



CANCER PREVENTION & RESEARCH
INSTITUTE OF TEXAS

Innovations in Cancer Imaging



Presenter



Katy Keenan, PhD

Project Leader

Quantitative Magnetic Resonance Imaging
National Institute of Standards and Technology

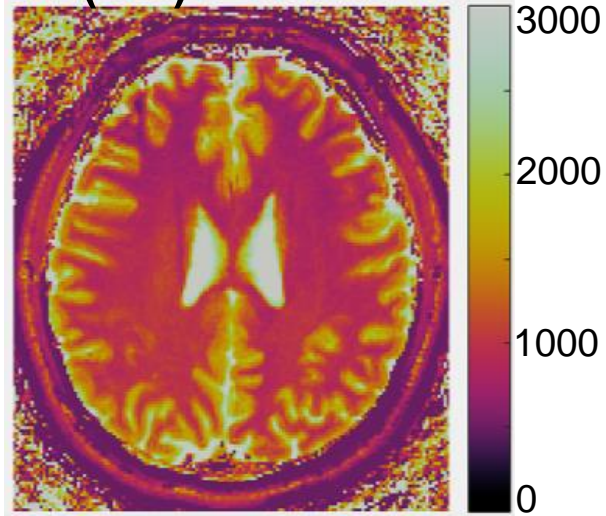
Innovations in Cancer Imaging

Kathryn Keenan, PhD

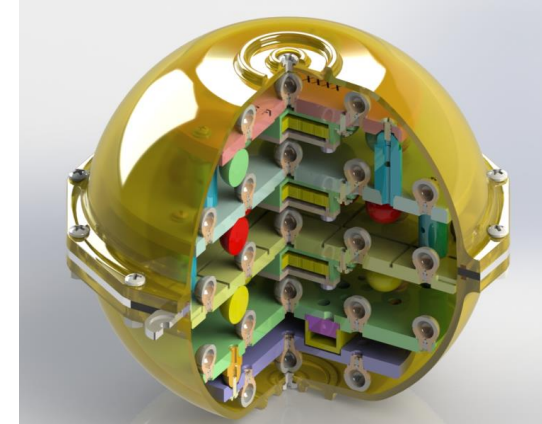
Project Leader, Quantitative MRI

Innovations in Cancer Imaging

T1 (ms)



More than a picture



How to implement quantitative MRI?



Expanding the use of MRI

Innovations in Cancer Imaging

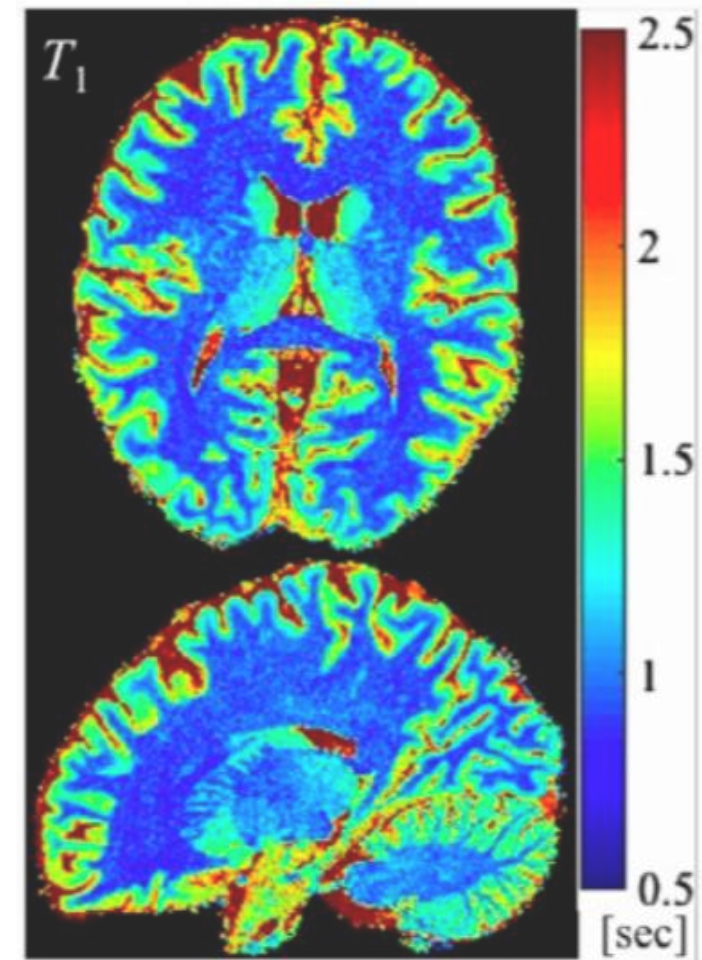
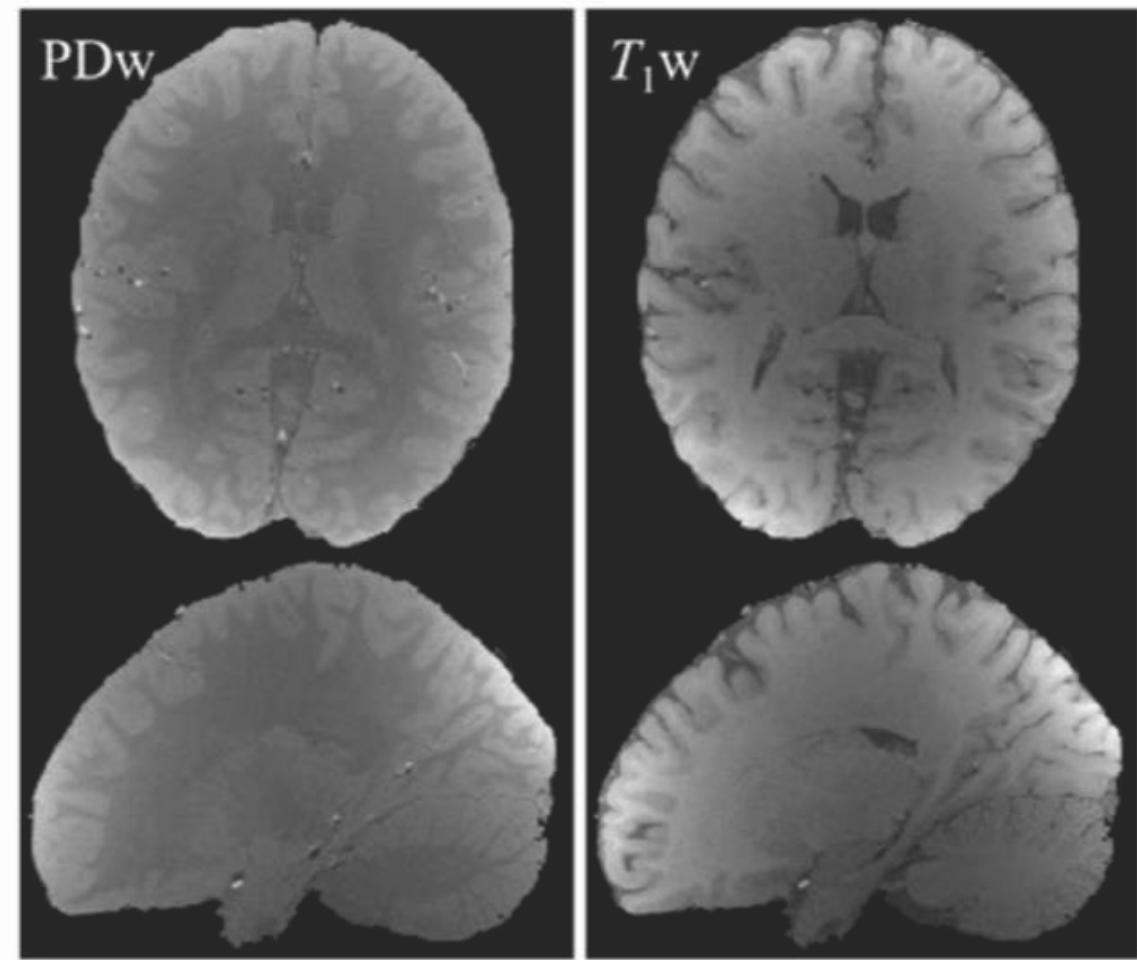
Part 1: More than a picture

Kathryn Keenan, PhD

Project Leader, Quantitative MRI

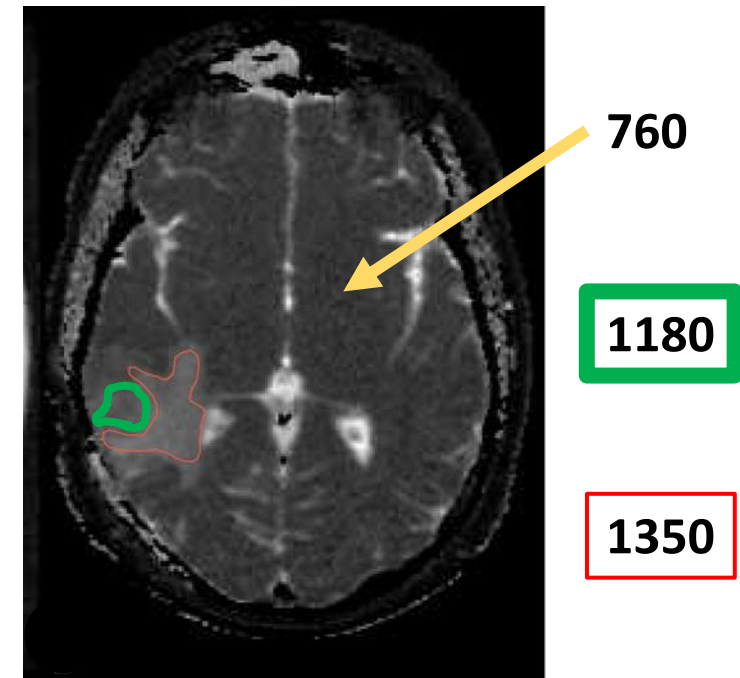
What is quantitative MRI?

Lee et al, MRM 2019

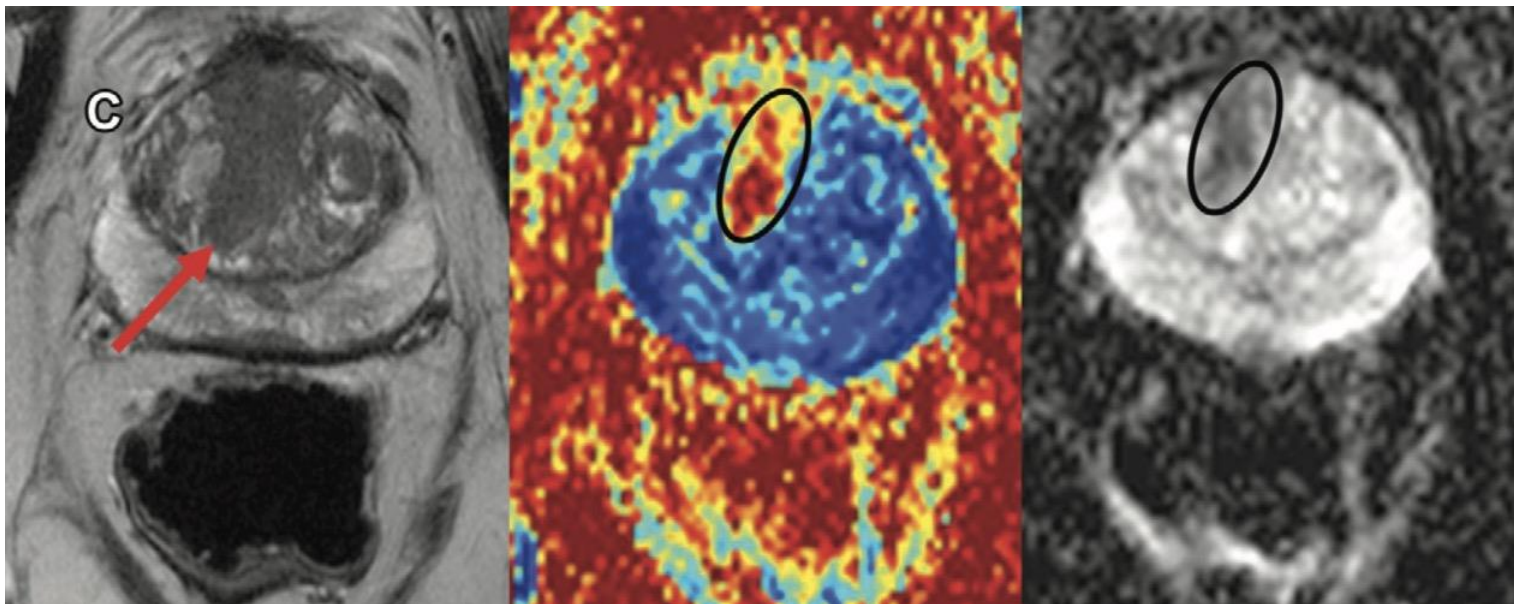


How are we using quantitative MRI?

Apparent Diffusion
Coefficient ($10^{-6} \text{ mm}^2/\text{s}$)



How are we using quantitative MRI?



T2-weighted

Fractional Intracellular
volume (FIC) map

Apparent Diffusion
Coefficient map

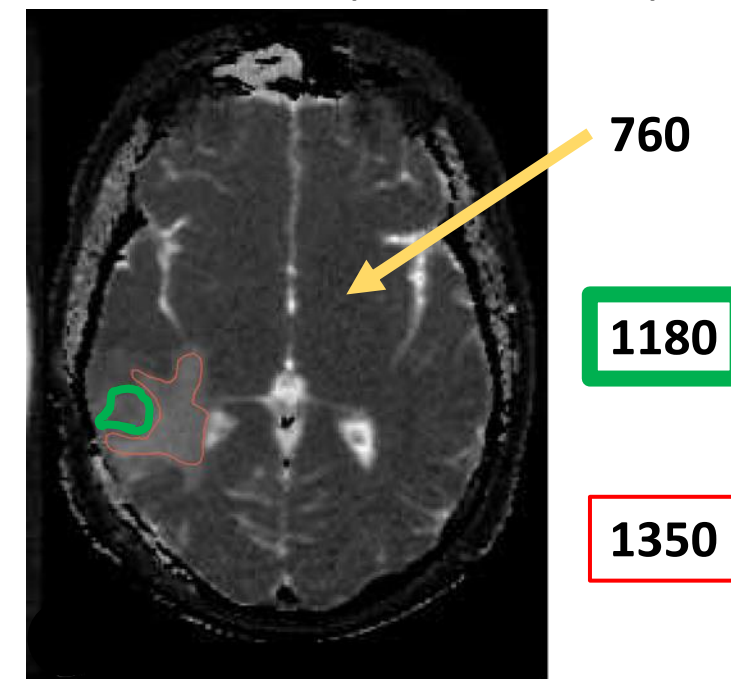
Radiology

ORIGINAL RESEARCH • GENITOURIN

Avoiding Unnecessary Biopsy after Multiparametric Prostate MRI with VERDICT Analysis: The INNOVATE Study

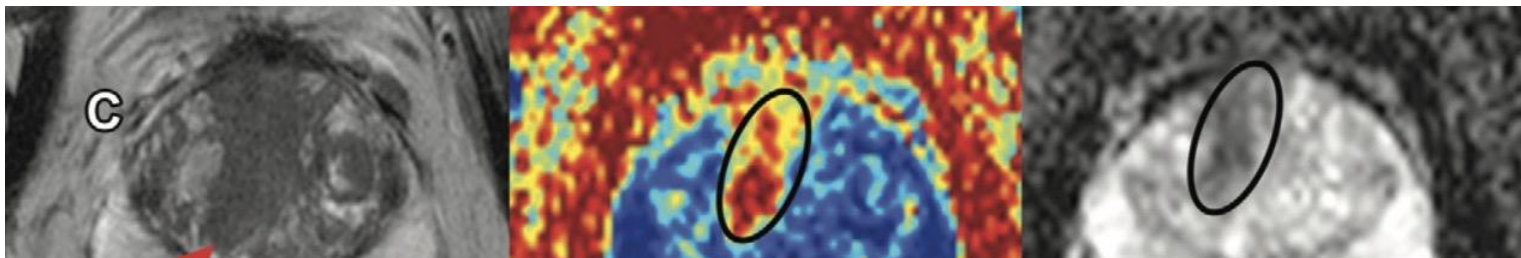
Saurabh Singh, PhD, FRCR • Harriet Rogers, PhD • Baris Kanber, PhD • Joey Clemente, PhD • Hayley Pye, PhD • Edward W. Johnston, PhD, FRCR • Tom Parry, MSc • Alistair Grey, FRCS • Eoin Dinneen, MRCS • Greg Shaw, MD, FRCS • Susan Heavey, PhD • Urszula Stopka-Farooqui, MRes • Aiman Haider, FRCPath • Alex Freeman, FRCPath • Francesco Giganti, MD, PhD • David Atkinson, PhD • Caroline M. Moore, MD, FRCS • Hayley C. Whitaker, PhD • Daniel C. Alexander, PhD • Eleftheria Panagiotaki, PhD • Shonit Punwani, PhD, MRCP, FRCR

Apparent Diffusion
Coefficient ($10^{-6} \text{ mm}^2/\text{s}$)



Maier S et al, Diffusion Imaging of Brain Tumors
NMR Biomed 2010

How are we using quantitative MRI?

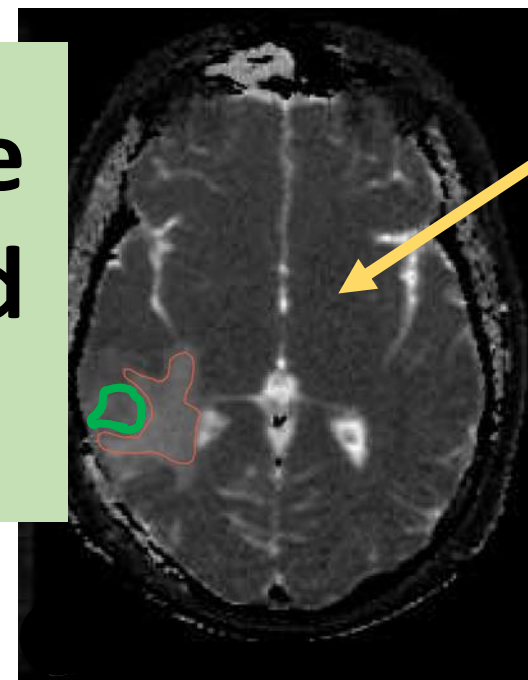


T2-weighted

Fractional volume

Quantitative MRI can be used for *diagnostics* and *treatment response*.

