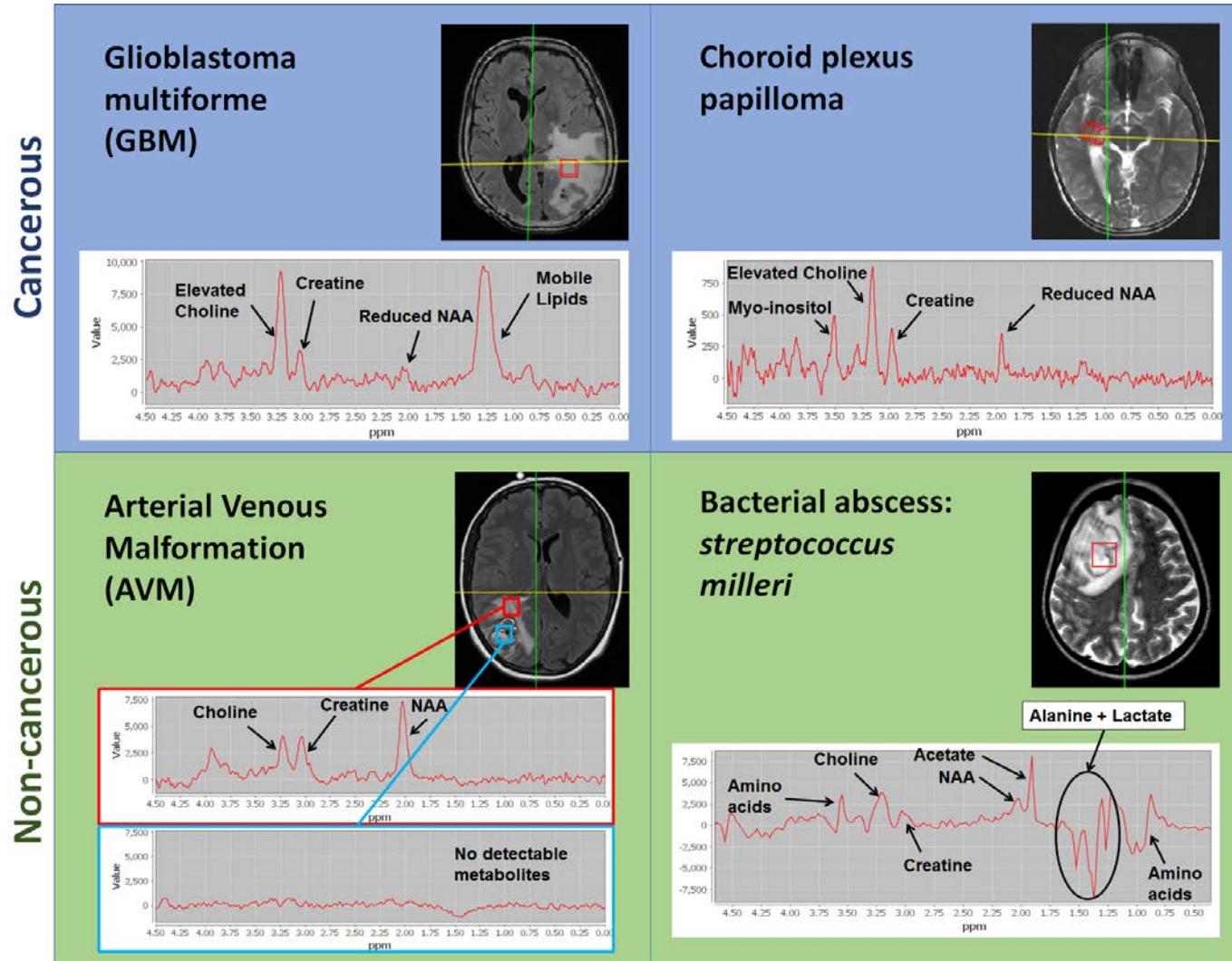


MRS in brain tumours

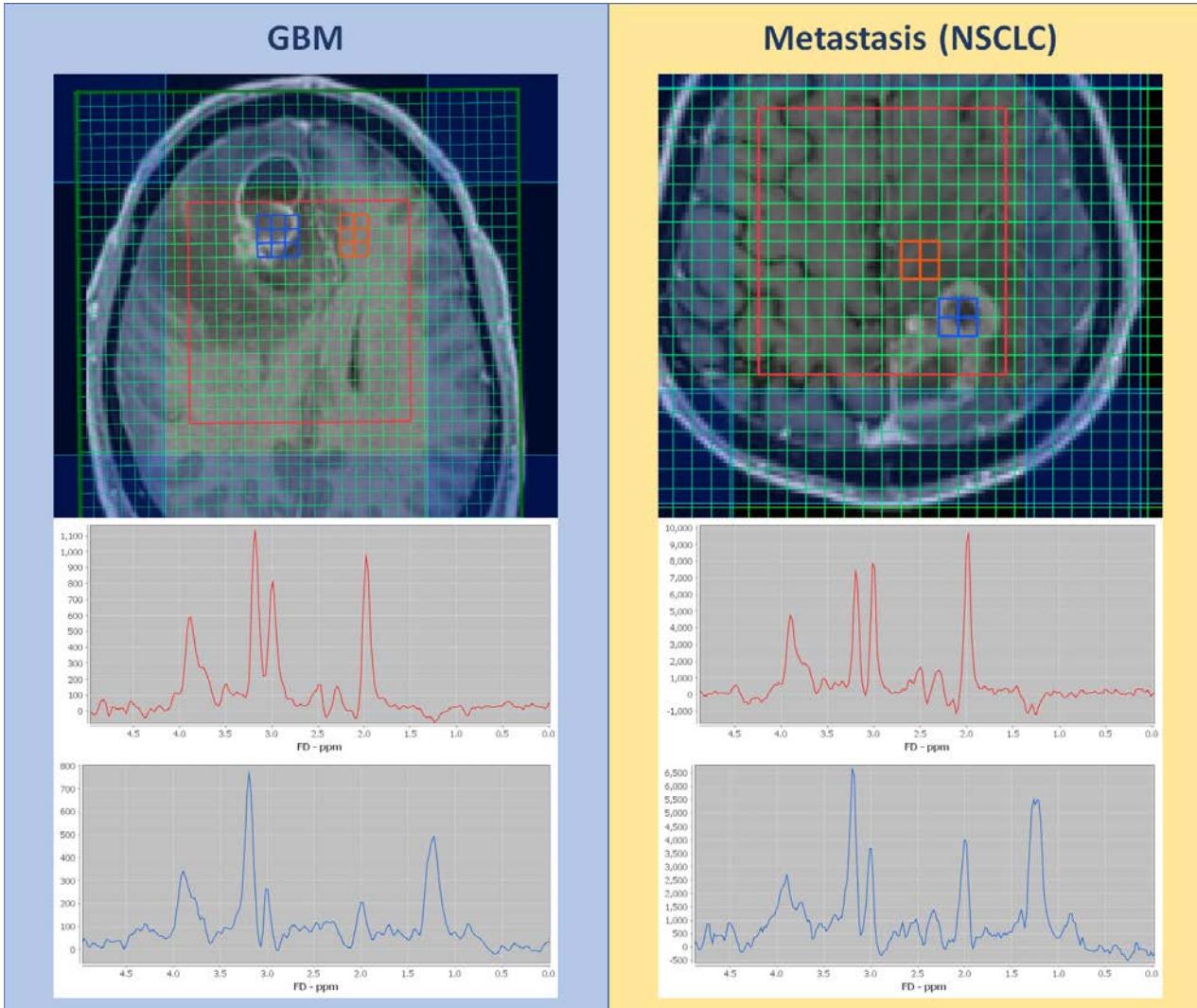
Main applications:

1. Tumor vs non-cancerous lesion;
2. Metastasis vs high-grade tumor;
3. Low-grade vs high-grade tumor;
4. Tumor-progression vs radiation necrosis;
5. Tumor border delineation;