Apparent Diffusion Coefficient ($10^{-6} \text{ mm}^2/\text{s}$)



760

1180

1350

ORIGINAL RESEARCH • GENITOURINARY

Radiology

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Possibilities of diagnostic quantitative MRI

Possibilities of diagnostic quantitative MRI

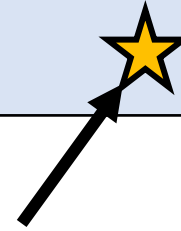
**Range of
qMRI value:**

Possibilities of diagnostic quantitative MRI

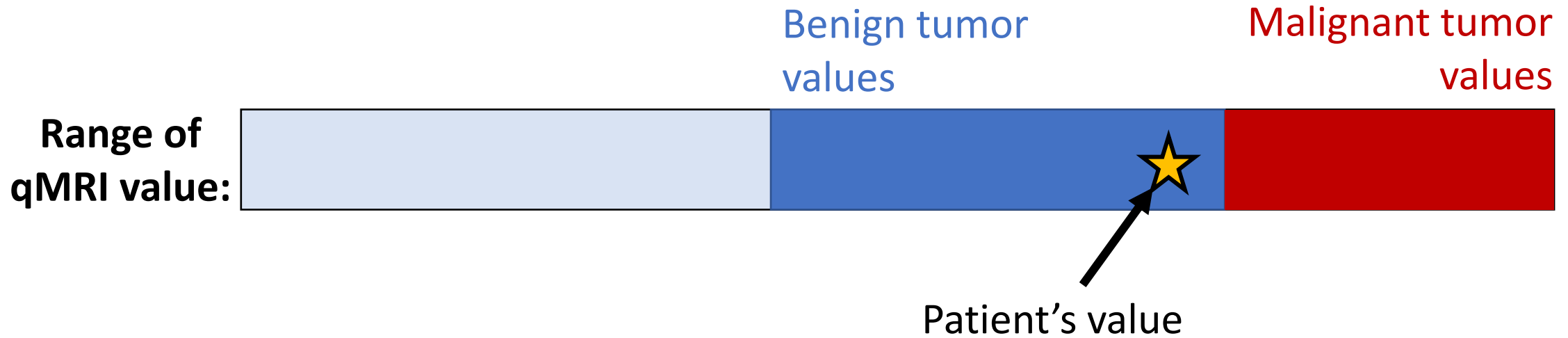
**Range of
qMRI value:**



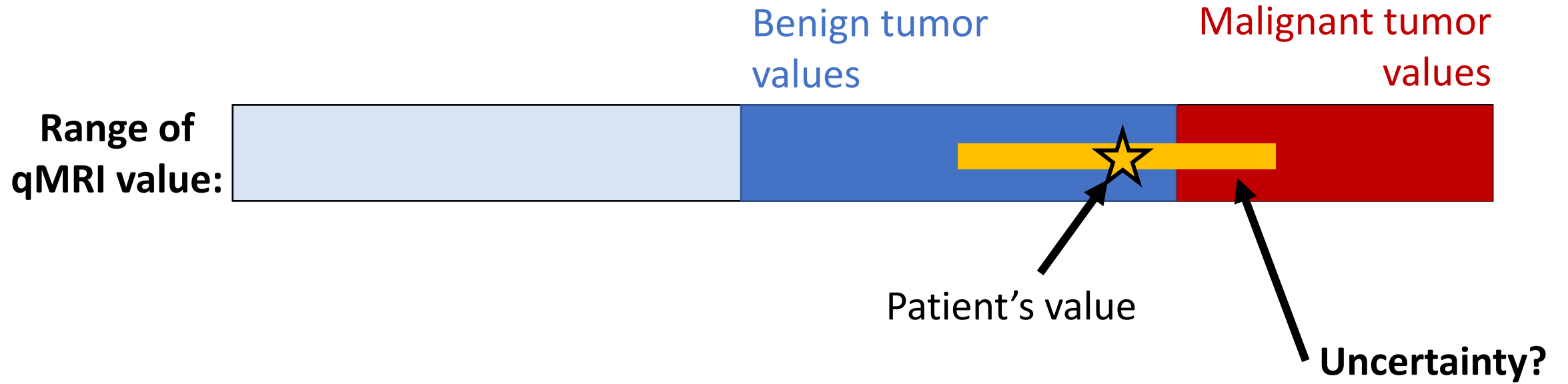
Patient's value



Possibilities of diagnostic quantitative MRI

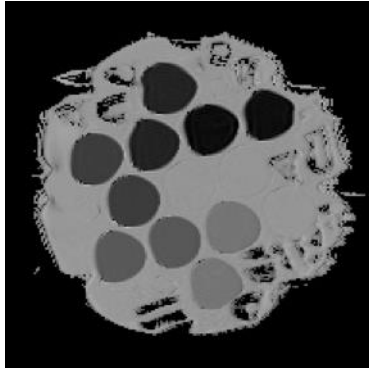


Possibilities of diagnostic quantitative MRI



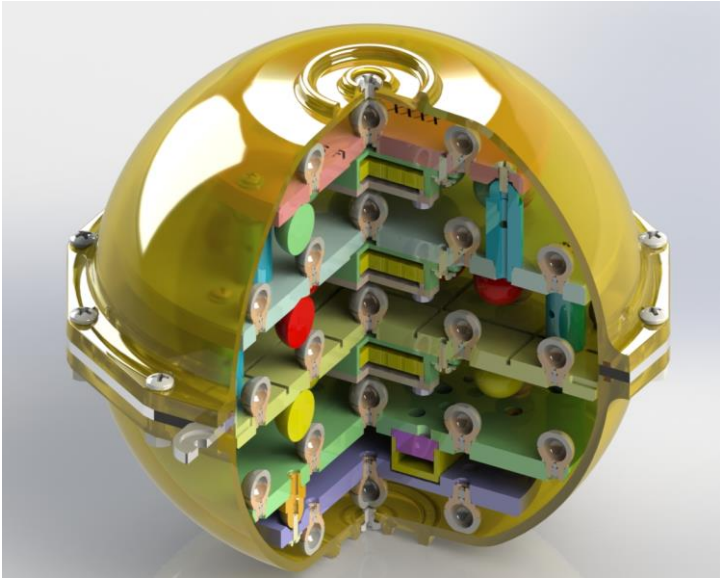
NIST's efforts in quantitative MRI

NIST's efforts in quantitative MRI



NIH National Institute of Biomedical Imaging and Bioengineering
Creating Biomedical Technologies to Improve Health

Isotropic diffusion phantom



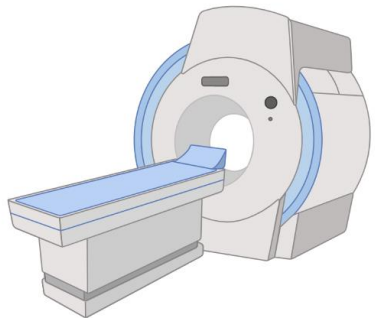
MRI System phantom



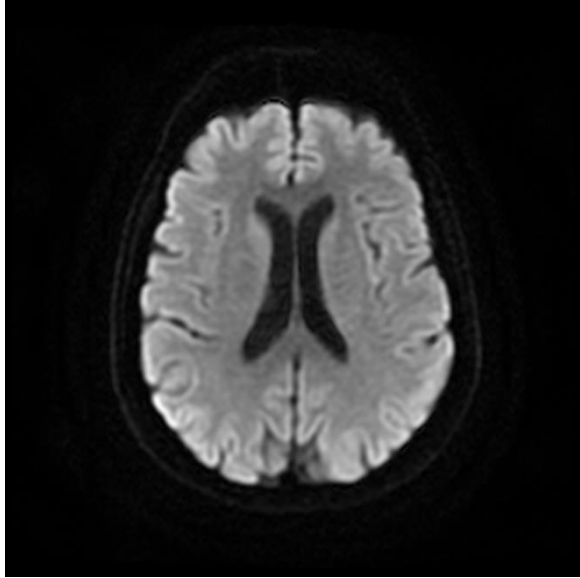
Breast phantom for isotropic diffusion and T1 mapping

Diffusion phantom T1 relaxation phantom

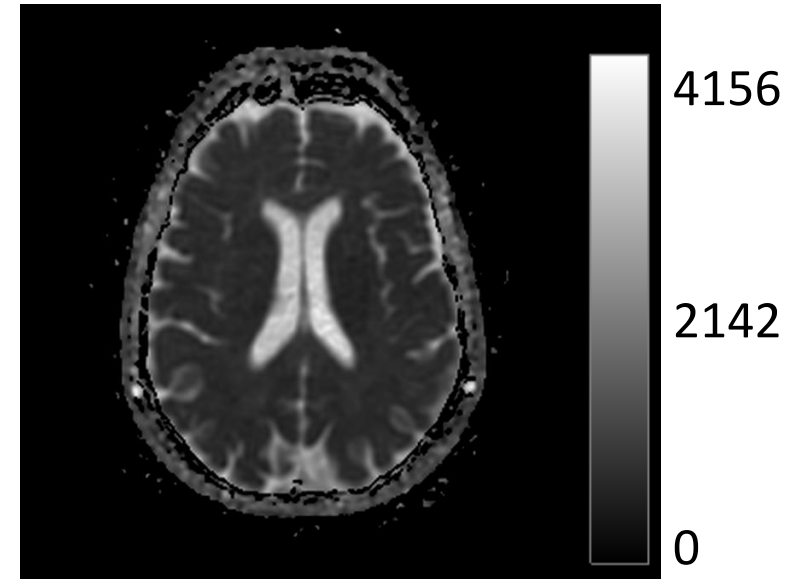


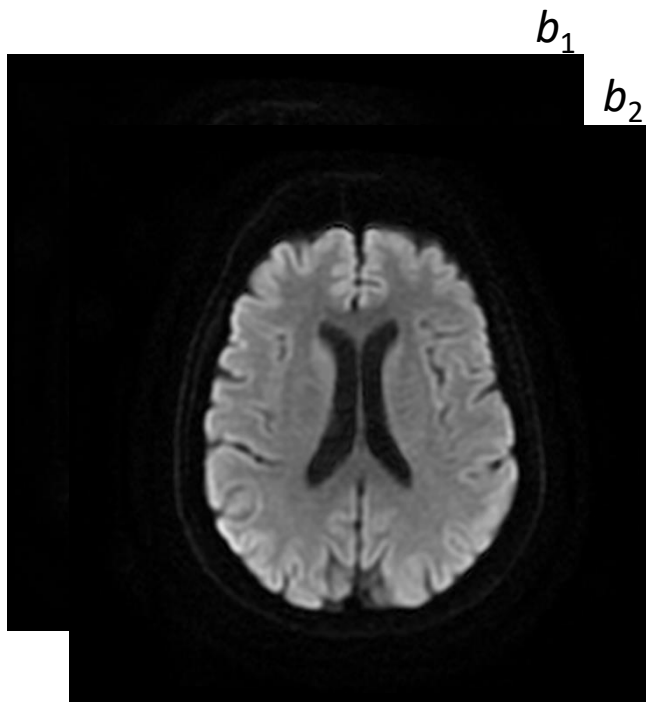


b_1

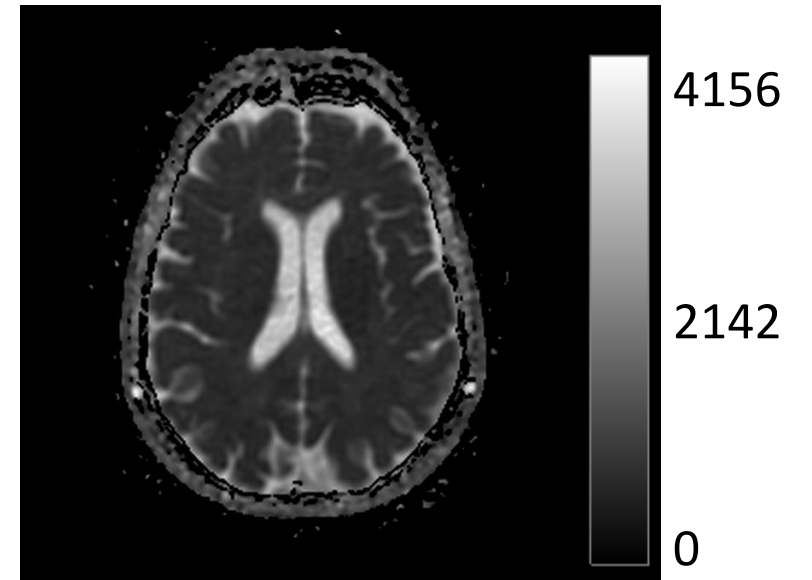


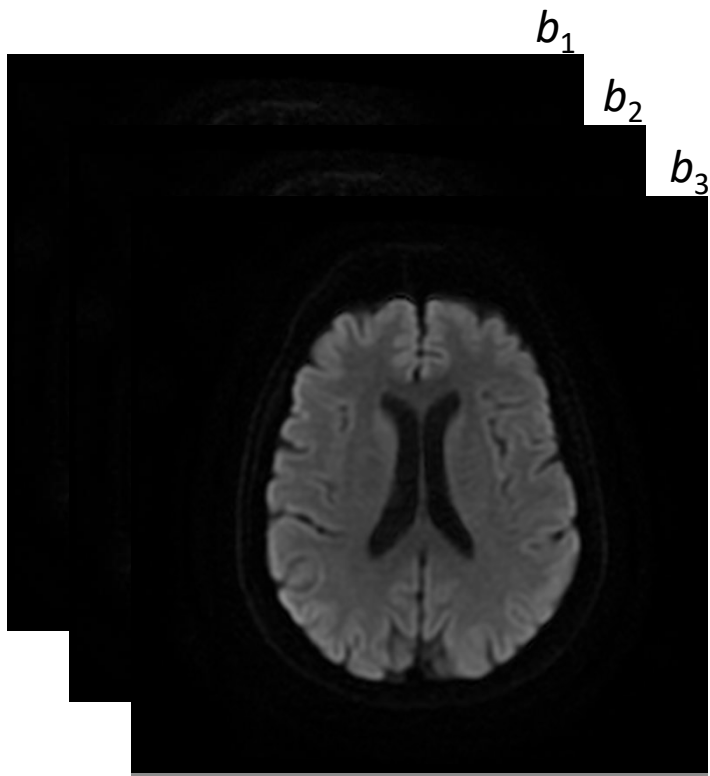
Apparent Diffusion
Coefficient ($10^{-6} \text{ mm}^2/\text{s}$)



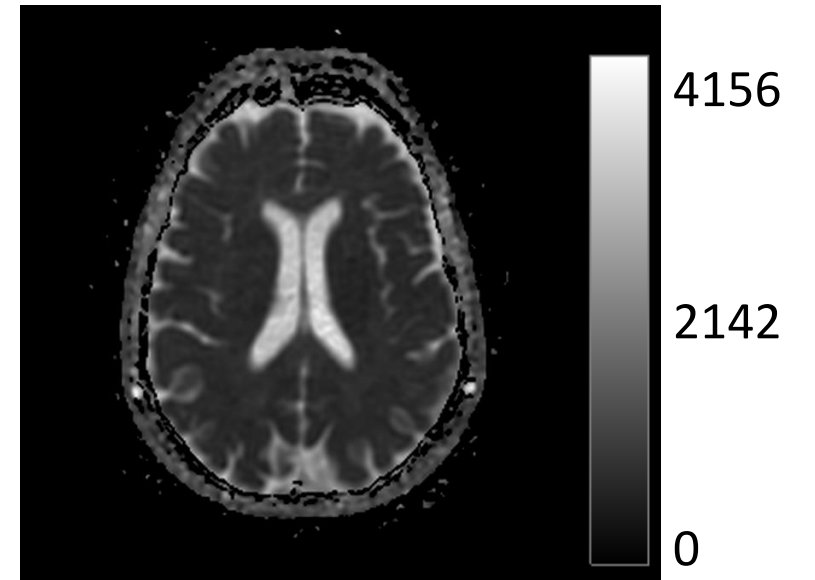


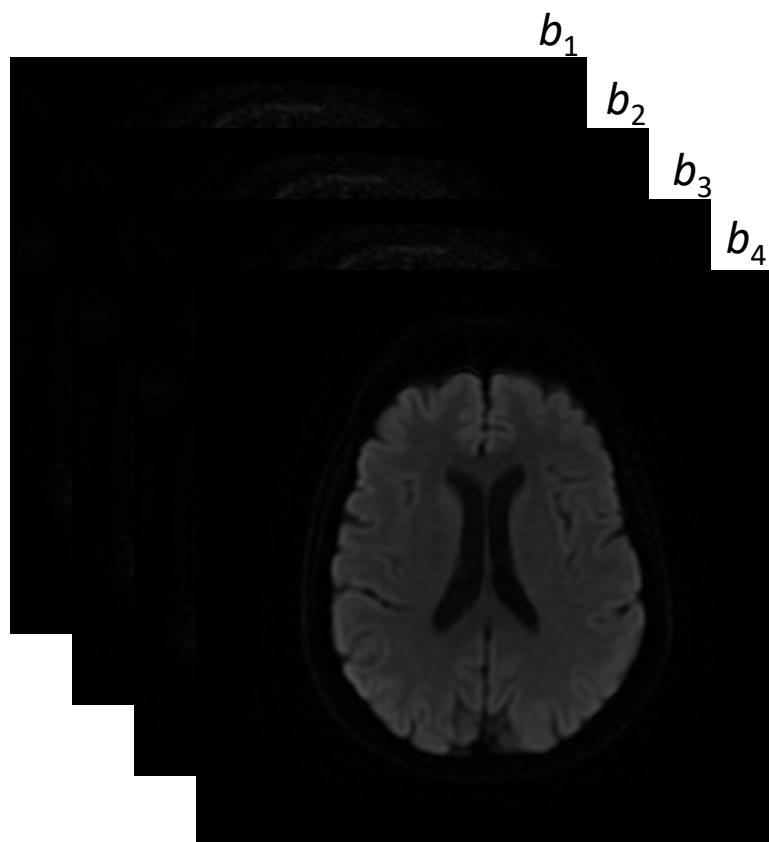
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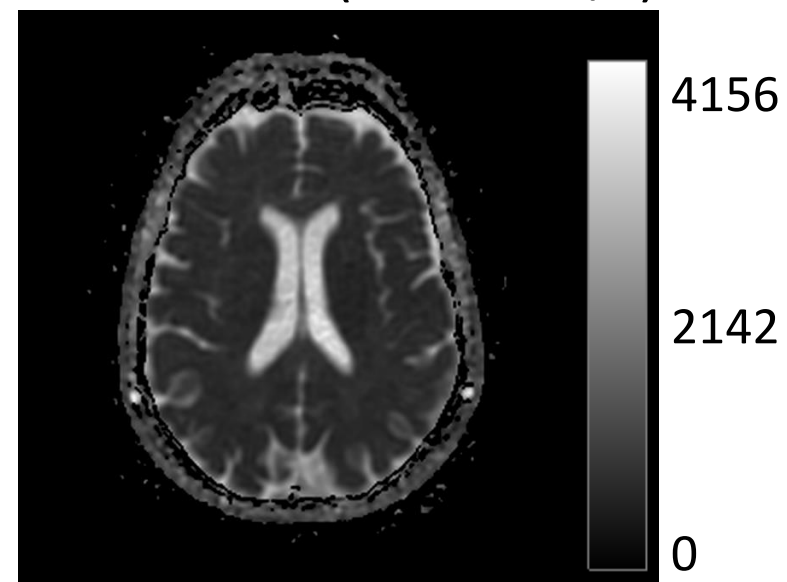