Tumor vs non-cancerous lesion



GBM vs Metastasis



MRS, the pitfalls

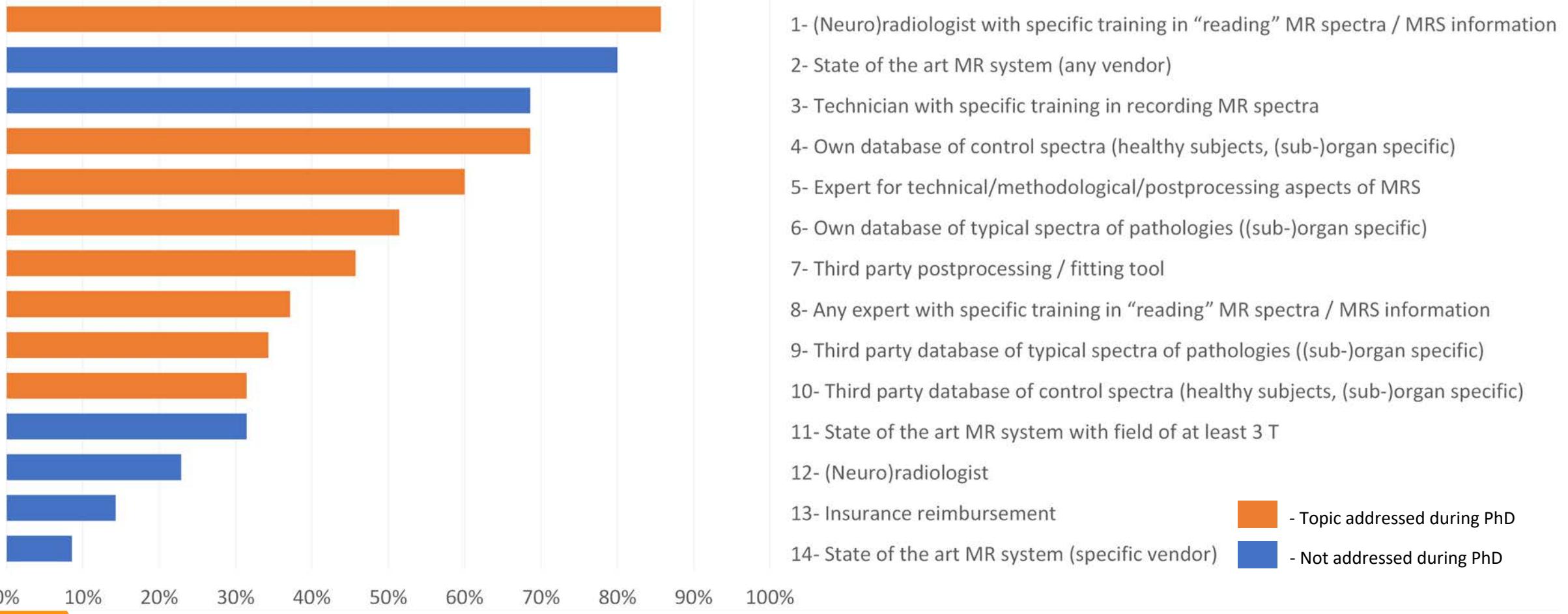
- Low SNR (signals from metabolites with much lower concentration than water - 10000x smaller!)
- Only a few metabolites can be measured *in vivo*;
- Complexity (Acquisition, Post-processing, Interpretation);
- Time-consuming (Acquisition, Post-processing);
- Very sensitive to field inhomogeneities;
- Niche market, mainly used in a few University Hospitals and in research centres;
- Limited tools available for processing MRS;

Survey

- *"What does it take for an MR site to perform MRS exams that can be useful for patient management?"*
- Roland Kreis, 2012
- 35 professionals from various hospitals
- 15 different countries
- Each participant could select any number of items from a predefined list

Survey

"What it takes for MRS?" survey by R. Kreis 2012



Research article

Received: 12 August 2015, Revised: 25 November 2015, Accepted: 25 November 2015, Published online in Wiley Online Library: 29 February 2016
(wileyonlinelibrary.com) DOI: 10.1002/nbm.3470

Automatic quality control in clinical ^1H MRSI of brain cancer

Nuno Pedrosa de Barros*, Richard McKinley, Urs Peter Knecht,
Roland Wiest and Johannes Slotboom

MRSI grids frequently show spectra with poor quality, mainly because of the high sensitivity of MRS to field inhomogeneities. These poor quality spectra are prone to quantification and/or interpretation errors that can have a significant impact on the clinical use of spectroscopic data. Therefore, quality control of the spectra should always precede their clinical use. When performed manually, quality assessment of MRSI spectra is not only a tedious and time-consuming task, but is also affected by human subjectivity. Consequently, automatic, fast and reliable methods for spectral quality assessment are of utmost interest. In this article, we present a new random forest-based method for automatic quality assessment of ^1H MRSI brain spectra, which uses a new set of MRS signal features. The random forest classifier was trained on spectra from 40 MRSI grids that were classified as acceptable or non-acceptable by two expert spectroscopists. To account for the effects of intra-rater reliability, each spectrum was rated for quality three times by each rater. The automatic method classified these spectra with an area under the curve (AUC) of 0.976. Furthermore, in the subset of spectra containing only the cases that were classified every time in the same way by the spectroscopists, an AUC of 0.998 was obtained. Feature importance for the classification was also evaluated. Frequency domain skewness and kurtosis, as well as time domain signal-to-noise ratios (SNRs) in the ranges 50–75 ms and 75–100 ms, were the most important features. Given that the method is able to assess a whole MRSI grid faster than a spectroscopist (approximately 3 s versus approximately 3 min), and without loss of accuracy (agreement between classifier trained with just one session and any of the other labelling sessions, 89.88%; agreement between any two labelling sessions, 89.03%), the authors suggest its implementation in the clinical routine. The method presented in this article was implemented in JMRUI's Spectrlm plugin. Copyright © 2016 John Wiley & Sons, Ltd.

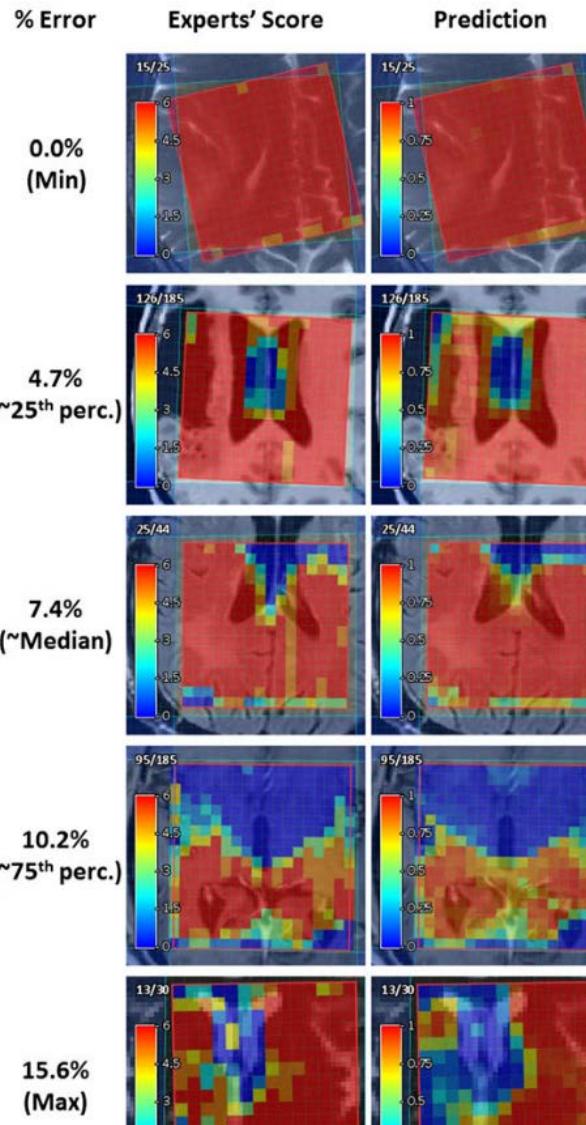
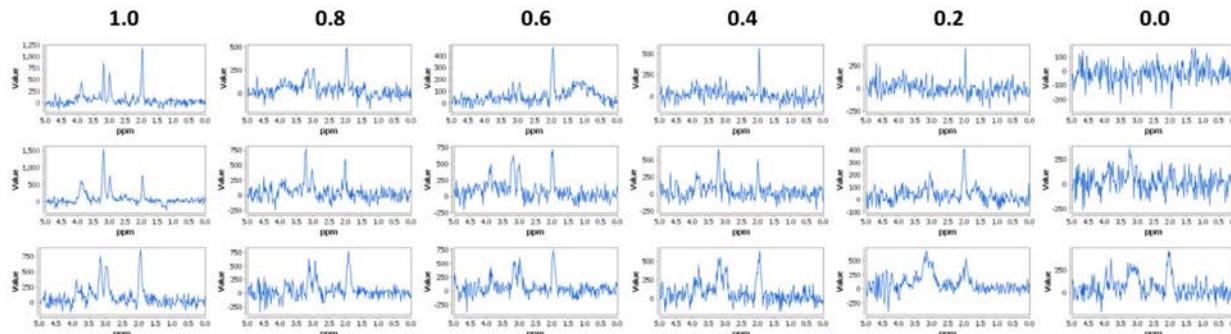
Keywords: MRSI; quality control; brain cancer; pattern recognition; automatic classification; spectral features

INTRODUCTION

Localised *in vivo* MRS provides important biochemical information on living tissues, and has proven its added value, for example, in brain tumour diagnostics and the evaluation of inborn diseases. However, *in vivo* MRS signals are very sensitive to susceptibility differences and, consequently, close to bone-tissue and tissue-air interfaces, as well as in the presence of post-operative paramagnetic particles, artefacts are often found (1). Other factors, such as bone marrow and subcutaneous lipid contamination, uncompensated eddy currents and poor water suppression, can negatively affect the quality of the spectra and consequently reduce their

concentrations of group data, as well as prevent the clinical use of MRS in any disease leading to low metabolite levels. Other metrics, such as ER-ARSOS (5,7), have been proposed for the estimation of the error in metabolite quantification using single-voxel spectroscopic (SVS) data. ER-ARSOS differs from theoretical error estimators, such as CRLB, in that it is obtained experimentally. Nevertheless, given that it requires multiple signals acquired in the process of signal averaging, it is specific to SVS.