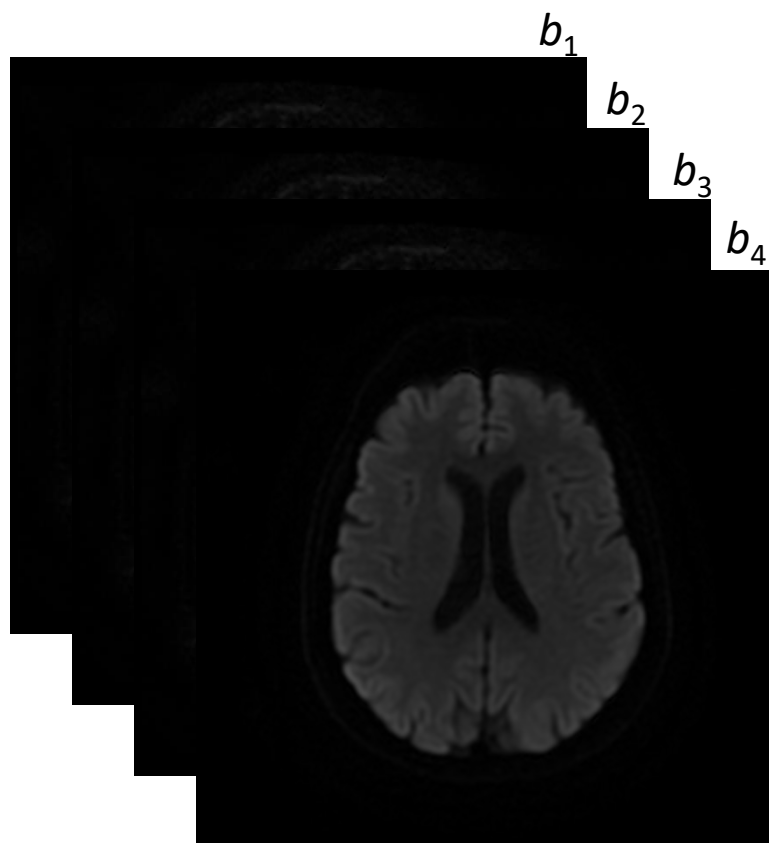
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Apparent Diffusion Coefficient ($10^{-6} \text{ mm}^2/\text{s}$)

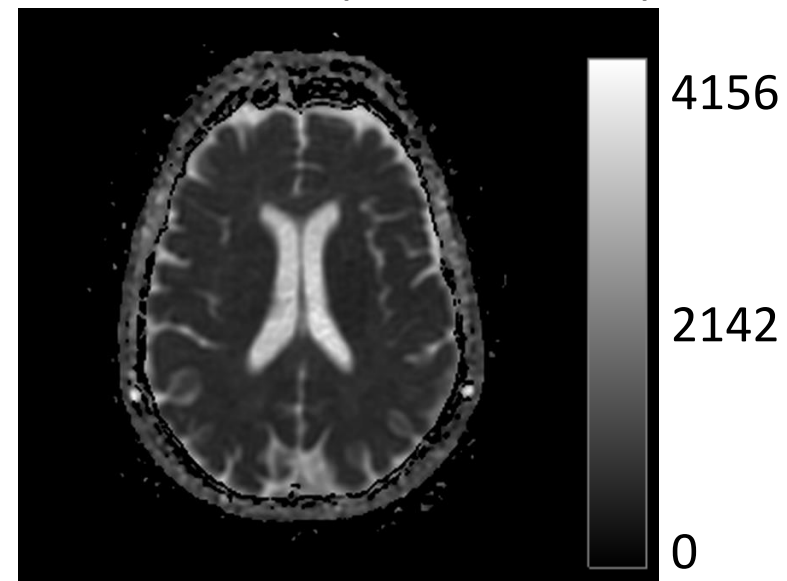


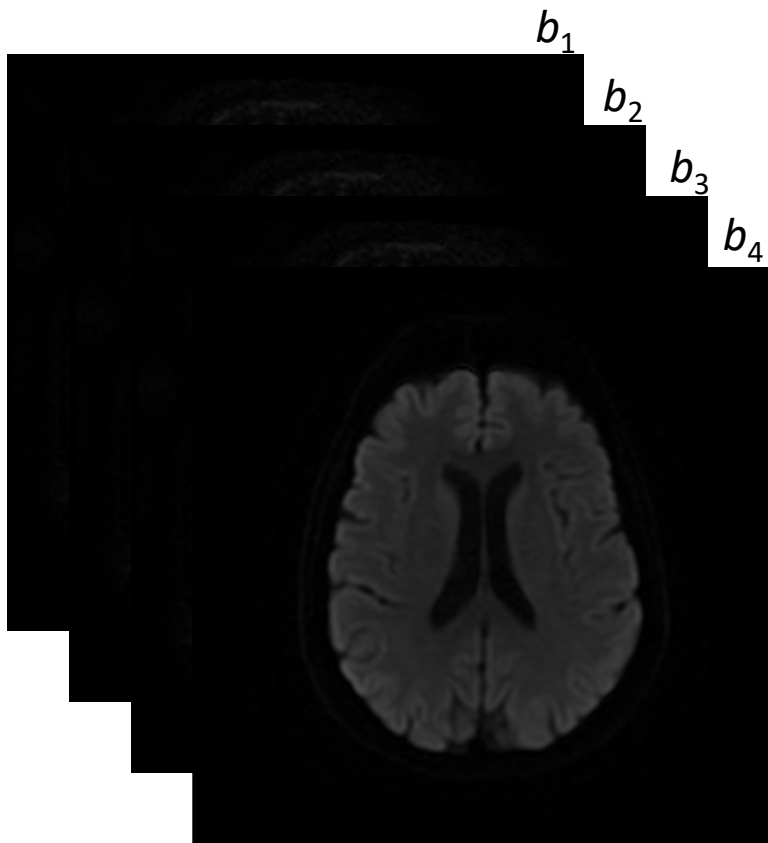


$$S = S_0 e^{-b \cdot ADC}$$

→

Apparent Diffusion
Coefficient ($10^{-6} \text{ mm}^2/\text{s}$)

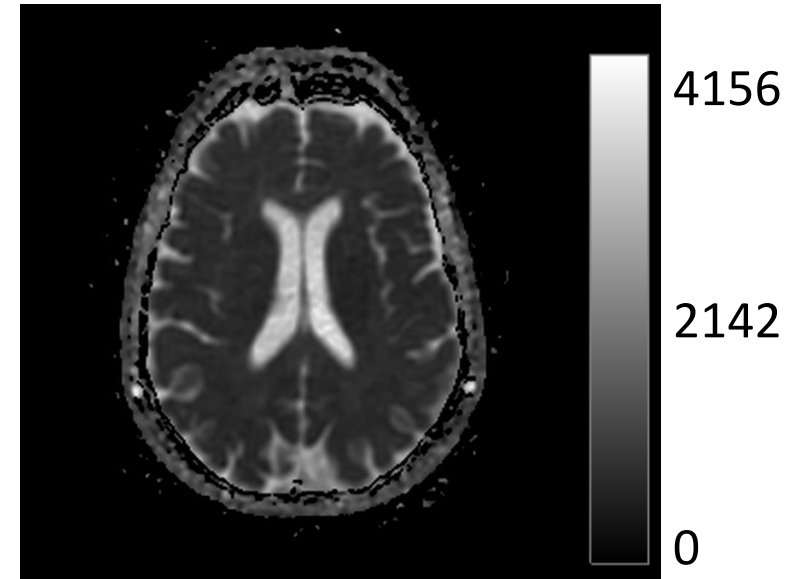


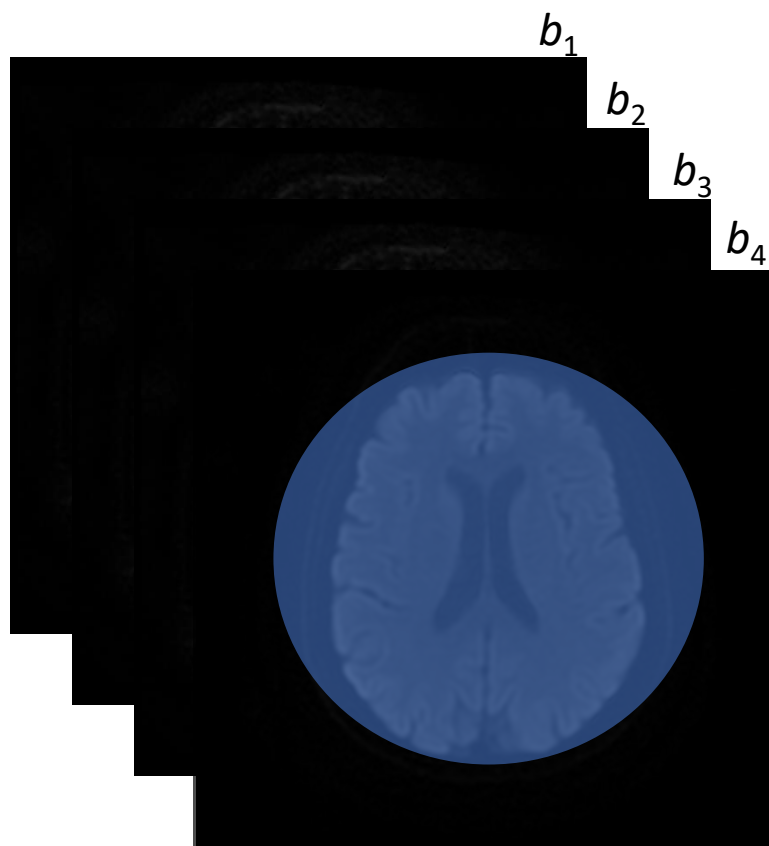


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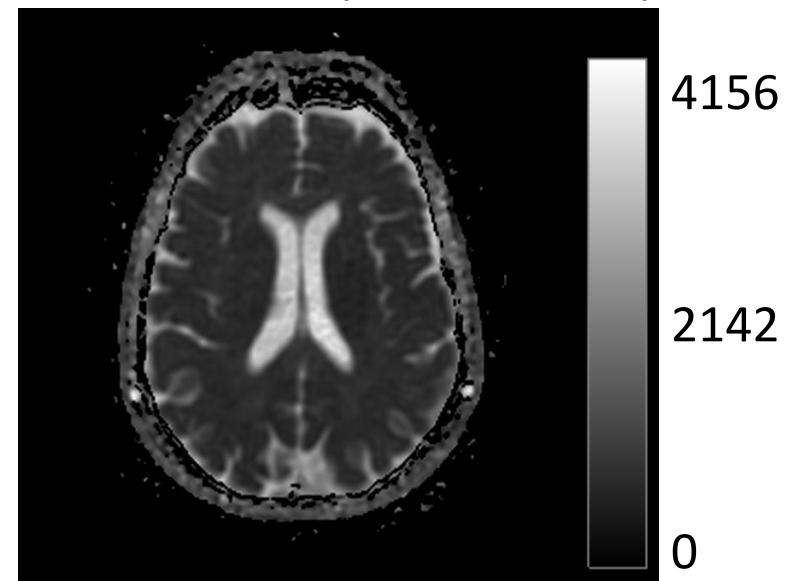


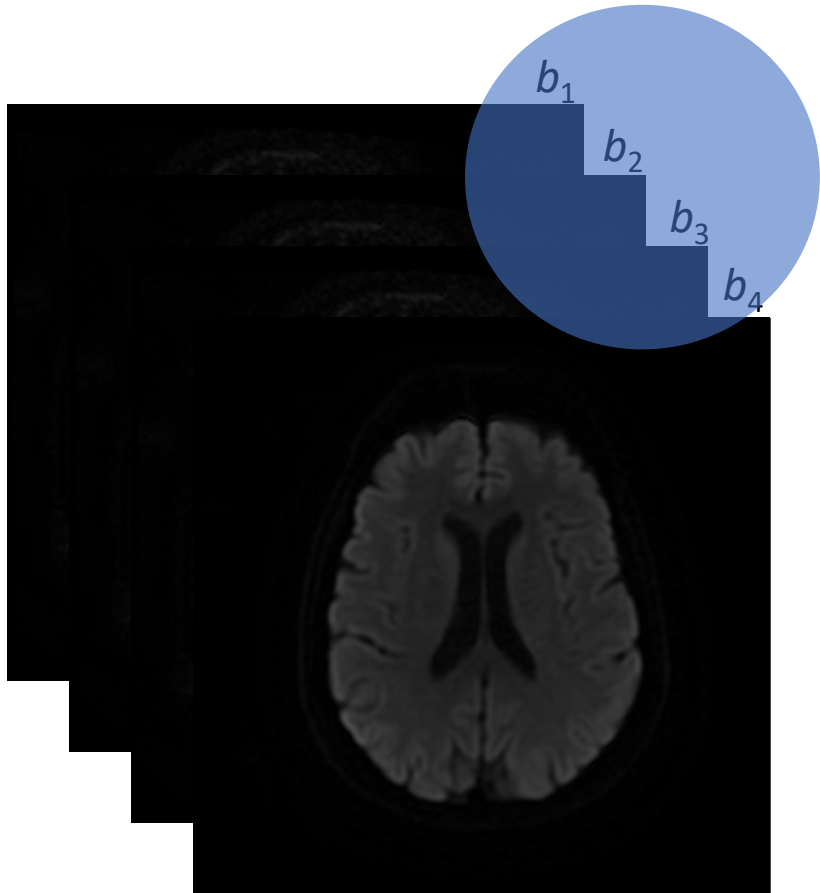


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Apparent Diffusion Coefficient ($10^{-6} \text{ mm}^2/\text{s}$)

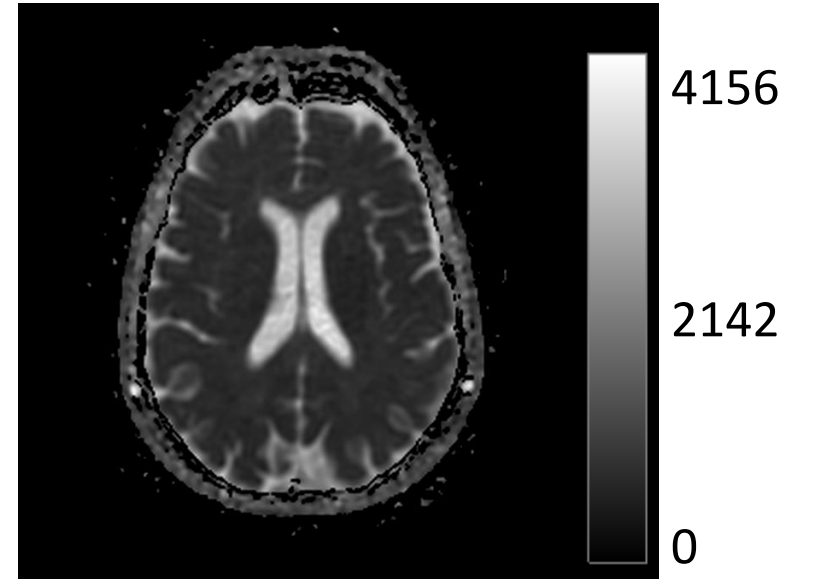


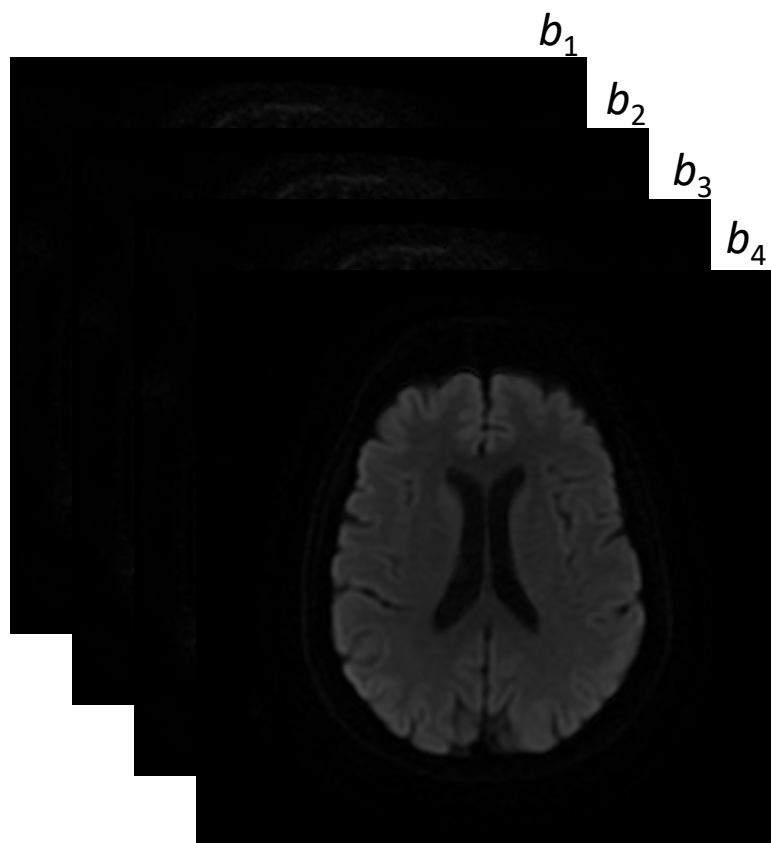


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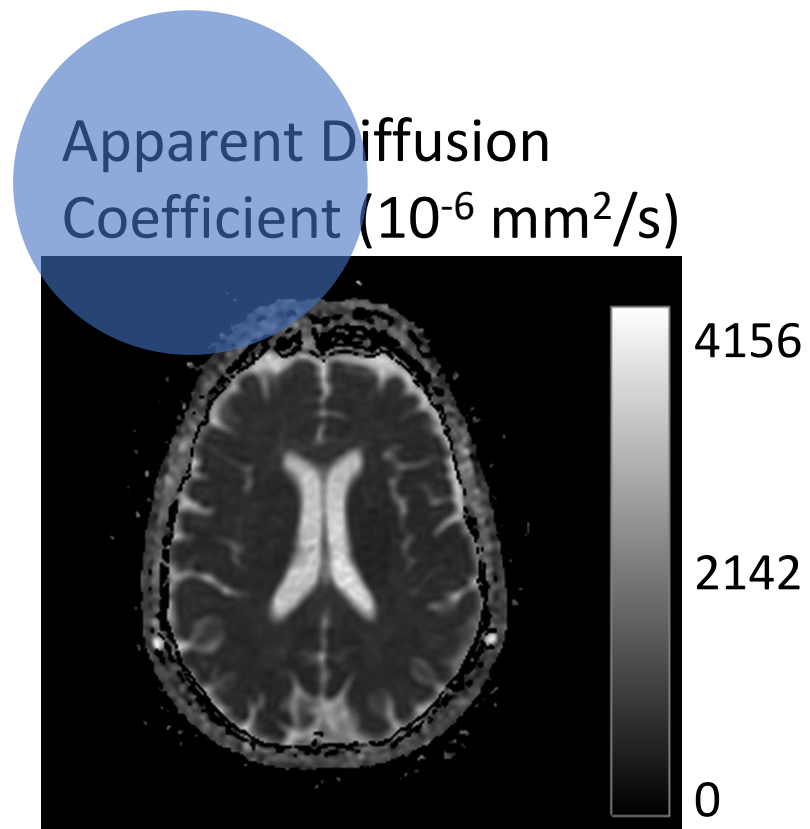
Apparent Diffusion Coefficient ($10^{-6} \text{ mm}^2/\text{s}$)