Manual quality checking of MRSI recordings requires much time, and can only be performed by expert users. What constitutes a good quality spectrum varies between MR users, mainly depending



Improving Labeling Efficiency in Automatic Quality Control of MRSI Data

Nuno Pedrosa de Barros,^{1,2*} Richard McKinley,^{1,2} Roland Wiest,^{1,2} and Johannes Slotboom^{1,2}

Purpose: To improve the efficiency of the labeling task in automatic quality control of MR spectroscopy imaging data.

Methods: 28/432 short and long echo time (TE) spectra (1.5 tesla; point resolved spectroscopy (PRESS); repetition time (TR)=1,500 ms) from 18 different brain tumor patients were labeled by two experts as either accept or reject, depending on their quality. For each spectrum, 47 signal features were extracted. The data was then used to run several simulations and test an active learning approach using *uncertainty sampling*. The performance of the classifiers was evaluated as a function of the number of patients in the training set, number of spectra in the training set, and a parameter α used to control the level of classification uncertainty required for a new spectrum to be selected for labeling.

Results: The results showed that the proposed strategy allows reductions of up to 72.97% for short TE and 62.09% for long TE in the amount of data that needs to be labeled, without significant impact in classification accuracy. Further reductions are possible with significant but minimal impact in performance.

Conclusion: Active learning using uncertainty sampling is an effective way to increase the labeling efficiency for training automatic quality control classifiers. *Magn Reson Med* 78:2399–2405, 2017. © 2017 International Society for Magnetic Resonance in Medicine.

Key words: MRSI; quality control; artifact detection; machine learning; active learning; labeling efficiency

INTRODUCTION

Bad-quality spectra are commonly observed in *in vivo* MRS. Multiple factors can cause MR spectroscopy signal artifacts, a topic that is extensively covered in the work of Kreis (1). Bad-quality spectra may prevent proper

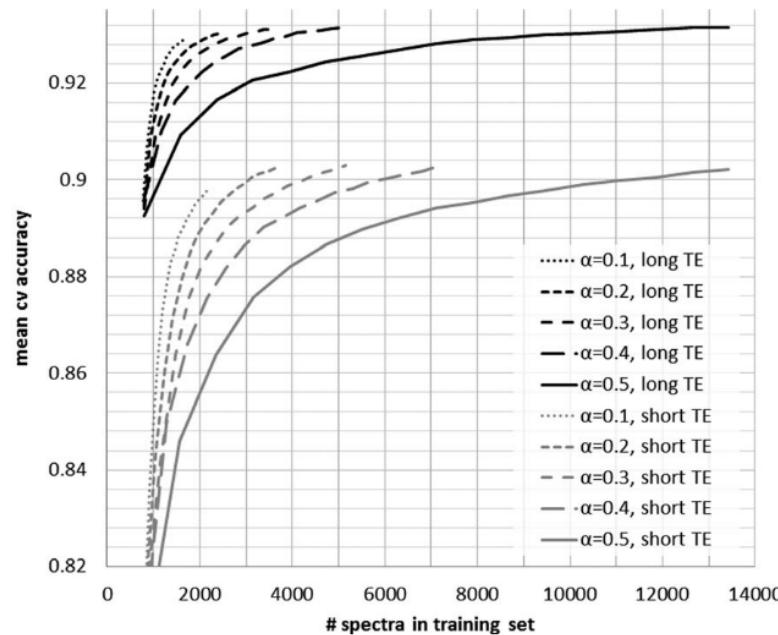
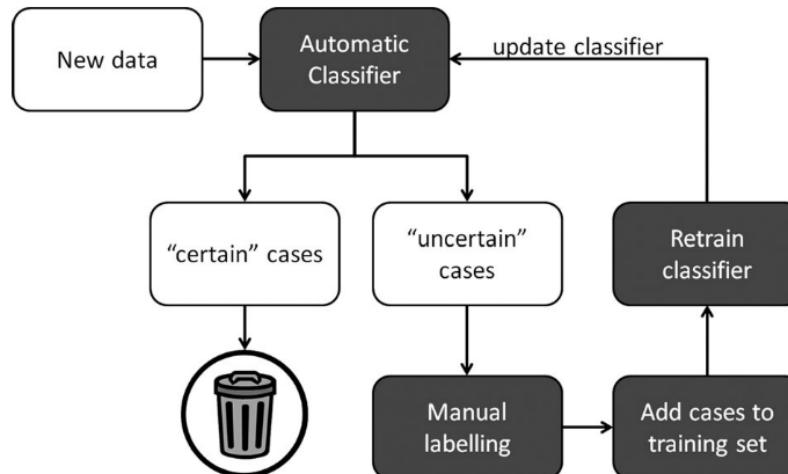
evaluation of the quality of the quantification (2) and the associated error (3–8). For the identification of artifacts, simple visual inspection is generally performed; nevertheless, this is only possible for single voxel acquisitions and when an expert is available. In the case of multi-voxel acquisitions, thousands of spectra are usually generated in just one acquisition, making the visual inspection of all the data a Sisyphean task.

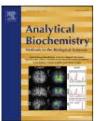
In order to automatize artifact and poor signal-to-noise ratio (SNR) detection in MRSI, a few machine-learning-based methods have been proposed (9–12). Such methods allow to check thousands of spectra in a matter of seconds with a performance that is identical to manual inspection (11,12) performed by human MRS experts. Besides the obvious time-saving potential of these methods, a considerable amount of time is needed for manually labeling the data that is used for training the automatic classifiers.

The selection of the training samples often is done by identifying a reasonable amount of MRSI acquisitions and by labeling all the corresponding spectra. However, not every individual spectrum provides relevant information to the learning algorithm, and the dependency that the training sample size has on the classifier performance often is not analyzed.

Labeling efficiency can be increased with the use of active learning approaches (13–19), where the learning method can actively select the subset of examples that need to be labeled by the user. This is an iterative process in which 1) the algorithm selects a subset of examples; 2) the user labels these selected examples; and 3) the learning method is updated with the new data before selecting again more data for labeling.

Uncertainty sampling (20) is a sampling strategy used in active learning that gives priority to the selection of those





Quality management in *in vivo* proton MRS

Nuno Pedrosa de Barros ^{a, b,*}, Johannes Slotboom ^b

^a University of Bern, Switzerland

^b Support Center for Advanced Neuroimaging, Inselspital, Bern, Switzerland



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ABSTRACT

The quality of MR-Spectroscopy data can easily be affected in *in vivo* applications. Several factors may produce signal artefacts, and often these are not easily detected, not even by experienced spectroscopists. Reliable and reproducible *in vivo* MRS-data requires the definition of quality requirements and goals, implementation of measures to guarantee quality standards, regular control of data quality, and a continuous search for quality improvement.

The first part of this review includes a general introduction to different aspects of quality management in MRS. It is followed by the description of a series of tests and phantoms that can be used to assure the quality of the MR system. In the third part, several methods and strategies used for *quality control* of the spectroscopy data are presented. This review concludes with a reference to a few interesting techniques and aspects that may help to further improve the quality of *in vivo* MR-spectra.

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1. Introduction

Quality management has four major components [1]:

- 1 Quality planning;
- 2 Quality assurance;
- 3 Quality control;
- 4 Quality improvement;

Quality planning consists in the definition of quality requirements and goals. *Quality assurance* deals with the prediction of possible errors and defines a set of measures to prevent them. *Quality control*, on the other hand, deals with situations where errors are created and its main aim is to detect them and avoid that these cause further complications. Finally, *quality improvement*

different sites, and frequently with different measurement conditions, is combined [2,3]. In multi-centre studies, apart from the quality management performed at the level of each centre, further measures need to be implemented to ensure data compatibility.

It is important to understand that *none* of the four quality management components are closed or independent. Tests performed in *quality assurance* can loosen or tighten quality requirements previously defined in *quality planning*, or even define new targets for *quality improvement*. Moreover, information collected in *quality control* may lead to new tests and prevention measures in *quality assurance*. And besides this, some actions may belong to more than one component. For example, as proposed by Milan Hájek et al. in Ref. [4], quantification calibration factors can be used both for *quality assurance*, improving the accuracy of the measurement, as well as for *quality control*, helping to detect

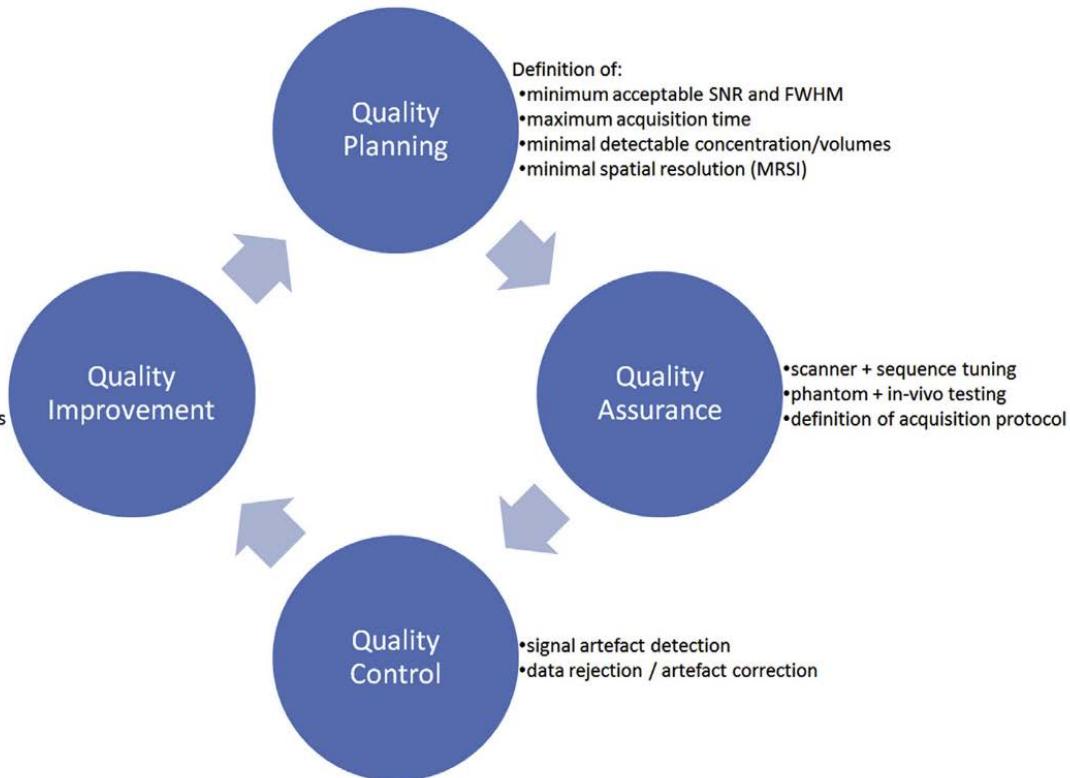
- hardware improvements
- sequence improvements
- evaluation of new sequences

Definition of:

- minimum acceptable SNR and FWHM
- maximum acquisition time
- minimal detectable concentration/volumes
- minimal spatial resolution (MRSI)

- scanner + sequence tuning
- phantom + *in-vivo* testing
- definition of acquisition protocol

- signal artefact detection
- data rejection / artefact correction



On the relation between MR spectroscopy features and the distance to MRI-visible solid tumor in GBM patients

Nuno Pedrosa de Barros¹ | Raphael Meier¹ | Martin Pletscher¹ | Samuel Stettler¹ | Urspeter Knecht¹ | Evelyn Herrmann² | Philippe Schucht³ | Mauricio Reyes⁴ | Jan Gralla¹ | Roland Wiest¹ | Johannes Slotboom¹

¹University Institute for Diagnostic and Interventional Neuroradiology, University of Bern, Bern, Switzerland

²Department of Radiation Oncology, University of Bern, Bern, Switzerland

³Department of Neurosurgery, University of Bern, Bern, Switzerland

⁴Institute for Surgical Technology and Biomechanics, University of Bern, Bern, Switzerland

Correspondence

Nuno Pedrosa de Barros, Neuroradiology, Inselspital, Freiburgstr. 4, CH-3010, Bern, Switzerland.
Email: nunopbarros@gmail.com
Twitter: @nunopbarros

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Purpose: To improve the detection of peritumoral changes in GBM patients by exploring the relation between MRSI information and the distance to the solid tumor volume (STV) defined using structural MRI (sMRI).

Methods: Twenty-three MRSI studies (PRESS, TE 135 ms) acquired from different patients with untreated GBM were used in this study. For each MRSI examination, the STV was identified by segmenting the corresponding sMRI images using BraTUMIA, an automatic segmentation method. The relation between different metabolite ratios and the distance to STV was analyzed. A regression forest was trained to predict the distance from each voxel to STV based on 14 metabolite ratios. Then, the trained model was used to determine the expected distance to tumor (EDT) for each voxel of the MRSI test data. EDT maps were compared against sMRI segmentation.

Results: The features showing abnormal values at the longest distances to the tumor were: %NAA, Glx/NAA, Cho/NAA, and Cho/Cr. These four features were also the most important for the prediction of the distances to STV. Each EDT value was associated with a specific metabolic pattern, ranging from normal brain tissue to actively proliferating tumor and necrosis. Low EDT values were highly associated with malignant features such as elevated Cho/NAA and Cho/Cr.

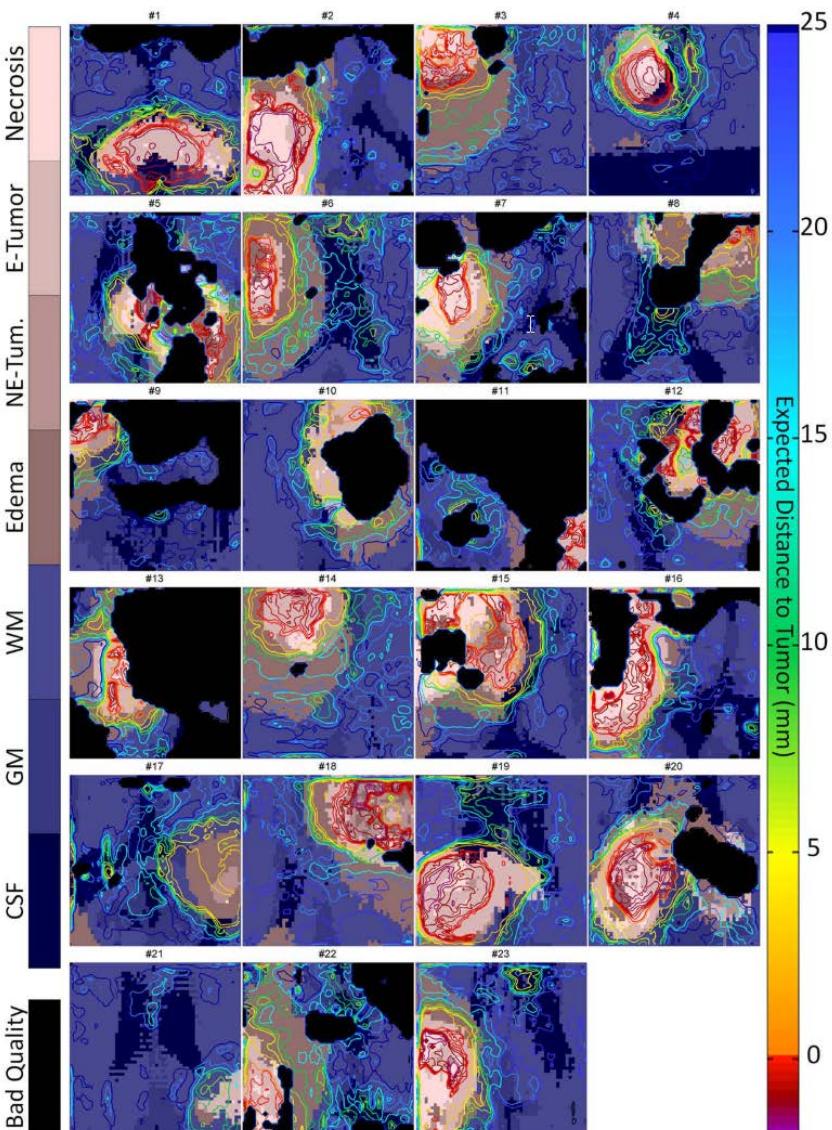
Conclusion: The proposed method enables the automatic detection of metabolic patterns associated with different distances to the STV border and may assist tumor delineation of infiltrative brain tumors such as GBM.