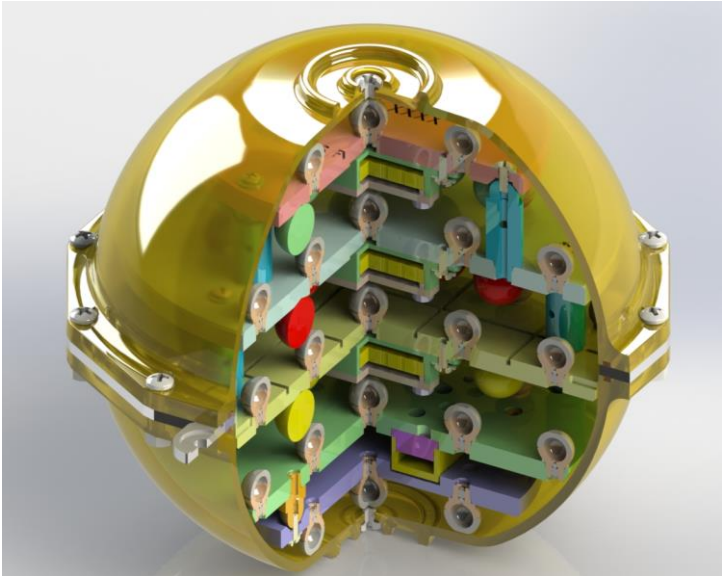


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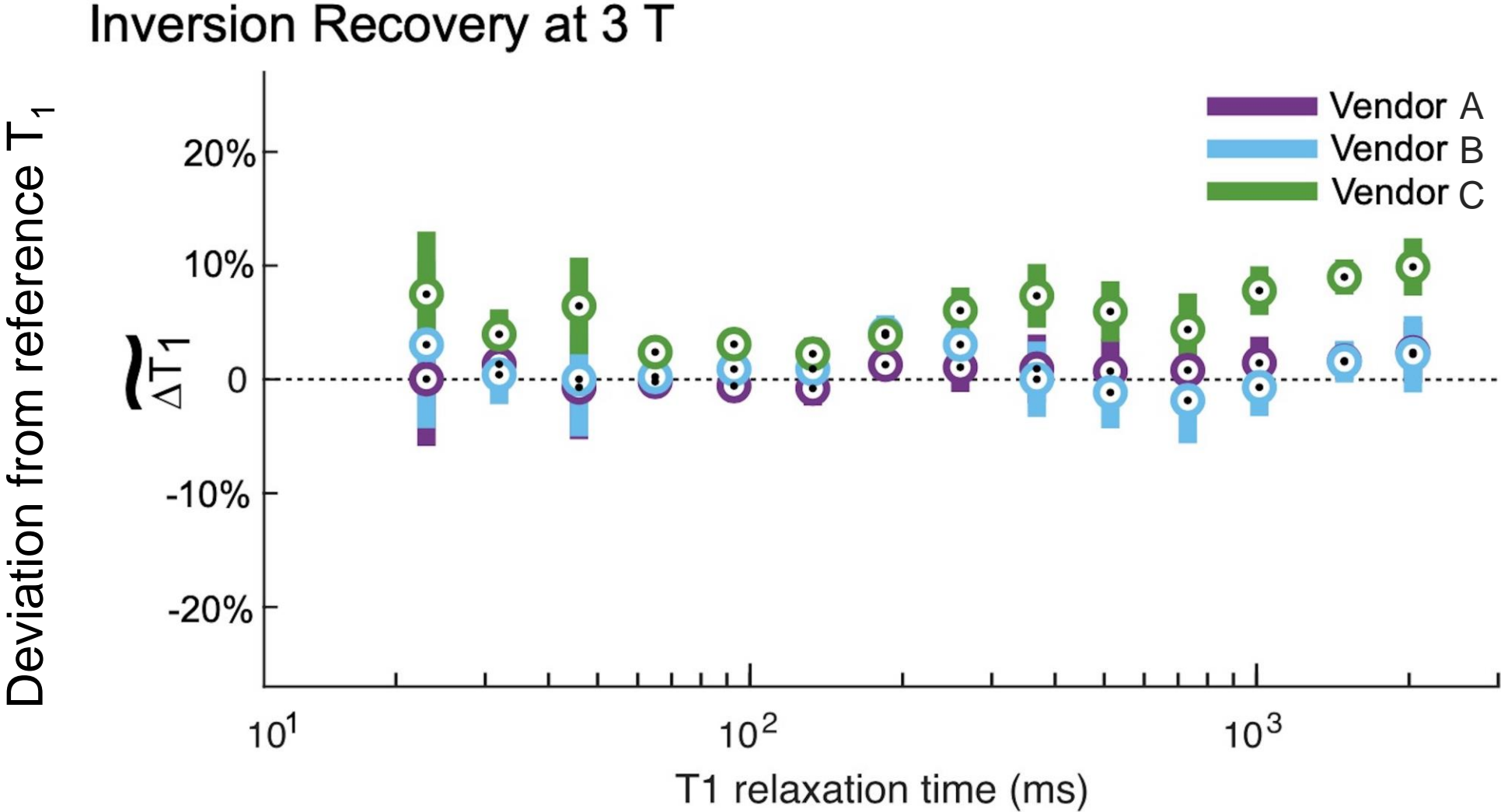
An arrow points from the equation to the right, indicating the transformation of the data.



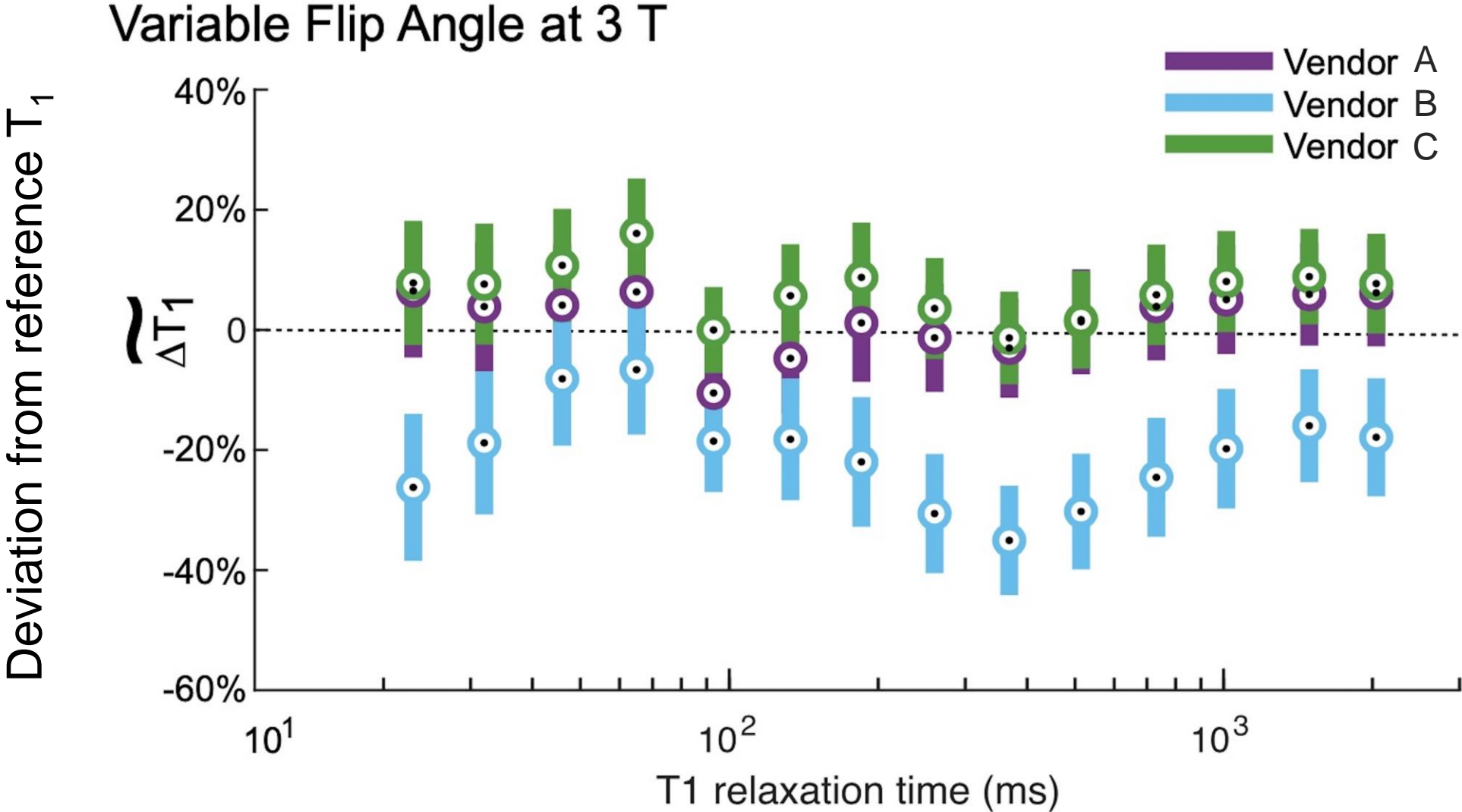
Multi-site T1 variability



Multi-site T1 variability



Multi-site T1 variability



MRI system bias

Received: 9 March 2018 | Revised: 28 May 2018 | Accepted: 4 June 2018

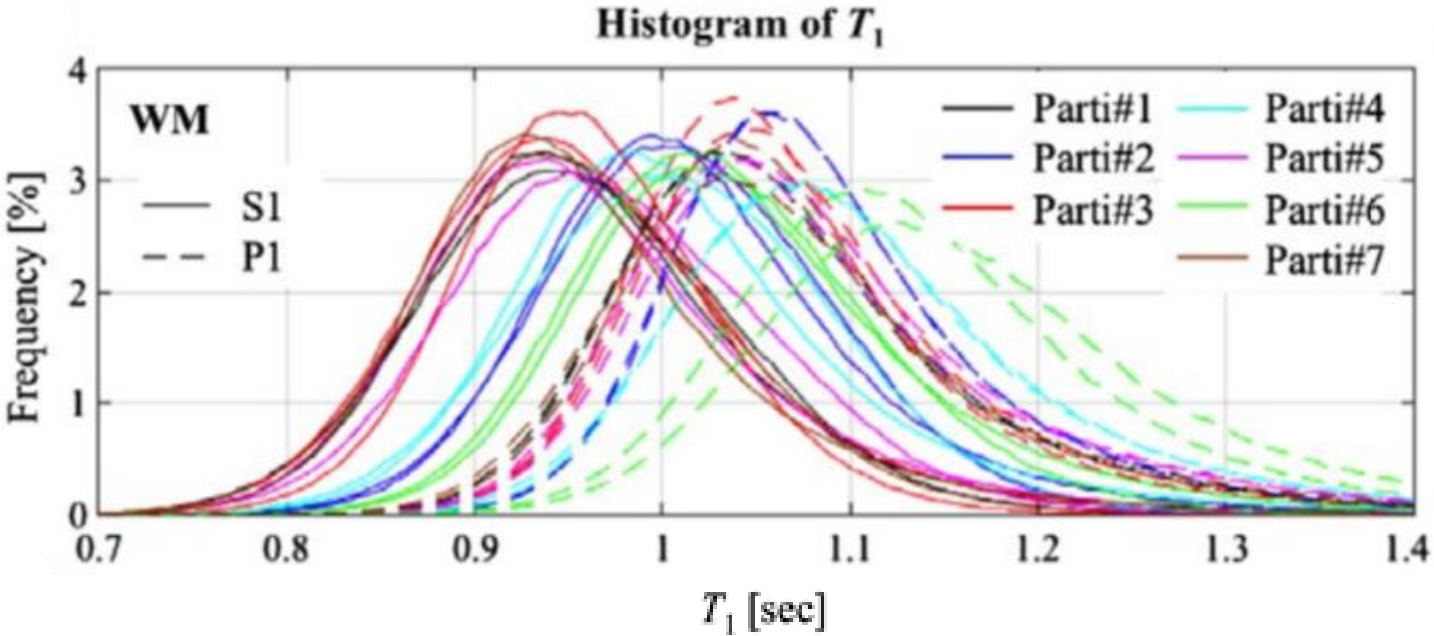
DOI: 10.1002/mrm.27421

FULL PAPER

Magnetic Resonance in Medicine

Establishing intra- and inter-vendor reproducibility of T_1 relaxation time measurements with 3T MRI

Yoojin Lee¹ | Martina F. Callaghan² | Julio Acosta-Cabronero² | Antoine Lutti³ | Zoltan Nagy¹



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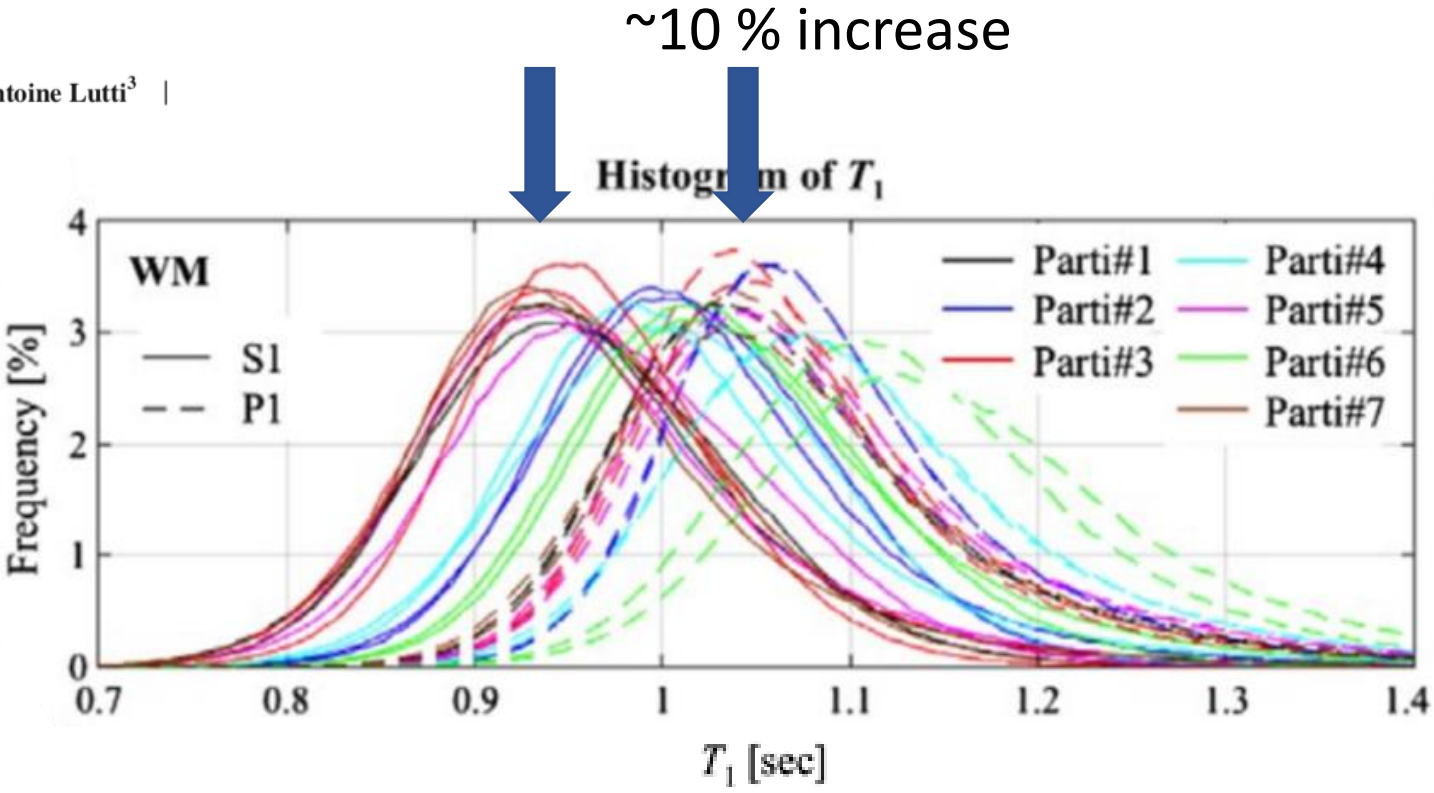
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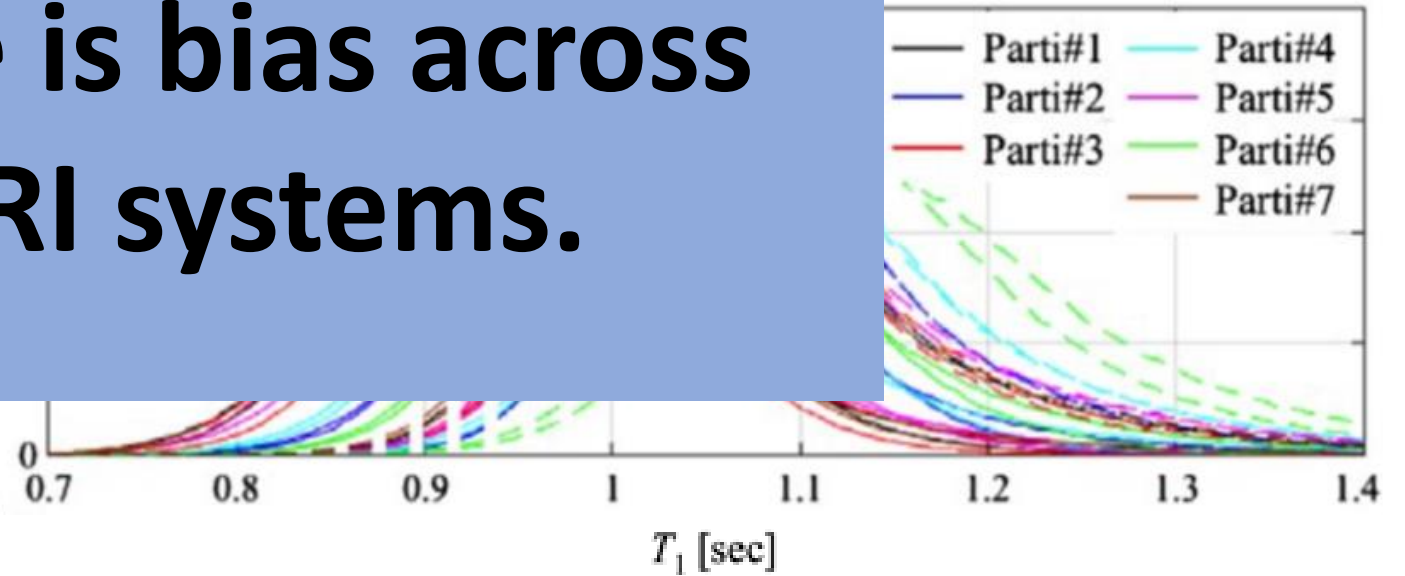
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Zoltan Nagy¹