KEY WORDS

expected distance to tumor, GBM, MRSI, nosologic imaging, tumor delineation

1 | INTRODUCTION

Glioblastoma multiforme (GBM) is the most aggressive type





RESEARCH ARTICLE

Analysis of metabolic abnormalities in high-grade glioma using MRSI and convex NMF

Nuno Pedrosa de Barros¹ | Raphael Meier¹ | Martin Pletscher¹ | Samuel Stettler¹ | Urspeter Knecht¹ | Mauricio Reyes² | Jan Gralla¹ | Roland Wiest¹ | Johannes Slotboom¹

¹Support Center for Advanced Neuroimaging (SCAN), Neuroradiology, University Hospital Inselspital, Bern, Switzerland

²Institute for Surgical Technology and Biomechanics (ISTB), University of Bern, Bern, Switzerland

Correspondence

Nuno Pedrosa de Barros, Support Center for Advanced Neuroimaging (SCAN), Neuroradiology, University Hospital Inselspital, Bern, Switzerland.
Email: nuno@barros@gmail.com

Funding information

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Clinical use of MRSI is limited by the level of experience required to properly translate MRSI examinations into relevant clinical information. To solve this, several methods have been proposed to automatically recognize a predefined set of reference metabolic patterns. Given the variety of metabolic patterns seen in glioma patients, the decision on the optimal number of patterns that need to be used to describe the data is not trivial. In this paper, we propose a novel framework to (1) separate healthy from abnormal metabolic patterns and (2) retrieve an optimal number of reference patterns describing the most important types of abnormality. Using 41 MRSI examinations (1.5 T, PRESS, T_E 135 ms) from 22 glioma patients, four different patterns describing different types of abnormality were detected: *edema*, *healthy without Glx*, *active tumor* and *necrosis*. The identified patterns were then evaluated on 17 MRSI examinations from nine different glioma patients. The results were compared against BraTumIL, an automatic segmentation method trained to identify different tumor compartments on structural MRI data. Finally, the ability to predict future contrast enhancement using the proposed approach was also evaluated.

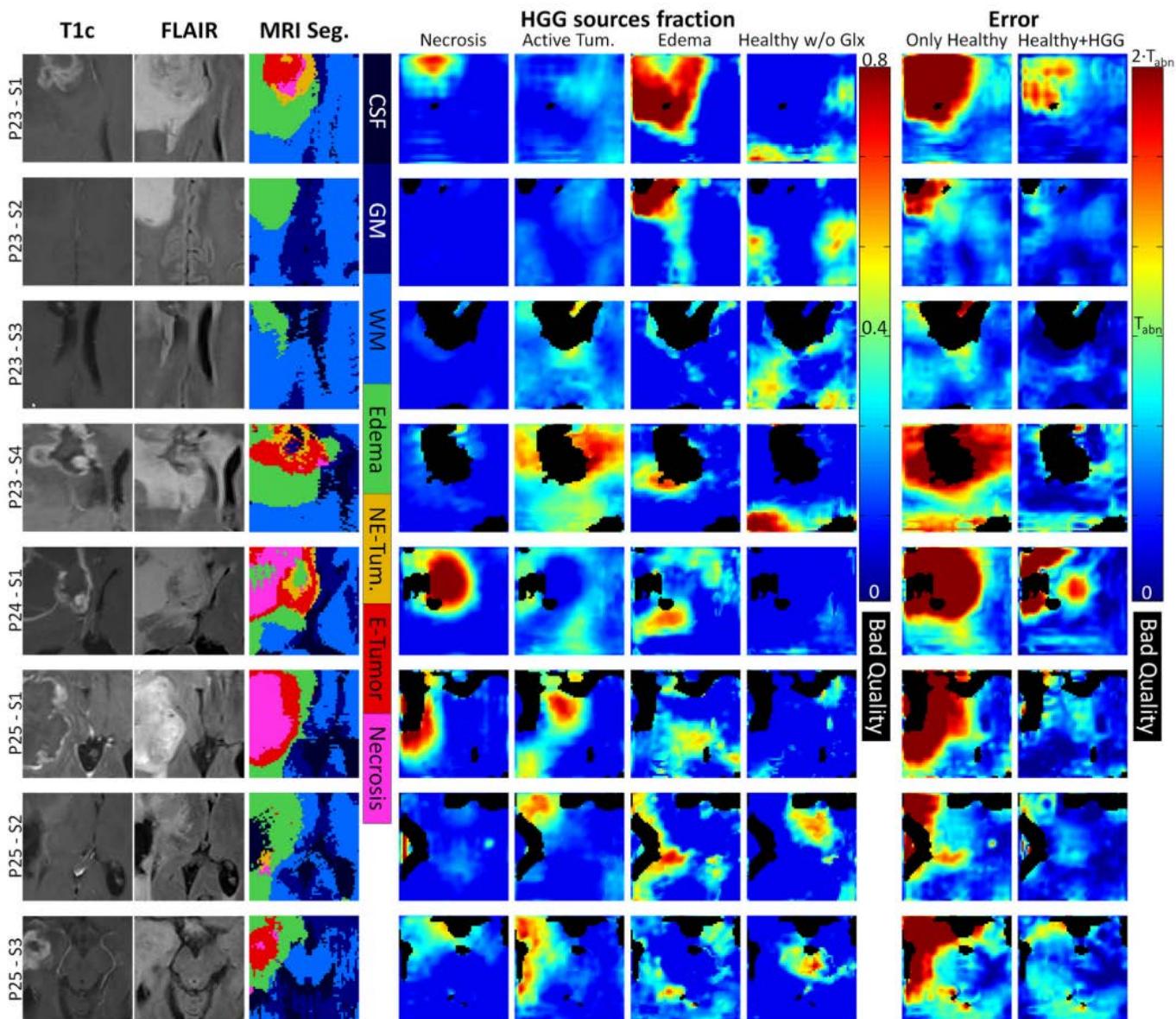
KEYWORDS

applications, cancer, head and neck cancer methods and engineering, MRS and MRSI methods, post-acquisition processing, spectroscopic imaging, visualization methods and engineering

1 | INTRODUCTION

MRS provides relevant metabolic information for the assessment of brain tumors, allowing us to distinguish different tumor types and grades,^{1–3} distinguish radiation effects (pseudoprogression) from true progression^{4,5} and identify regions with high tumor cellularity that are not visible in structural MRI.^{6–8} Many publications⁹ focus on the translation of one or two MRS features, such as choline (Cho)/NAA (N-acetyl aspartate) and Cho/Cr (creatinine), into clinically meaningful information for the tasks described above. Regardless of what can already be achieved with the analysis of individual metabolite ratios, the use of metabolic patterns for the identification of tissue types and diseases has the potential to allow more precise characterization of brain tumors.

Several approaches^{10–21} have been suggested for the analysis of metabolic patterns present in brain tumor MRS data. Before such methods



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^b
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Graduate School for Cellular and Biomedical Sciences
University of Bern

Improving the Clinical Use of Magnetic Resonance Spectroscopy for the Analysis of Brain Tumours using Machine Learning and Novel Post-Processing Methods

PhD thesis submitted by

Nuno Pedrosa de Barros

from Portugal

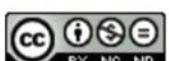
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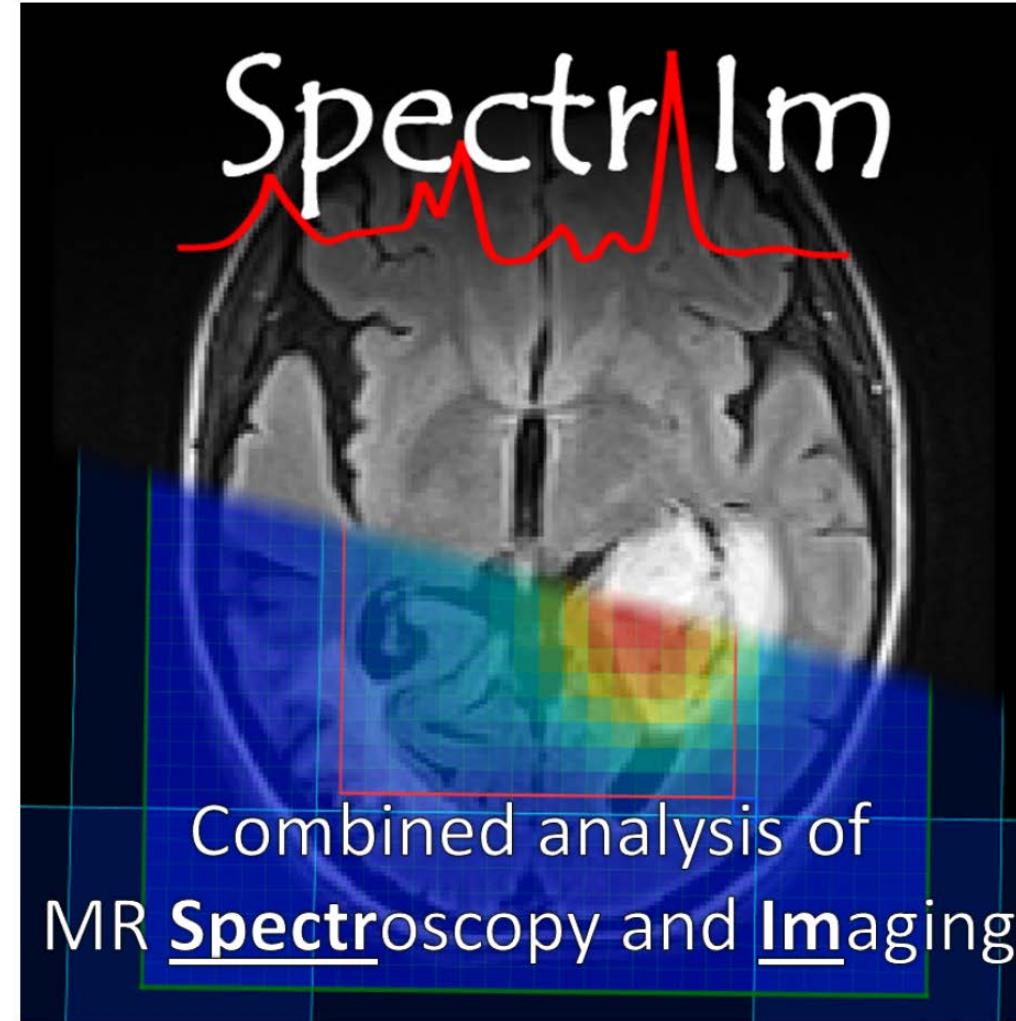
PhD in Biomedical Engineering

Supervisor: PD. Dr. Johannes Slotboom
Institute for Diagnostic and Interventional Neuroradiology
Faculty of Medicine of the University of Bern

Co-Advisor: Prof. Dr. Roland Kreis
Magnetic Resonance Spectroscopy and Methodology, Department of Clinical Research
Faculty of Medicine of the University of Bern

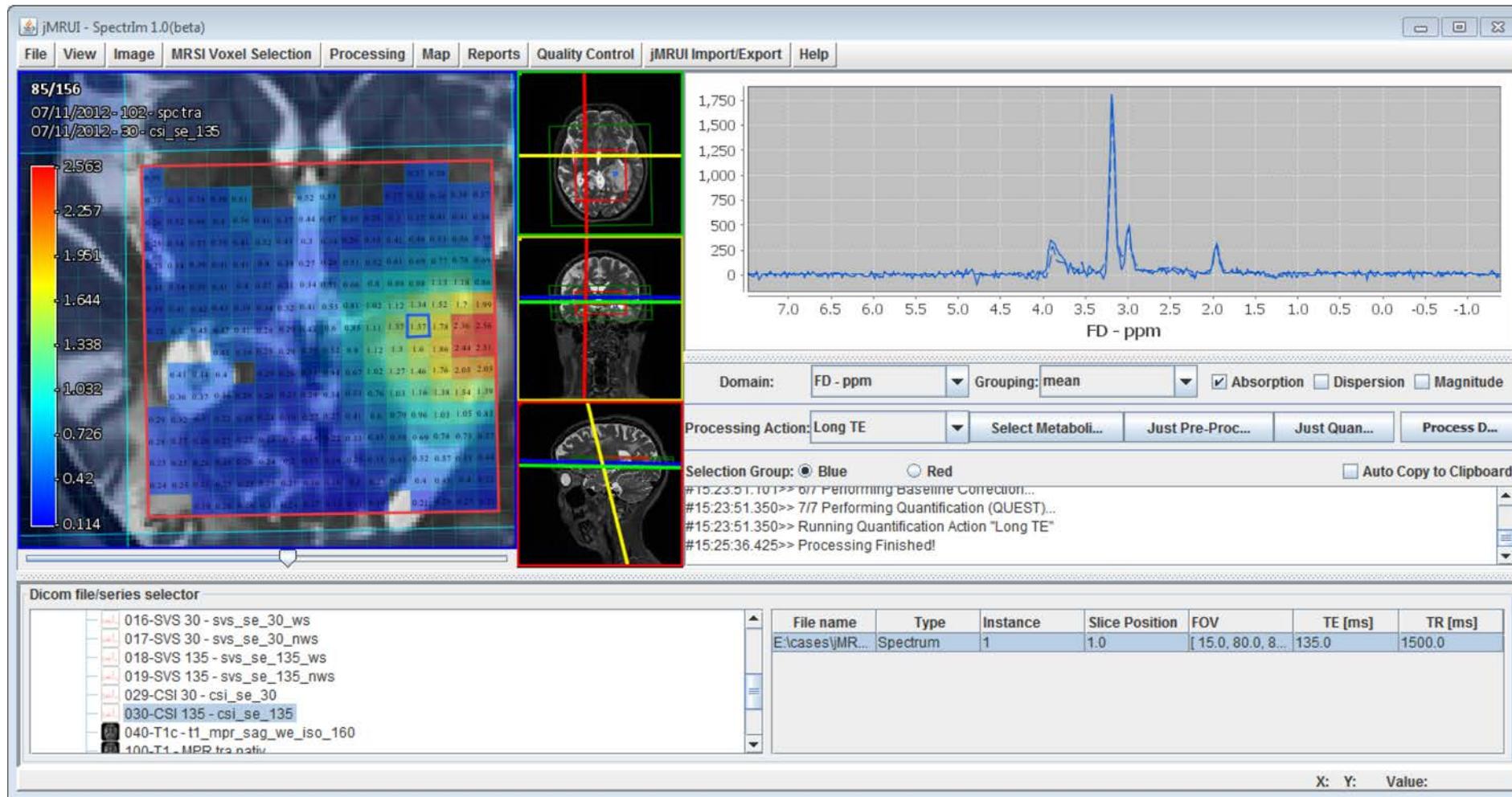
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Spectrlm

jMRUI
www.jmrui.eu





A few tips...

Find a clear goal!

- Having a clear goal will help you:
 - keep focus
 - keep motivated: getting closer to your goal will give you more energy to continue
 - making hard decisions: what options bring you closer to your goal?

Know the strengths of your institution!