**There is bias across
MRI systems.**



MRI system upgrades

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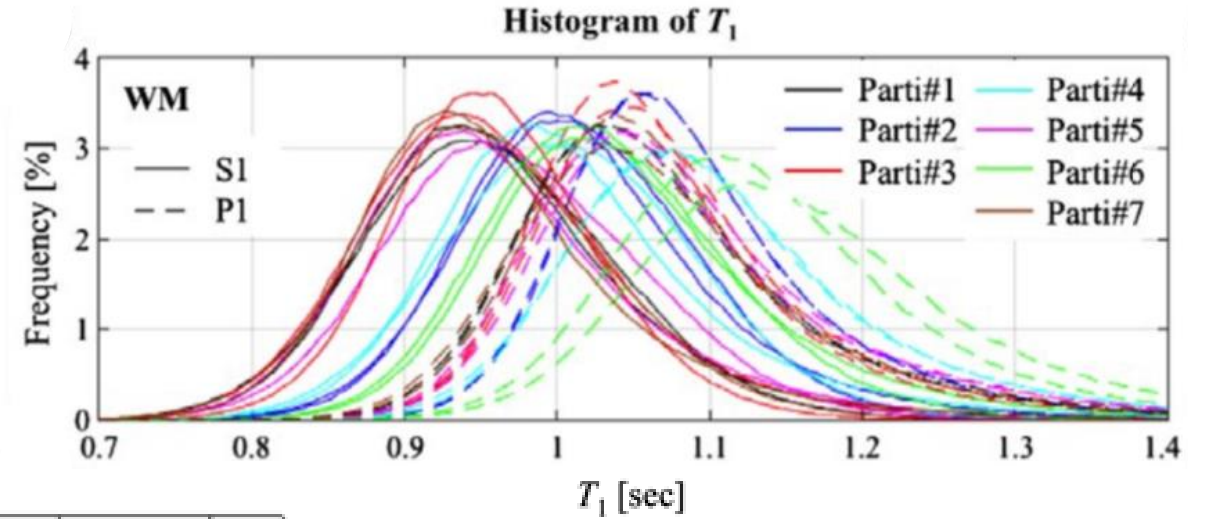
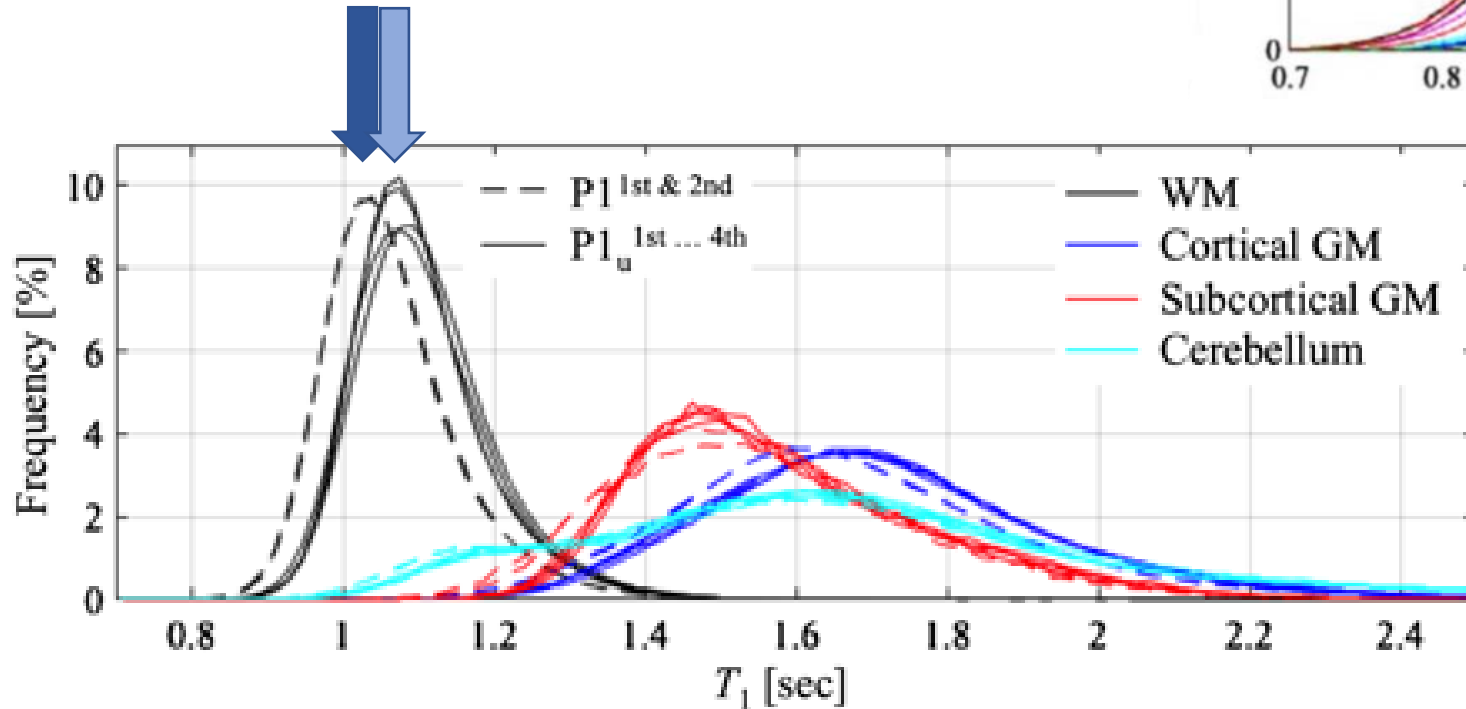
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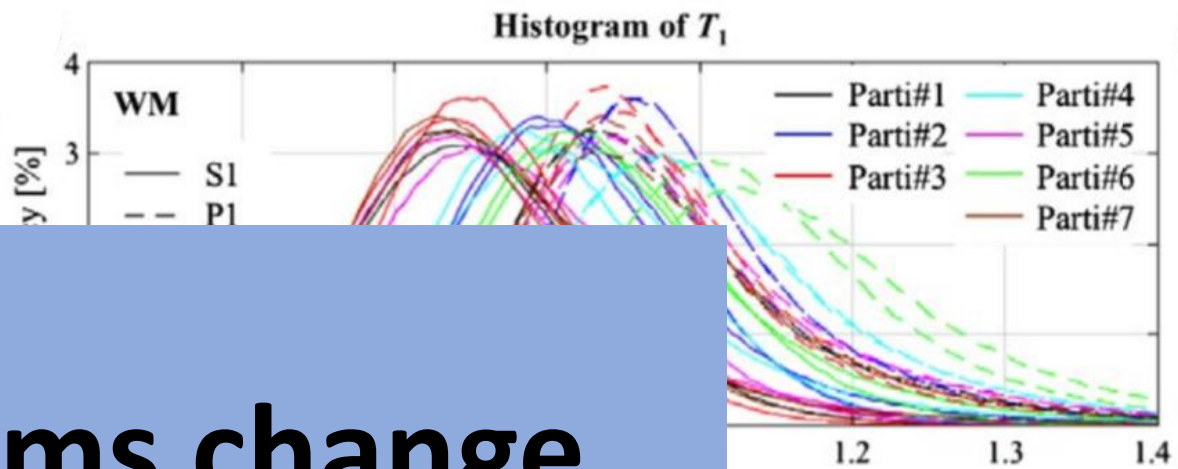
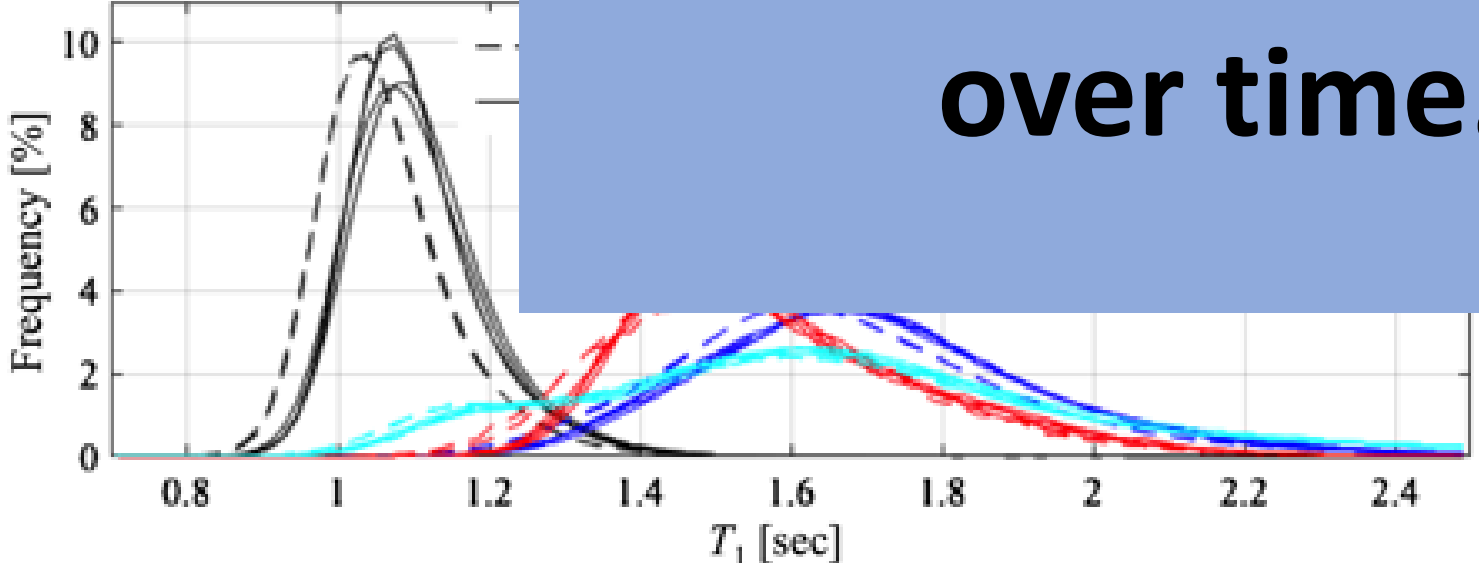
FULL PAPER

Magnetic Resonance in Medicine

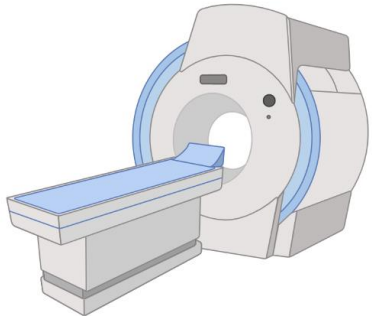
Establishing intra- and inter-vendor reproducibility of T_1 relaxation time measurements with 3T MRI

Yoojin Lee¹ | Martina F. Callaghan² | Julio Zoltan Nagy¹

MRI systems change over time.



What can you do?



Data acquisition

- > Pulse sequences
- > Hardware
- > Software

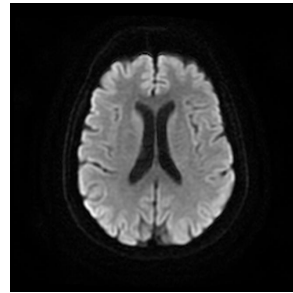
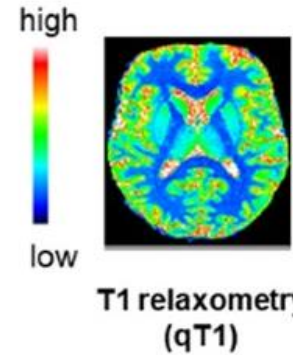


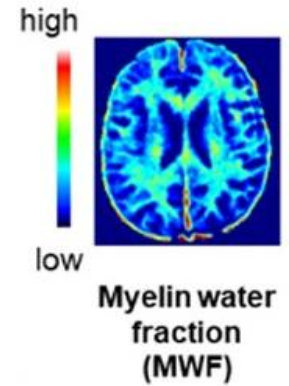
Image Reconstruction

- > Software
- > Can be tied to quantitative model
- > Data storage



Quantitative Modeling

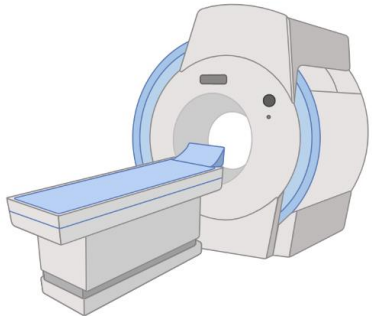
- > Model selection
- > Software



Using the information

- > Clinical work
- > Biophysical model
- > Software

What can you do?



Data acquisition

- > Pulse sequences
- > Hardware
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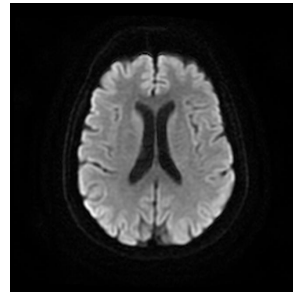
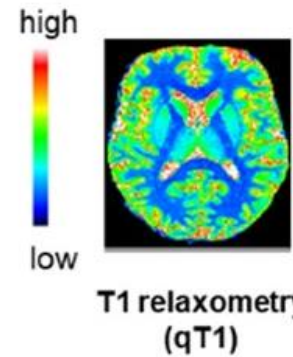


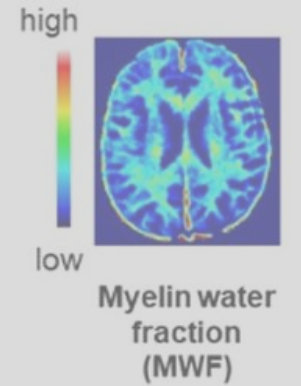
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Quantitative Modeling

- > Model selection
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Using the information

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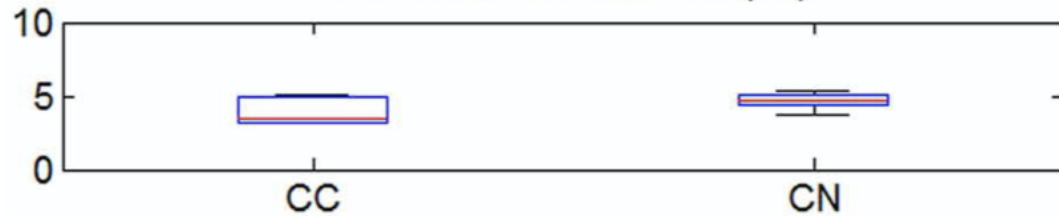
Controlling the acquisition



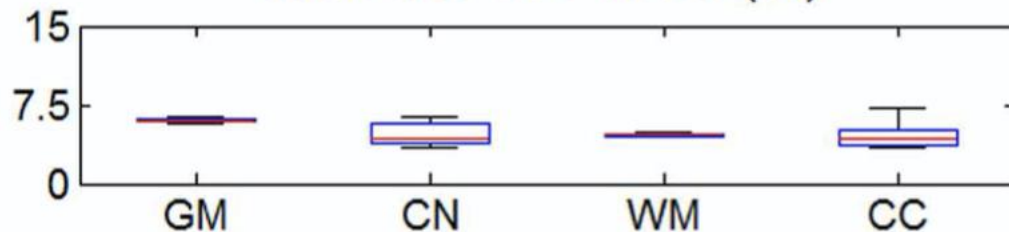
Quantitative multi-parameter mapping of R1, PD*, MT, and R2* at 3T: a multi-center validation

Nikolaus Weiskopf^{1*}, John Suckling^{2,3,4}, Guy Williams^{3,5}, Marta M. Correia⁶, Becky Inkster², Roger Tait³, Cinly Ooi^{2,3}, Edward T. Bullmore^{2,3,4,7} and Antoine Lutti^{1,8}

Intra-site CoV of R1 (%)



Inter-site CoV of R1 (%)



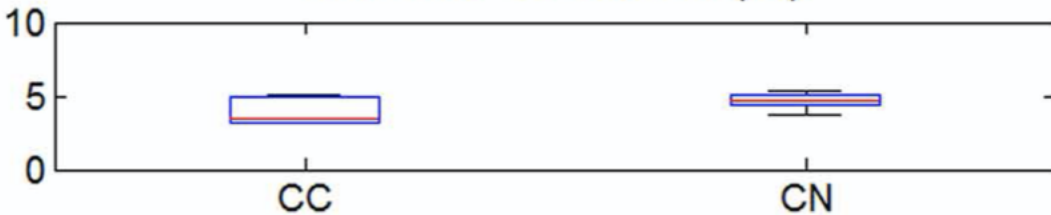
Controlling the acquisition



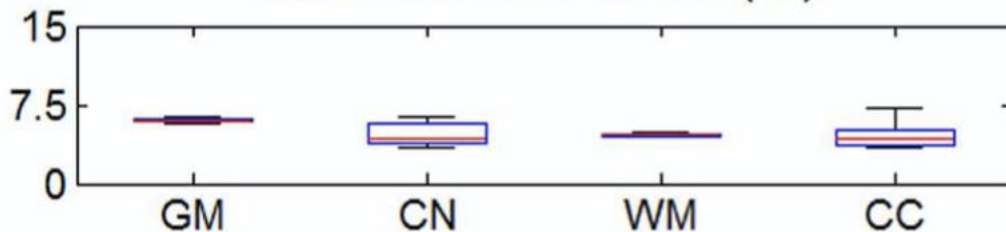
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Intra-site CoV of R1 (%)



Inter-site CoV of R1 (%)



How stable is quantitative MRI? – Assessment of intra- and inter-scanner-model reproducibility using identical acquisition sequences and data analysis programs

René-Maxime Gracien^{a, c, ✉}, Michelle Maiworm^{a, b, c}, Nadine Brüche^c, Manoj Shrestha^c, Ulrike Nöth^c, Elke Hattingen^b, Marlies Wagner^b, Ralf Deichmann^c

- Provided that identical acquisition sequences are used, discrepancies between qMRI data acquired with different scanner models are low.

Controlling the acquisition *isn't the whole solution*



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

NeuroImage

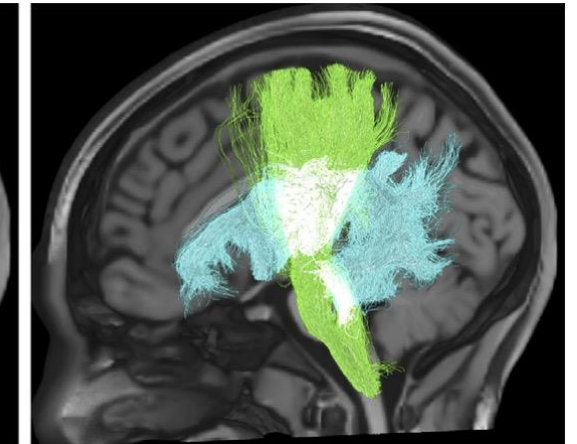
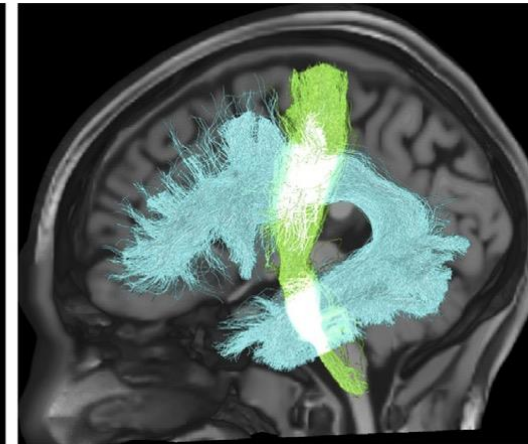
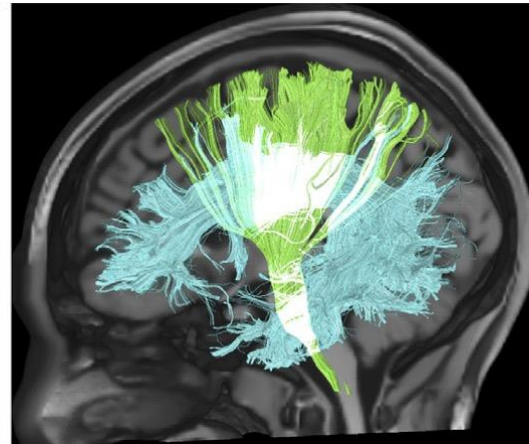
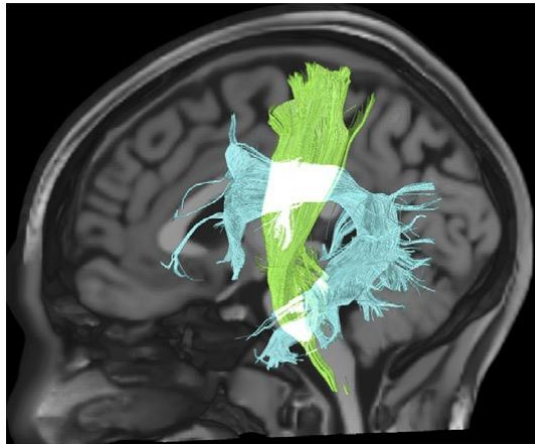
journal homepage: www.elsevier.com/locate/neuroimage



Tractography dissection variability: What happens when 42 groups dissect 14 white matter bundles on the same dataset?



Kurt G. Schilling^{a,*}, François Rheault^b, Laurent Petit^c, Colin B. Hansen^d, Vishwesh Nath^d, Fang-Cheng Yeh^e, Gabriel Girard^f, Muhamed Barakovic^g, Jonathan Rafael-Patino^h, Thomas Yu^h, Elda Fischi-Gomez^h, Marco Pizzolatoⁱ, Mario Ocampo-Pineda^j, Simona Schiavi^j, Erick J. Canales-Rodríguez^h, Alessandro Daducci^j, Cristina Granziera^g, Giorgio Innocenti^k, Jean-Philippe Thiran^h, Laura Mancini^l, Stephen Wastling^l, Sirio Cocozza^m, Maria Petraccaⁿ, Giuseppe Dentillo^m, Matteo Mancini^o, Sigurd B. Vos^p, Veeraj N. Vekheria^q, John S. Duncan^r



Controlling the acquisition *isn't the whole solution*

Brain Imaging and Behavior (2020) 14:1318–1327

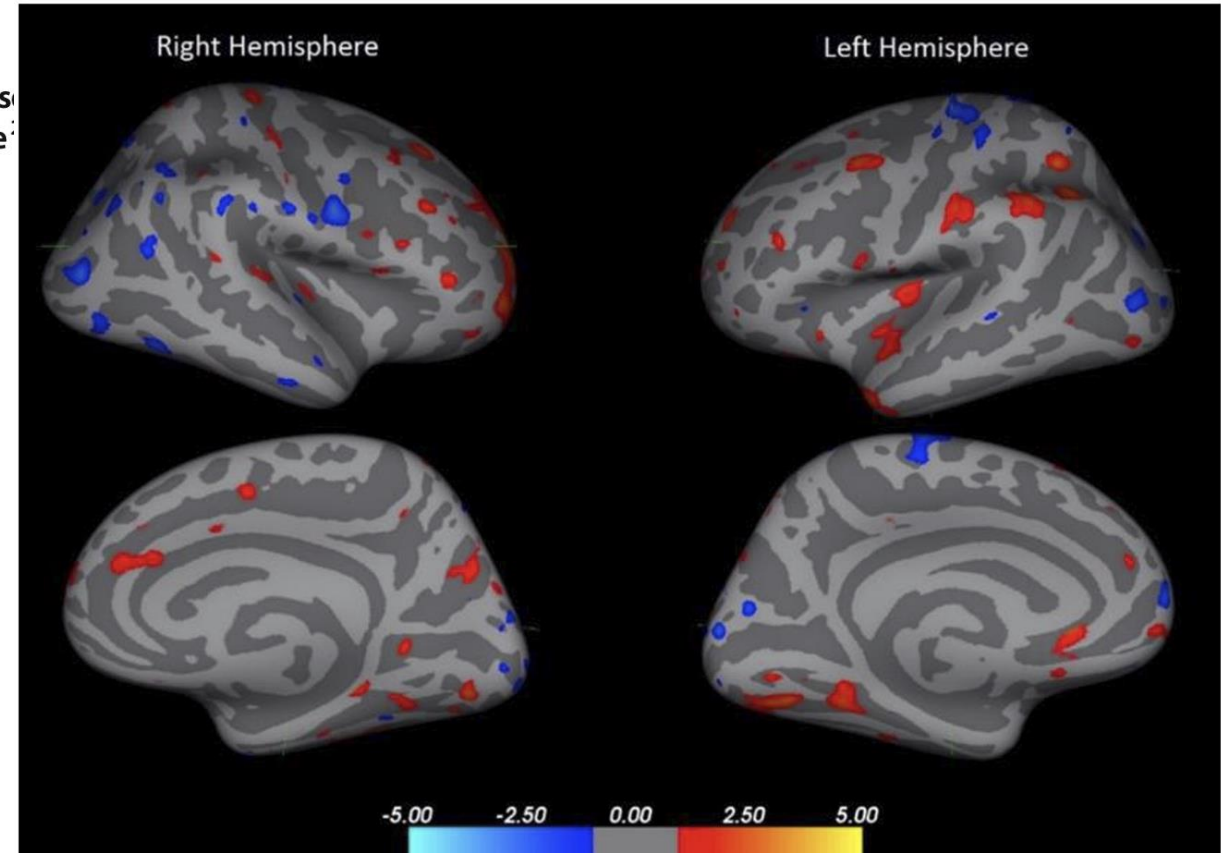
<https://doi.org/10.1007/s11682-018-9994-x>

ORIGINAL RESEARCH

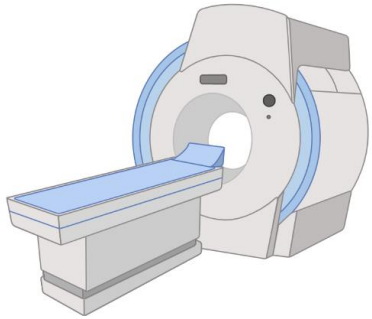


FreeSurfer 5.3 versus 6.0: are volumes comparable? A Chronic Effects of Neurotrauma Consortium study

Erin D. Bigler¹  · Marc Skiles¹ · Benjamin S. C. Wade^{2,3,4} · Tracy J. Abildskov¹ · Nick J. Tustis¹ · Mary R. Newsome⁶ · Andrew R. Mayer⁷ · James R. Stone⁵ · Brian A. Taylor⁸ · David F. Tate¹ · Harvey S. Levin⁶ · Elisabeth A. Wilde^{6,9}



What can you do?



Data acquisition

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- > Hardware
- > Software

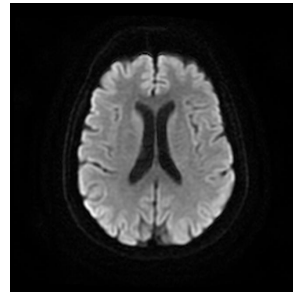
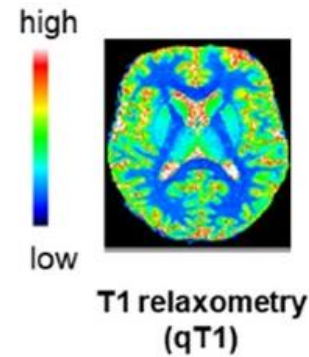


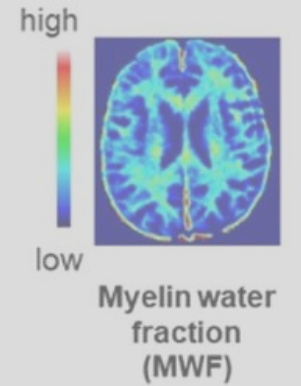
Image Reconstruction

- > Software
- > Can be tied to quantitative model
- > Data storage



Quantitative Modeling

- > Model selection
- > Software



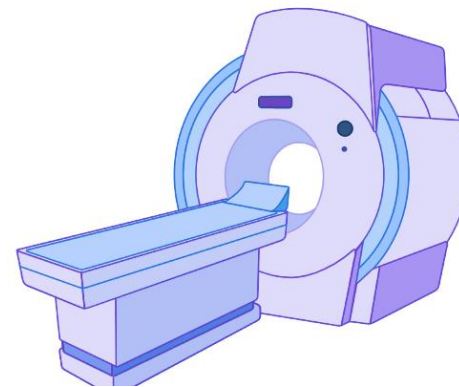
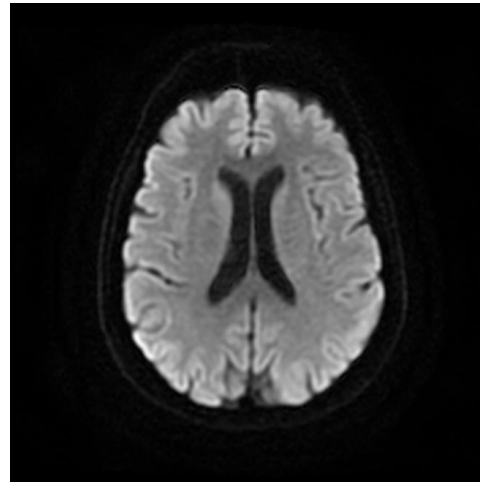
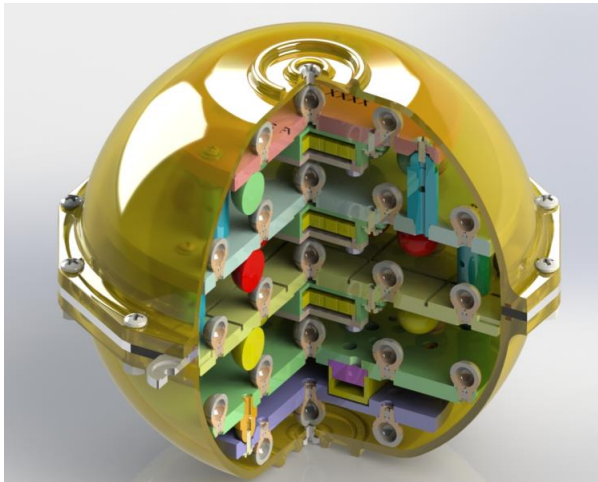
Using the information

- > Clinical work
- > Biophysical model
- > Software

Implementing quantitative MRI

Use a phantom and a repeatable pipeline.

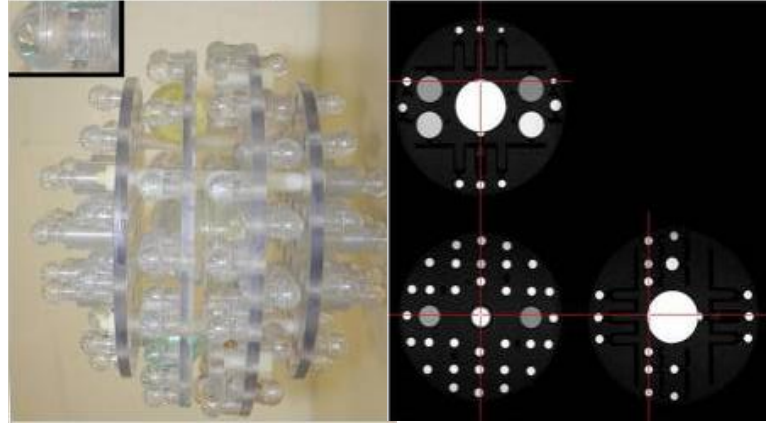
Quantitative
Imaging
Biomarkers
Alliance



Use phantoms!

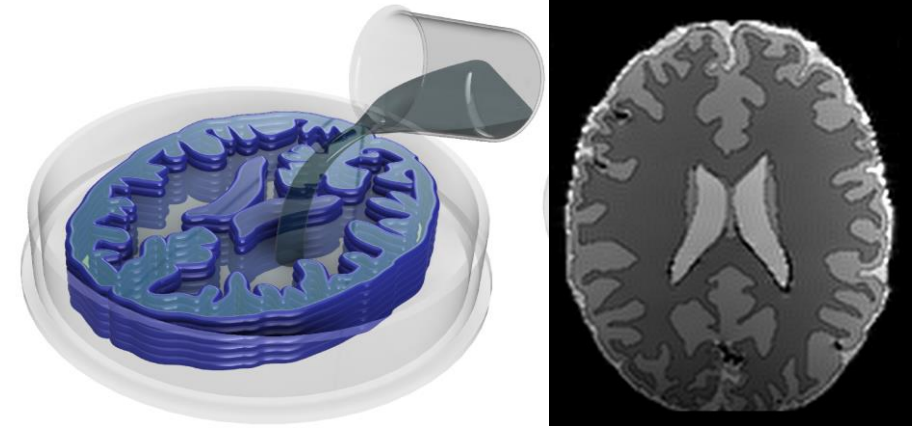


Isotropic diffusion phantom



ADNI phantom

Gunter JL et al., Med Phys 2009



3D Printed, Agarose-filled phantom

K. Gopalan, J. I. Tamir, A. Arias, M. Lustig, MRM 2021

phantoms.martinos.org



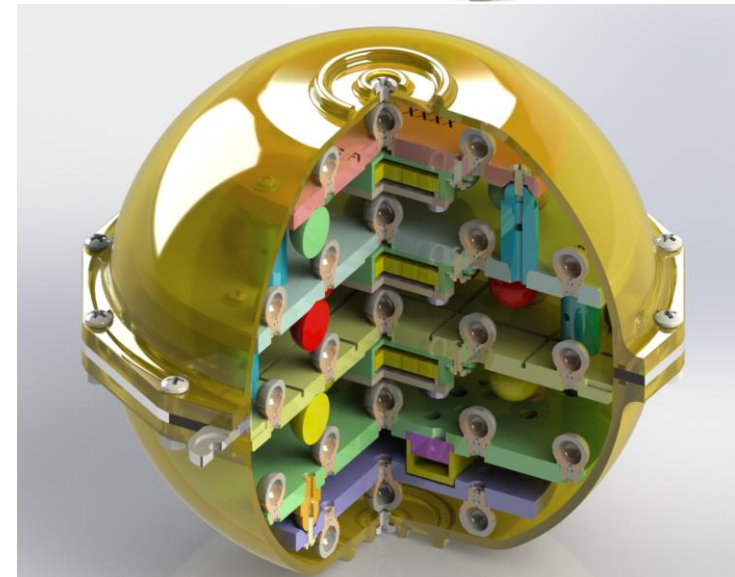
Proton Density Fat Fraction & R2* phantom

Hernando D et al., MRM 2016

How can we use a phantom?

- Select a phantom for your application
- Test the pipeline that you plan to use for participants
- Site qualification for image acquisition

- Adds logistical complexity
- Doesn't always represent in vivo imaging





Medical Phantom Lending Library

<https://www.nist.gov/programs-projects/nistnibib-medical-imaging-phantom-lending-library>

How the PLL works:

- Easy to use: go to web site, check availability calendar, submit request for review by NIST.
- 2-to-6-week loans recommended
- Sharing data to common database encouraged
- Currently only ship within North America

NIST Search NIST Menu

PROJECTS/PROGRAMS

NIST/NIBIB Medical Imaging Phantom Lending Library

Summary

As part of the MRI Biomarker Measurement Service, traceable magnetic resonance imaging (MRI) phantoms are available for loan at a minimal cost, plus shipping. Two copies each of the MRI system phantom developed by NIST and the International Society of Magnetic Resonance in Medicine (ISMRM) and the MRI diffusion phantom developed by NIST, the Radiological Society of North America (RSNA), and the National Institutes of Health (NIH) are available for check out. Contact MRIStandards@nist.gov to schedule a loan. A two-week loan at each site is suggested and during the initial startup there will be no charge for the loan. Analysis code, sample images, calibration data, and references can be found at <https://github.com/MRIStandards/PhantomViewer>. Additional phantoms will be added to the lending library as requested by customers, please email MRIStandards@nist.gov to submit requests for additional phantoms.

[View Phantom Availability Calendar](#)

ORGANIZATIONS

Physical Measurement Laboratory
Applied Physics Division
Magnetic Imaging Group

NIST STAFF

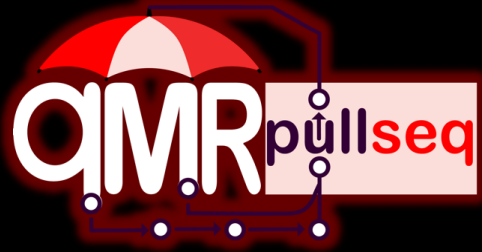
Stephen E. Russek
Kathryn Keenan
Karl Stupic

CONTACT

Contact: stephen.russek@nist.gov

Control the entire pipeline

Control the entire pipeline



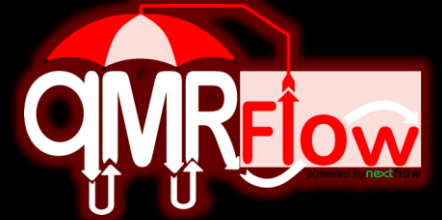
Open-source
implementation



Unified
user interface



Community
data standards



Fully transparent
workflow



Vendor-neutral sequences (VENUS)

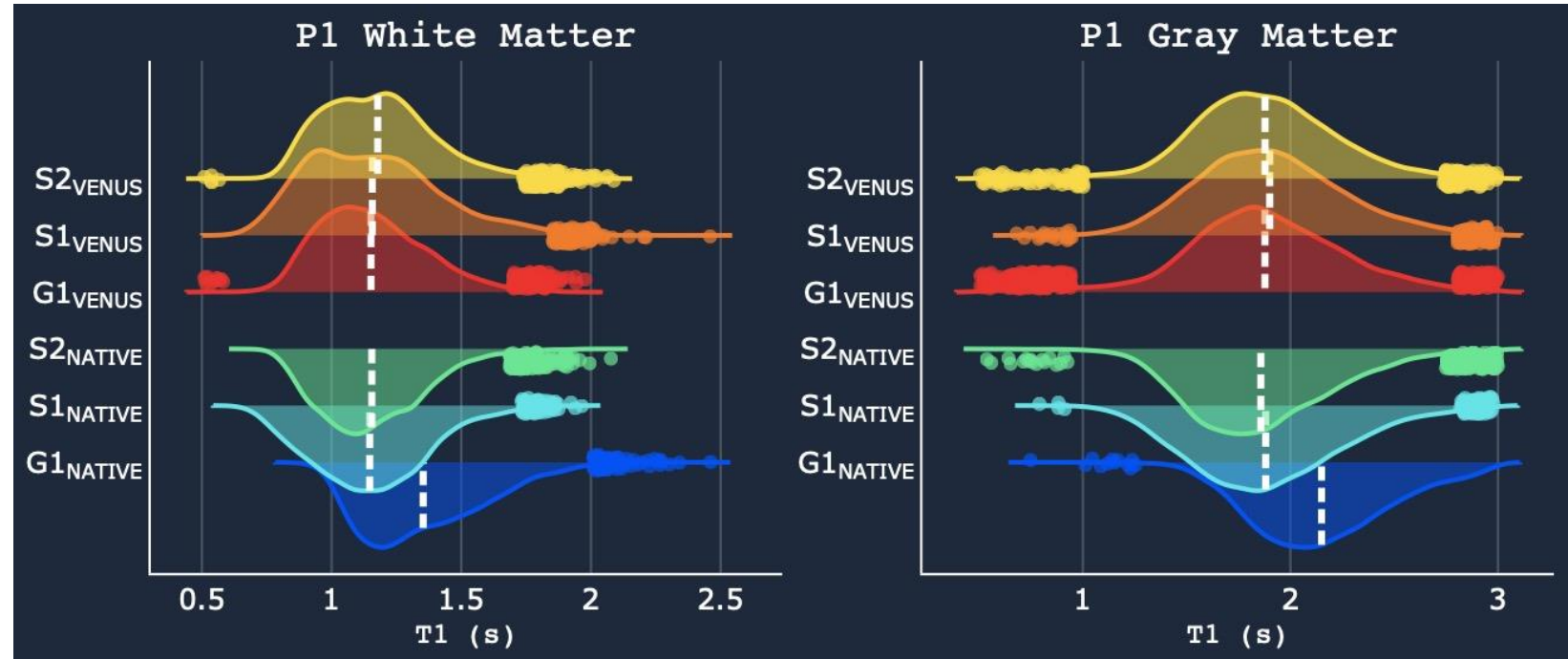
Karakuzu et al. <https://zenodo.org/record/6860878>

VENUS: <https://onlinelibrary.wiley.com/doi/abs/10.1002/mrm.29292>

qMRI-BIDS: <https://www.nature.com/articles/s41597-022-01571-4>

qMRLab: <https://joss.theoj.org/papers/10.21105/joss.02343>

Control the entire pipeline



Vendor-neutral sequences (VENUS)