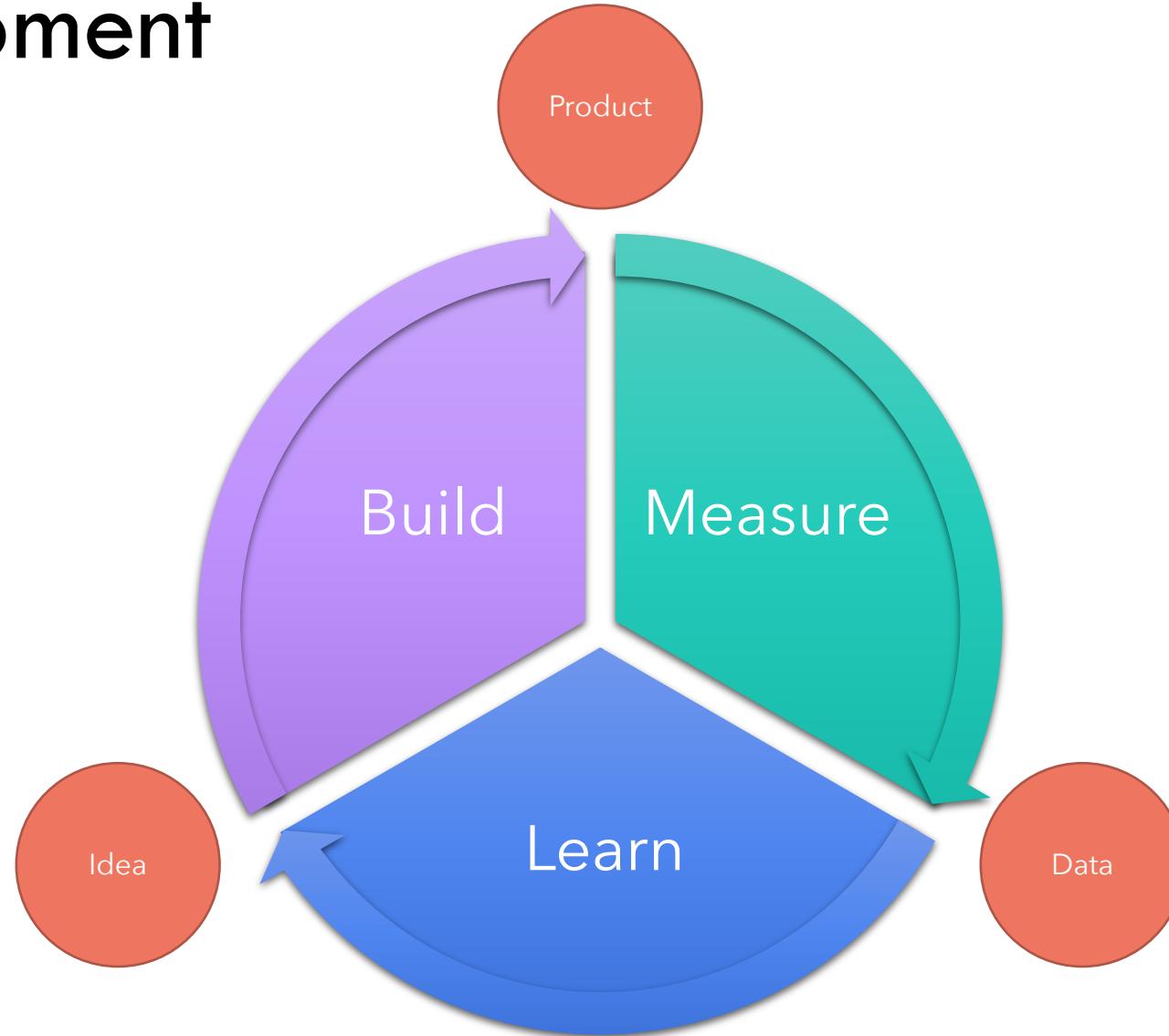


- Access to MRI scanners
- Access to local clinical data
- Direct collaboration with Clinicians

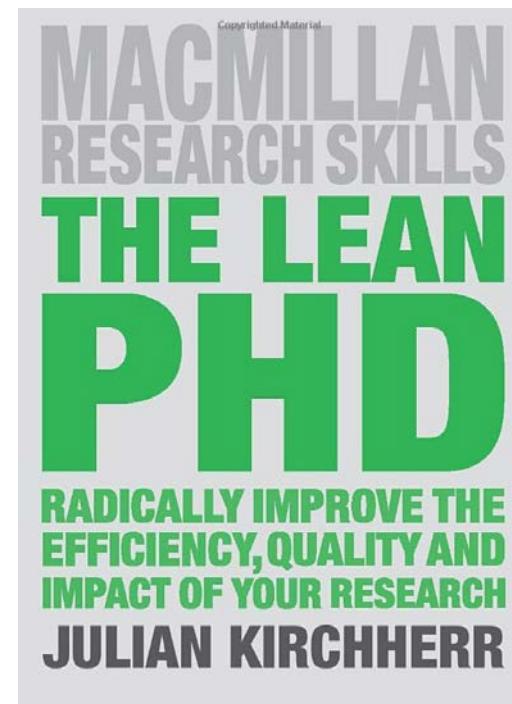
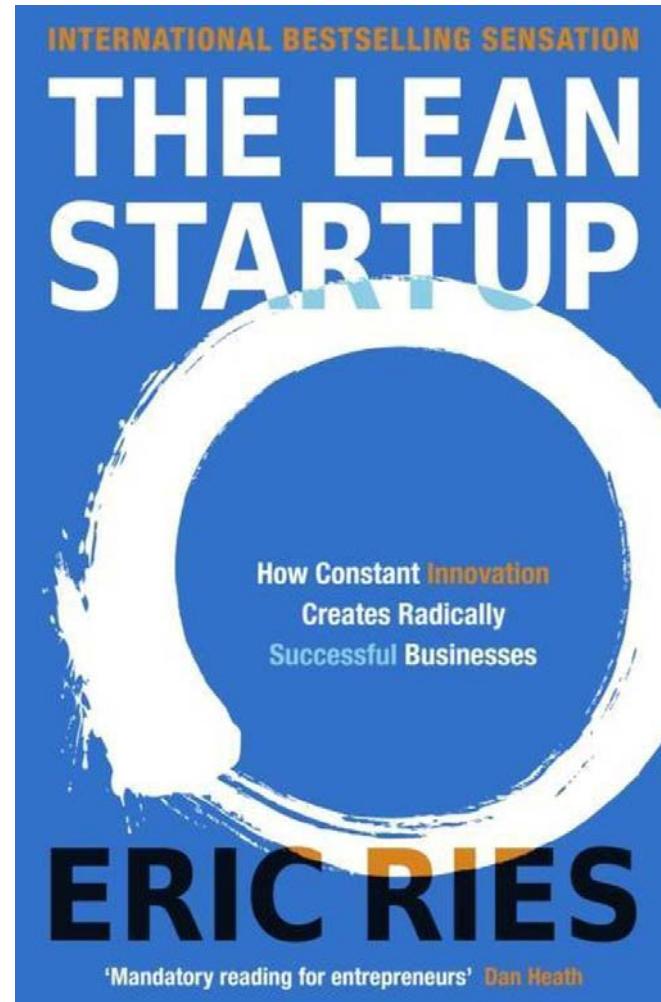


- Access to large imaging datasets
- Collaboration with IT, sales, marketing
- Clinical software development and certification know-how

Lean development

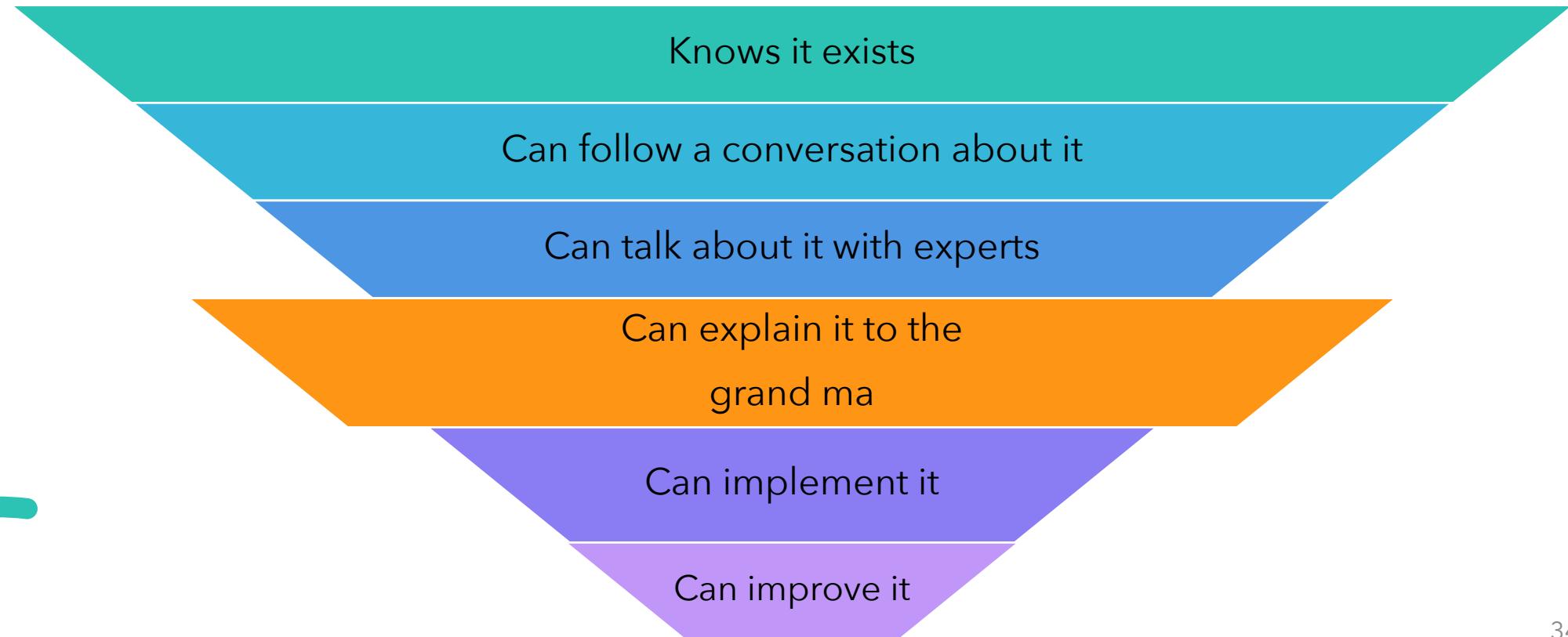


Lean development



Explain your research to your grandma!

Levels of mastery (method)



... or the general public



Supervise master students

- As you progress in your PhD the time needed for new ideas and the time available to test them will become increasingly different
- Transform small projects in internships or master thesis
- Students ask questions! If you don't know the answers you will learn them
- If well supervised, good students will help you move faster

Know the PhD and ITN perks

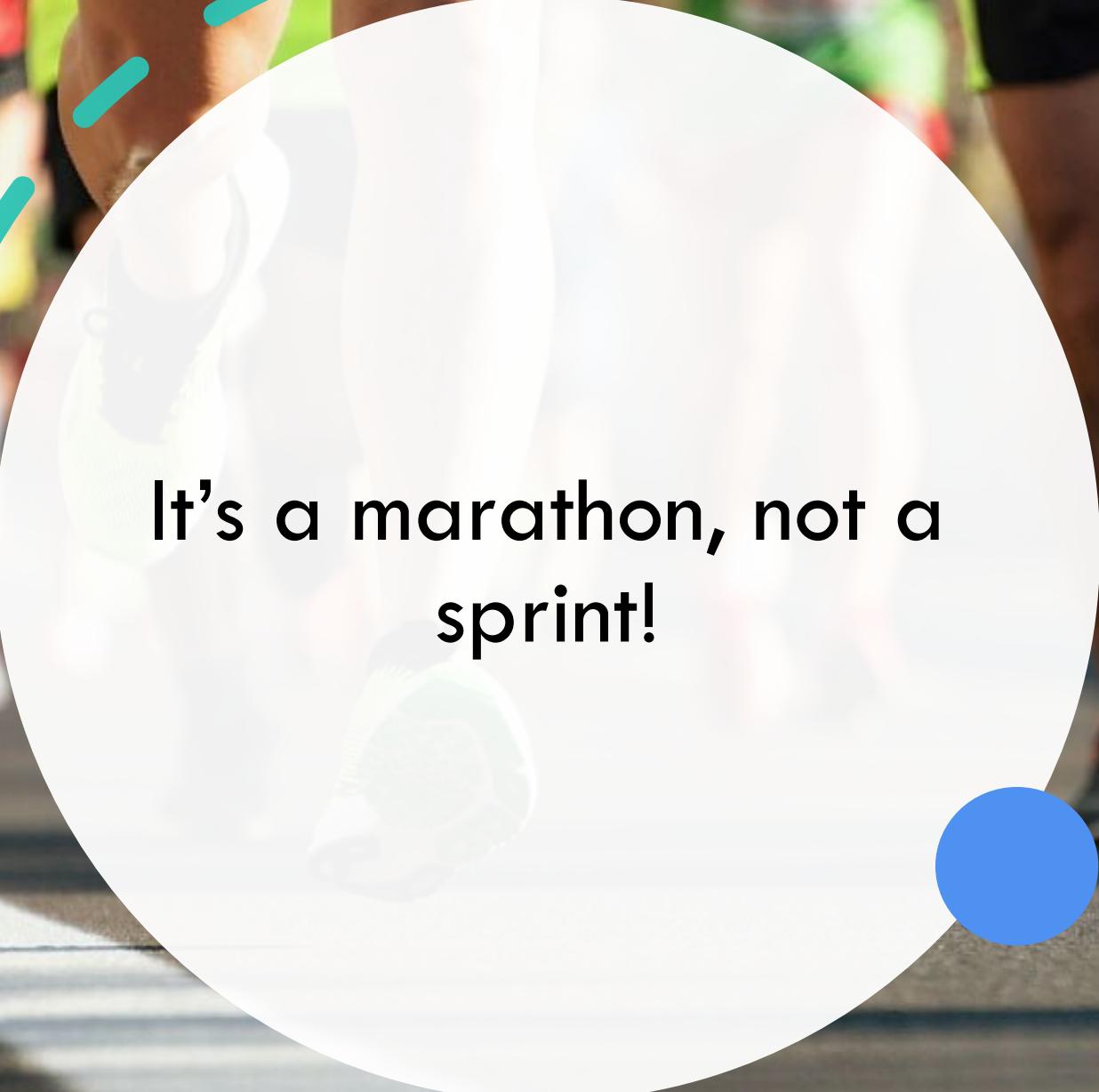
- Access to a vast number of courses, sometimes from multiple universities (Switzerland)
- Language courses
- Internships or courses with external partners (e.g. Siemens Sequence Programming)
- Other courses (start-up creation, project management...)
- Discounts in gyms, swimming pools, ...

Conferences

- Go to different types of conferences
 - Clinical, specialist, technical, big and small
- Alternate between conferences:
 - E.g. 1 year ISMRM, 1 year MICCAI

Translate research into tangible products

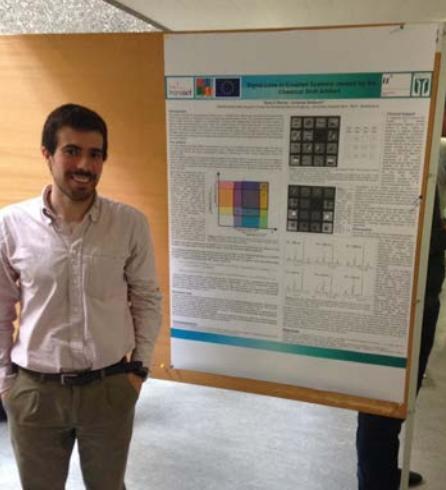
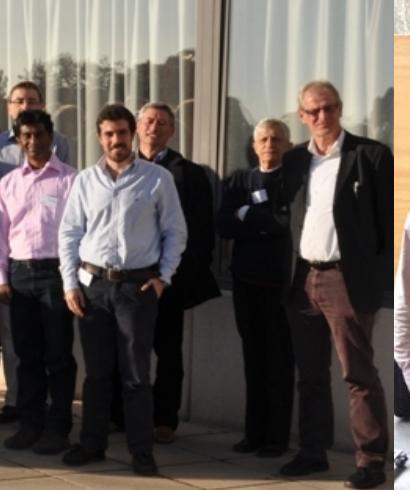
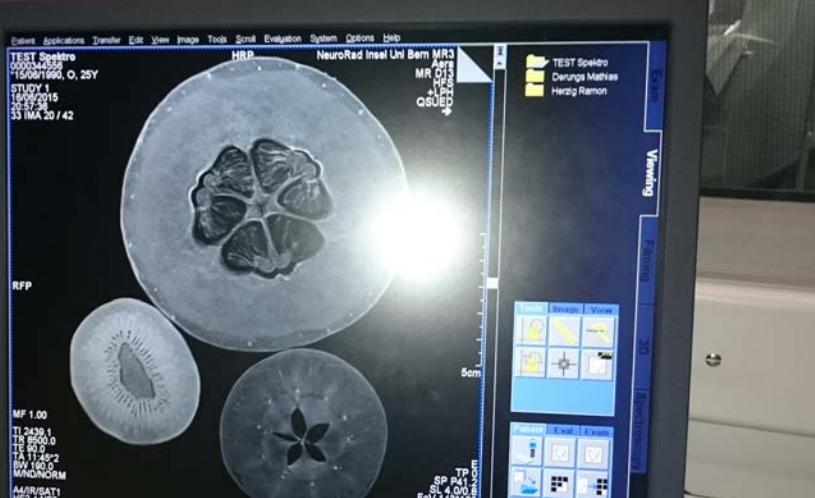
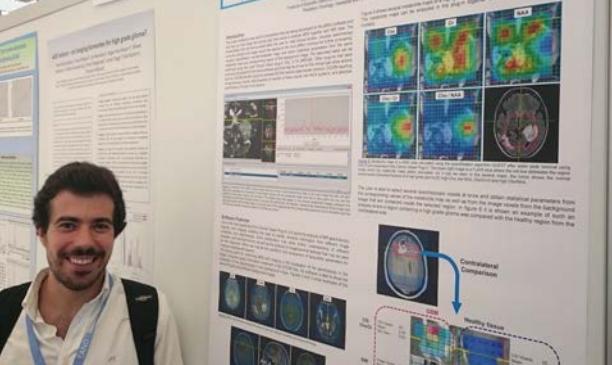
- Manuscripts
- Datasets
- Open software
- IP, patents



**It's a marathon, not a
sprint!**

It's a marathon not a sprint

- Keep yourself motivated
- (Develop a software tool or code library)
- Find healthy routines that help you maintain productivity
- Practice sport, sleep enough, eat well and meet your friends and family



Good luck!