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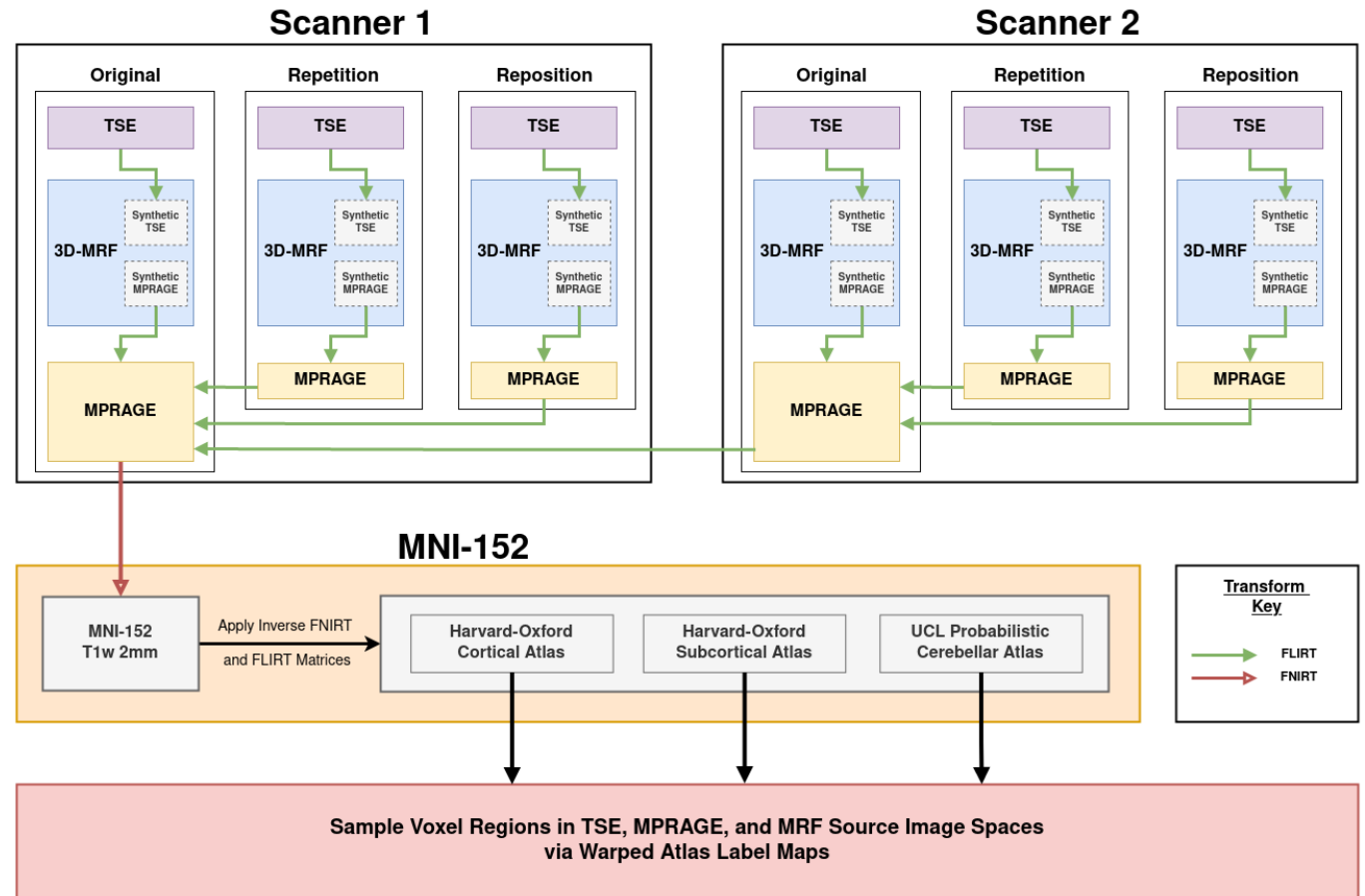
qMRI-BIDS: <https://www.nature.com/articles/s41597-022-01571-4>

qMRLab: <https://joss.theoj.org/papers/10.21105/joss.02343>

Use a method with high repeatability and reproducibility

Use a method with high repeatability and reproducibility

- Acquire TSE, MPRAGE, and MRF data for various scenarios on two scanners
- Linearly register scanners to each other via “original” MPRAGE images
- Nonlinearly register all images to MNI-152-2mm via scanner 1 “original” MPRAGE images



Use a method with high repeatability and reproducibility

MRF is reproducible whether a scan is repeated:

- immediately
- after reposition on the same scanner
- repeated on a different scanner or day

Weighted Mean/StdDev by Region Size

| mean \pm std dev (bias \pm agreement) | Intrascanner | | Interscanner |
|--|-------------------------|-------------------------|-------------------------|
| | Same-Session | Cross-Session | Cross-Session |
| T1 (%) | 0.22 \pm 2.83 | -0.07 \pm 2.22 | -1.01 \pm 2.62 |
| T2 (%) | 1.06 \pm 4.38 | 1.41 \pm 4.04 | -3.51 \pm 4.22 |
| MPRAGE (%) | -1.26 \pm 6.00 | -3.64 \pm 6.38 | -2.25 \pm 7.91 |
| TSE (%) | -0.40 \pm 5.59 | -1.70 \pm 5.89 | -0.39 \pm 7.90 |

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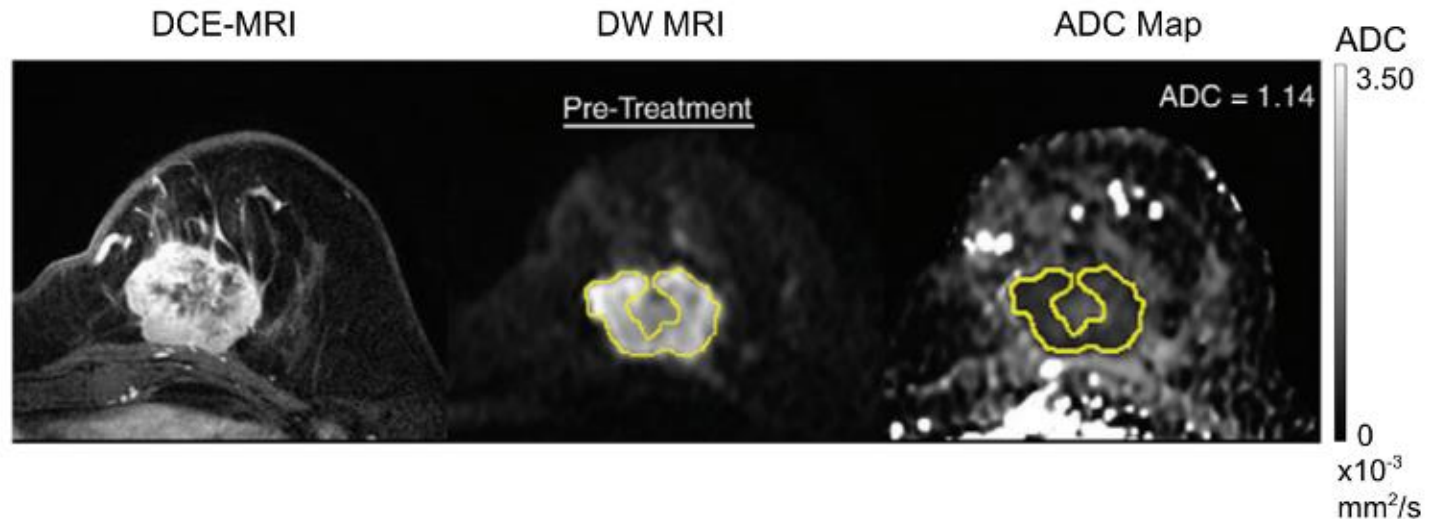
Quantitative
Imaging
Biomarkers
Alliance

RSNA®

Why does this matter?

Diffusion-weighted MRI Findings Predict Pathologic Response in Neoadjuvant Treatment of Breast Cancer: The ACRIN 6698 Multicenter Trial

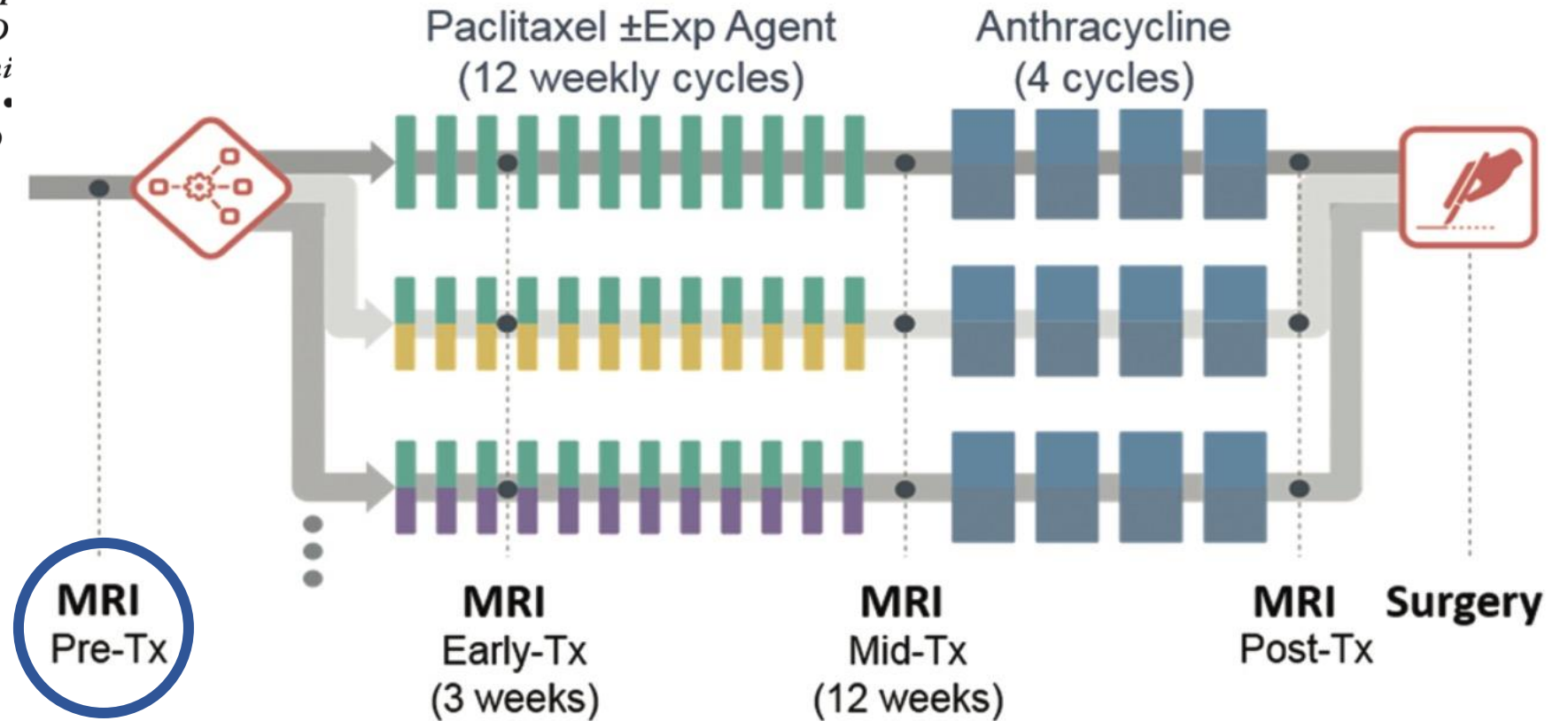
Savannah C. Partridge, PhD • Zheng Zhang, PhD • David C. Newitt, PhD • Jessica E. Gibbs, BA • Thomas L. Chenevert, PhD • Mark A. Rosen, MD, PhD • Patrick J. Bolan, PhD • Helga S. Marques, MS • Justin Romanoff, MA • Lisa Cimino, RT • Bonnie N. Joe, MD, PhD • Heidi R. Umphrey, MD • Haydee Ojeda-Fournier, MD • Basak Dogan, MD • Karen Oh, MD • Hiroyuki Abe, MD, PhD • Jennifer S. Drukteinis, MD • Laura J. Esserman, MD, MBA • Nola M. Hylton, PhD • For the ACRIN 6698 Trial Team and I-SPY 2 Trial Investigators



Why does this matter?

Diffusion-weighted MRI Findings Predict Pathologic Response in Neoadjuvant Treatment of Breast Cancer: The ACRIN 6698 Multicenter Trial

Savannah C. Partridge, PhD • Zheng Zhang, I Chenevert, PhD • Mark A. Rosen, MD, PhD Romanoff, MA • Lisa Cimino, RT • Bonni MD • Basak Dogan, MD • Karen Oh, MD • Esserman, MD, MBA • Nola M. Hylton, PhD



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ADC response were evident during treatment (Fig 4a). Δ ADC was not predictive of pCR at early treatment/3 weeks (AUC = 0.53; 95% CI: 0.45, 0.61; $P = .48$). By midtreatment/12 weeks, mean Δ ADC was greater in patients with pCR than in patients without pCR ($50\% \pm 49$ and $36\% \pm 44$, respectively) and was predictive of pCR, with AUC = 0.60 (95% CI: 0.52, 0.68; $P = .017$). Δ ADC at posttreatment was similarly predictive, with AUC = 0.61 (95% CI: 0.52, 0.69, $P = .013$) (Table 2), although neither Δ ADC at midtreatment nor Δ ADC at posttreatment was significant after multiple-comparison adjustment.

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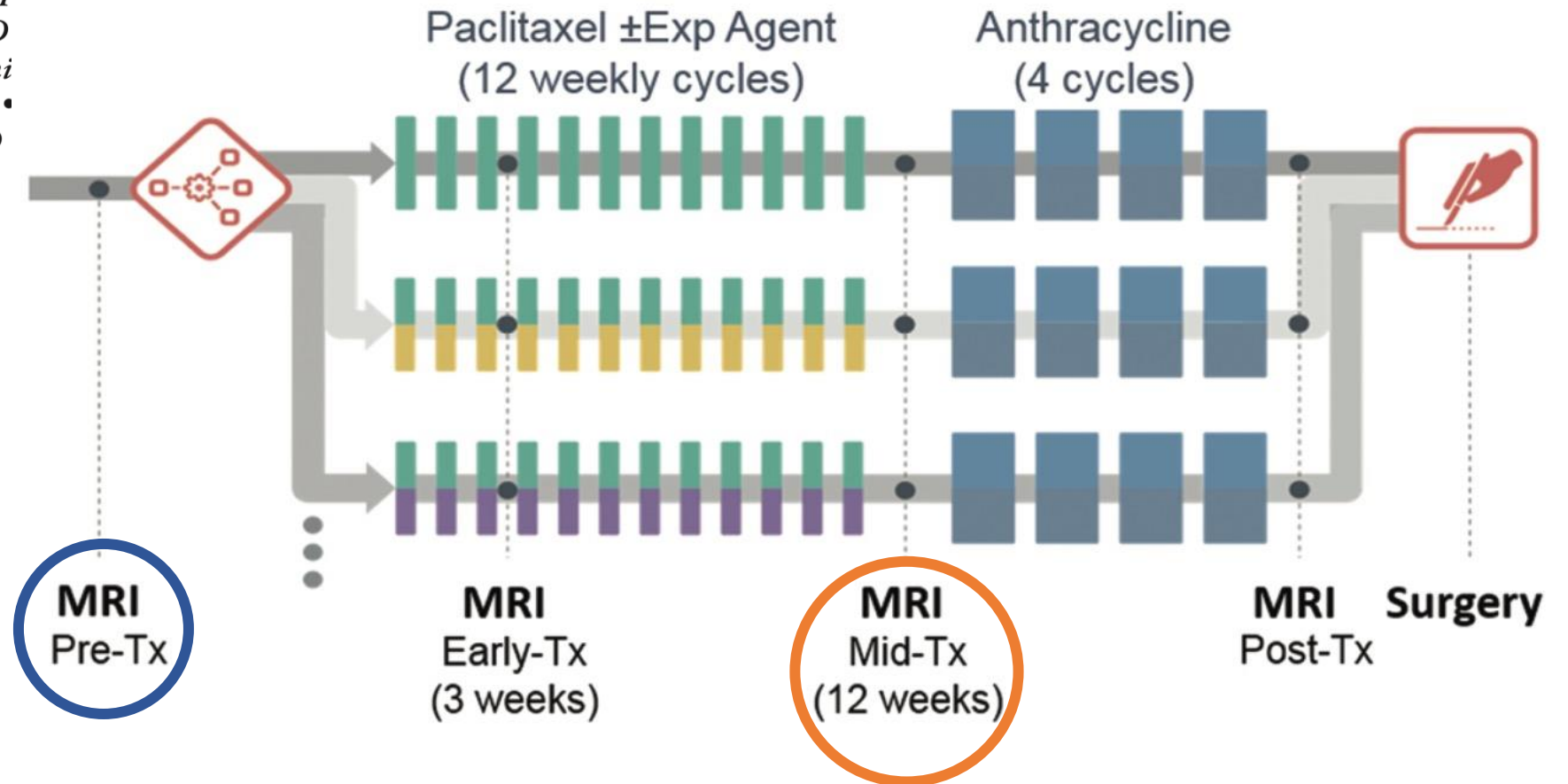
Savannah C. Partridge, PhD • Zheng Zhang, PhD • David C. Newitt, PhD • Jessica E. Gibbs, BA • Thomas L. Chenevert, PhD • Mark A. Rosen, MD, PhD • Patrick J. Bolan, PhD • Helga S. Marques, MS • Justin Romanoff, MA • Lisa Cimino, RT • Bonnie N. Joe, MD, PhD • Heidi R. Umphrey, MD • Haydee Ojeda-Fournier, MD • Basak Dogan, MD • Karen Oh, MD • Hiroyuki Abe, MD, PhD • Jennifer S. Drukteinis, MD • Laura J. Esserman, MD, MBA • Nola M. Hylton, PhD • For the ACRIN 6698 Trial Team and I-SPY 2 Trial Investigators

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Is this actually happening?

Is this actually happening?

YES

Is this actually happening?

YES

Clinical Research Organizations (CROs)

Is this actually happening?

YES

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Eur Radiol (2017) 27:3662–3668
DOI 10.1007/s00330-017-4736-9

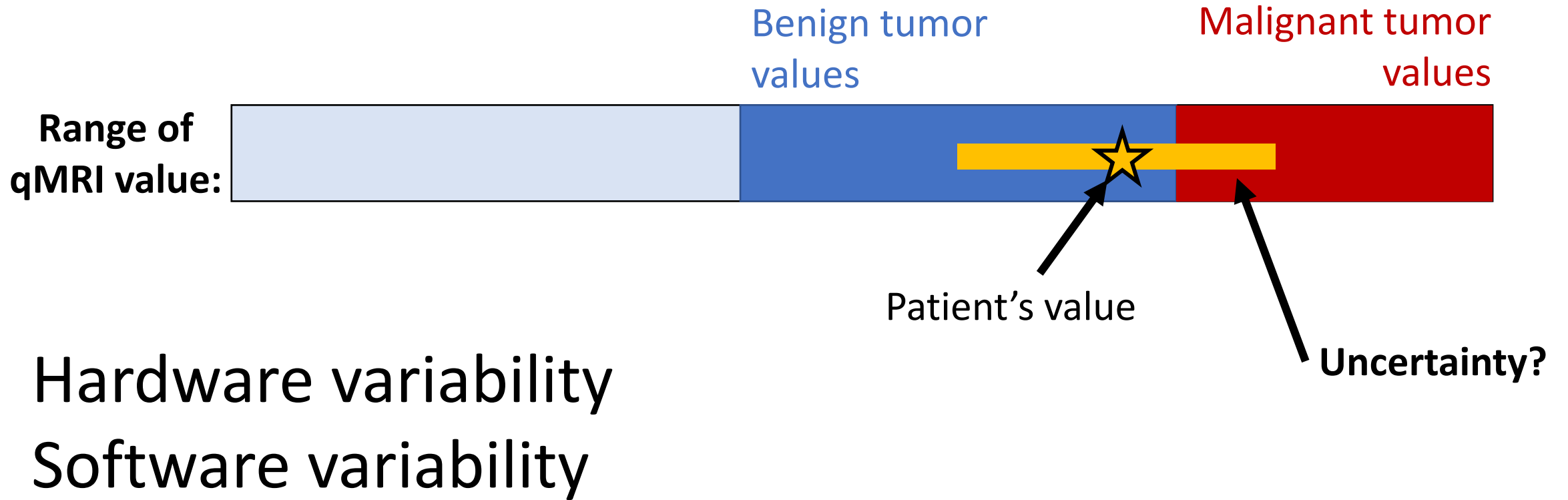
MUSCULOSKELETAL

Repeatability and response to therapy of dynamic contrast-enhanced magnetic resonance imaging biomarkers in rheumatoid arthritis in a large multicentre trial setting

John C. Waterton^{1,2} · Meilien Ho³ · Lars H. Nordenmark⁴ · Martin Jenkins⁵ · Julie DiCarlo⁶ · Gwenael Guillard⁷ · Caleb Roberts⁸ · Giovanni Buonaccorsi⁸ · Geoffrey J. M. Parker^{1,8} · Michael A. Bowes⁷ · Charles Peterfy⁶ · Herbert Kellner⁹ · Peter C. Taylor¹⁰

MRI biomarkers [13] pose different challenges to soluble biomarkers. Biomarker quality and validity depends on operation of an MRI device not primarily designed for quantitative work, perhaps in a manner unfamiliar to users in trial sites. Encouraging measures of repeatability and response to therapy in small studies in single expert centres may not translate to real-world multicentre trials. It is therefore necessary to evaluate [14] these biomarkers specifically in the multicentre setting.

Possibilities of diagnostic quantitative MRI



Moving quantitative MRI to the clinic

**There is bias
across MRI
systems.**

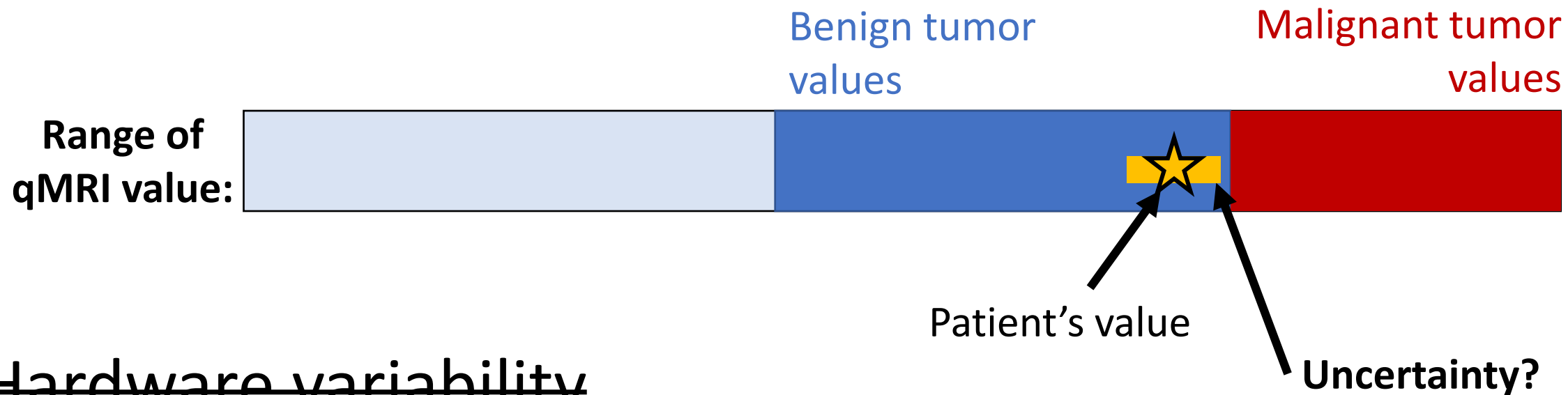
**MRI systems
change over time.**

**Use a phantom and a
controlled pipeline.**

**We can use repeatable &
reproducible methods.**

**We can do regular QA
on our MRI systems.**

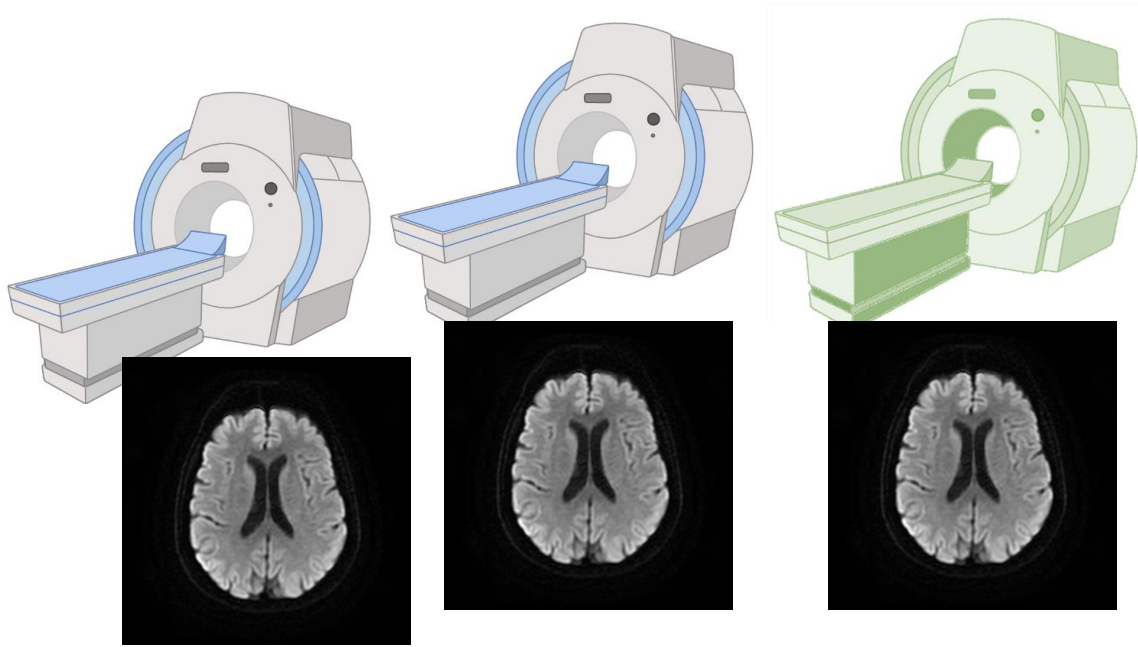
Moving quantitative MRI to the clinic



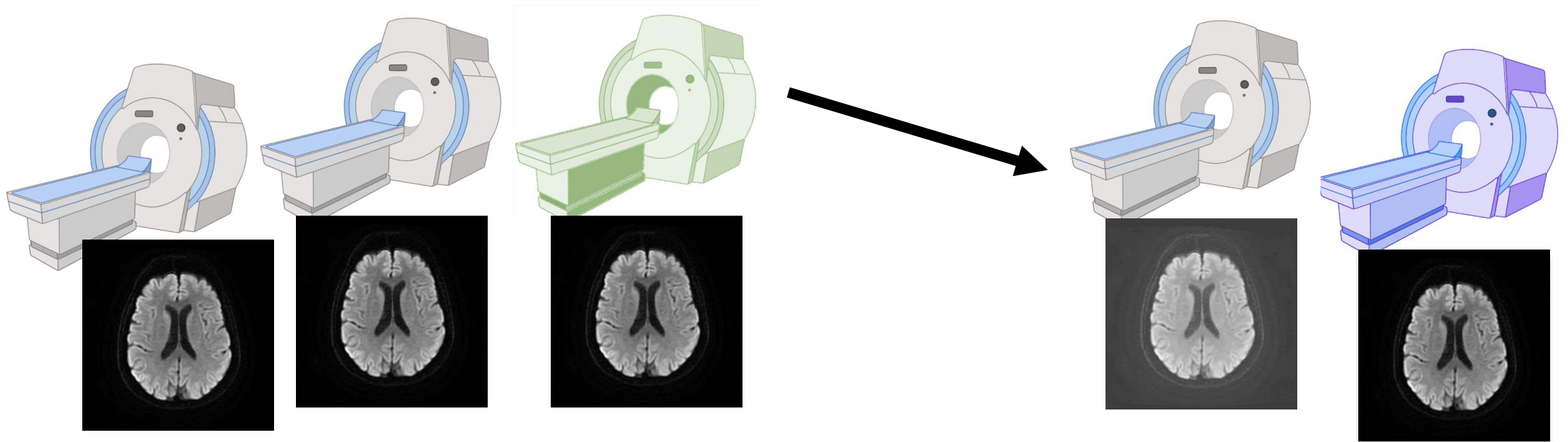
~~Hardware variability~~

~~Software variability~~

Implementing *clinical* quantitative MRI



Implementing *clinical* quantitative MRI

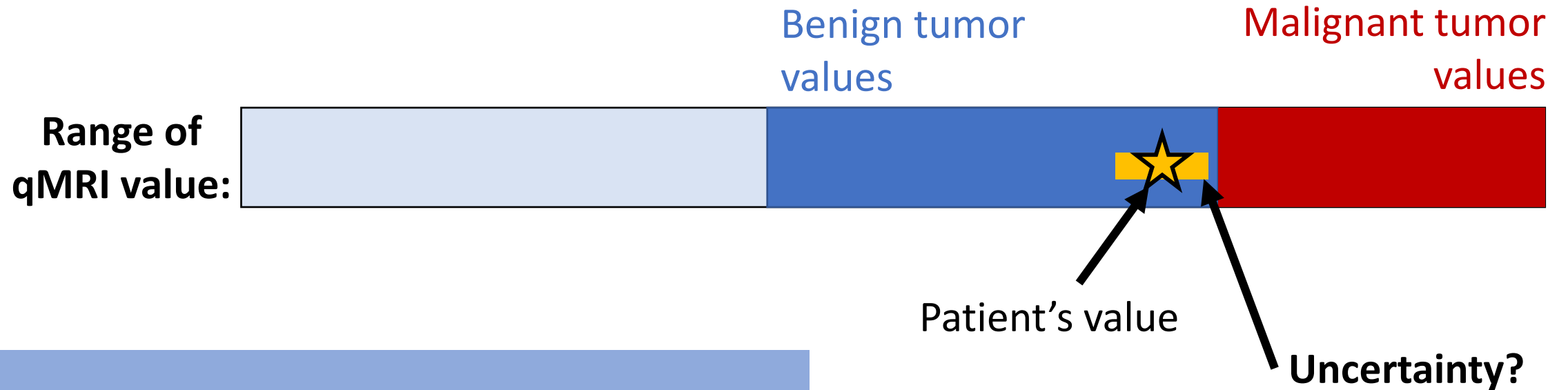


Implementing *clinical* quantitative MRI



**How do we translate
qMRI success to the
clinic?**

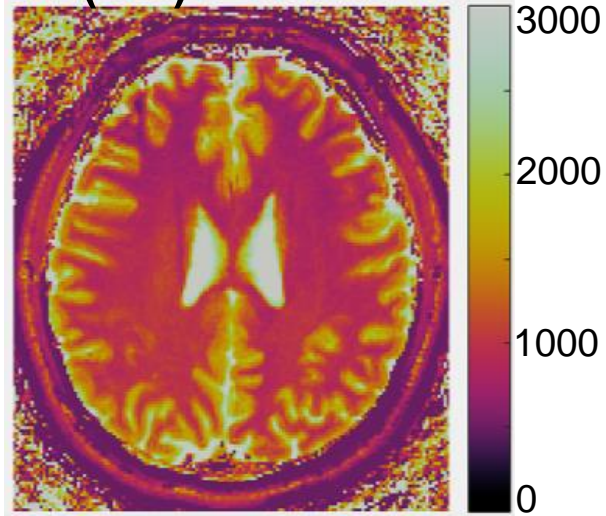
Moving quantitative MRI to the clinic



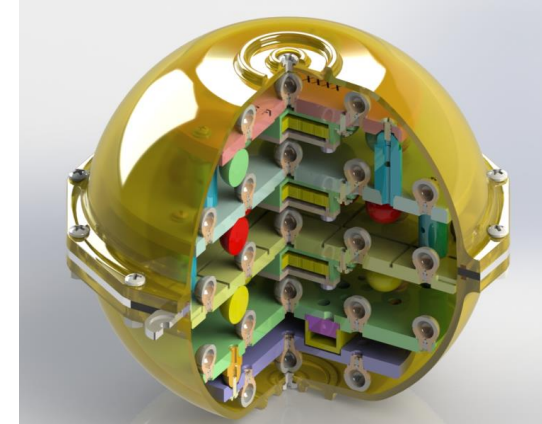
Need clinically actionable values.

Innovations in Cancer Imaging

T1 (ms)



More than a picture



How to implement quantitative MRI?



Expanding the use of MRI

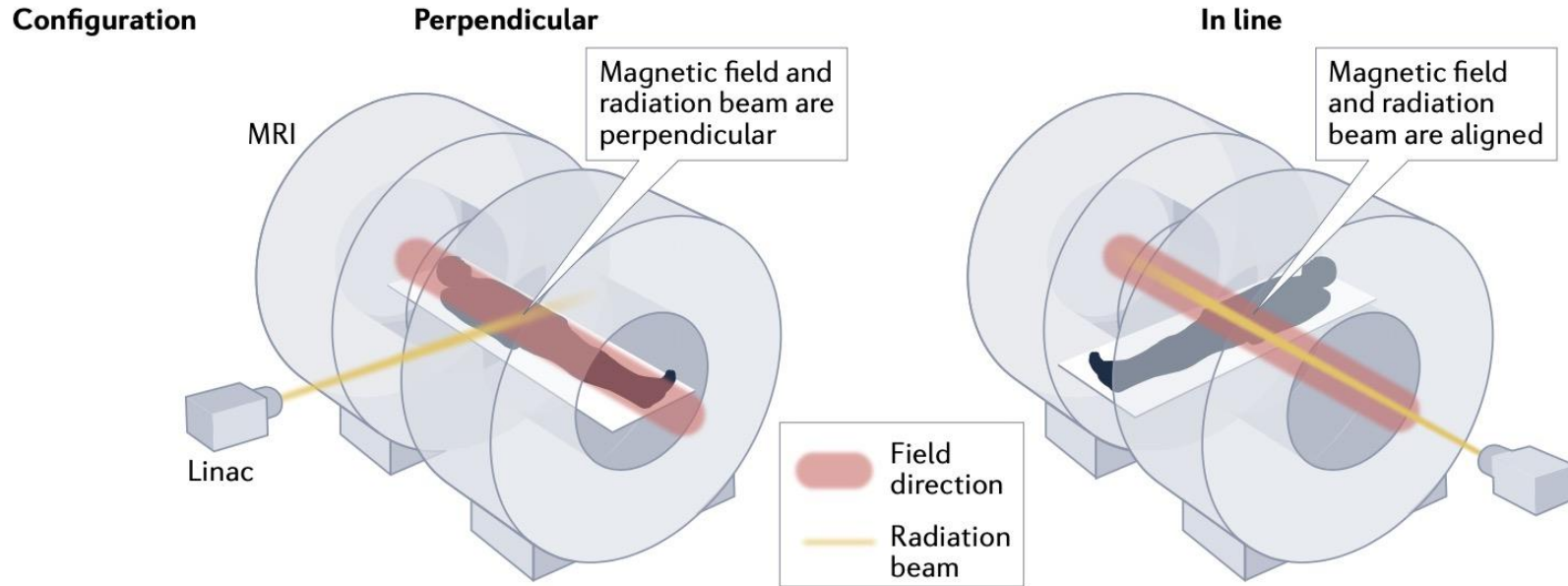
Innovations in Cancer Imaging

Part 2: Expanding the use of MRI

Kathryn Keenan, PhD

Project Leader, Quantitative MRI

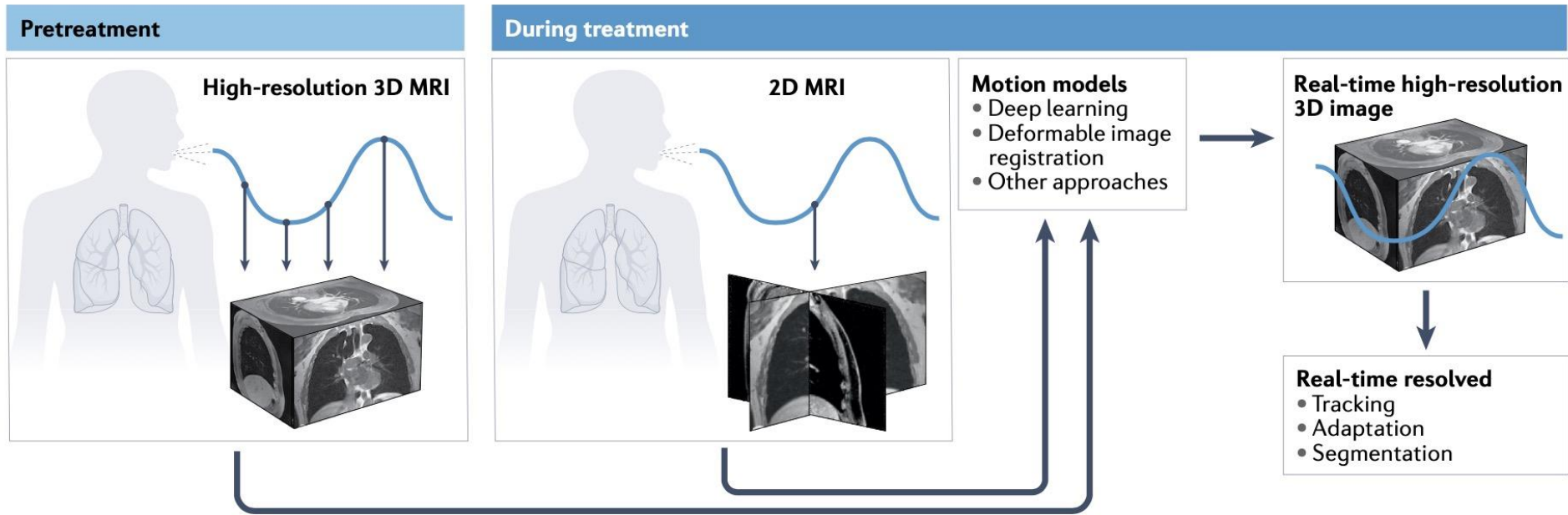
MRI-guided radiotherapy



Integrated MRI-guided radiotherapy — opportunities and challenges

Paul J. Keall¹✉, Caterina Brighi¹, Carri Glide-Hurst², Gary Liney³, Paul Z. Y. Liu¹, Suzanne Lydiard¹, Chiara Paganelli⁴, Trang Pham⁵, Shanshan Shan¹, Alison C. Tree⁶, Ulke A. van der Heide⁷, David E. J. Waddington¹ and Brendan Whelan¹

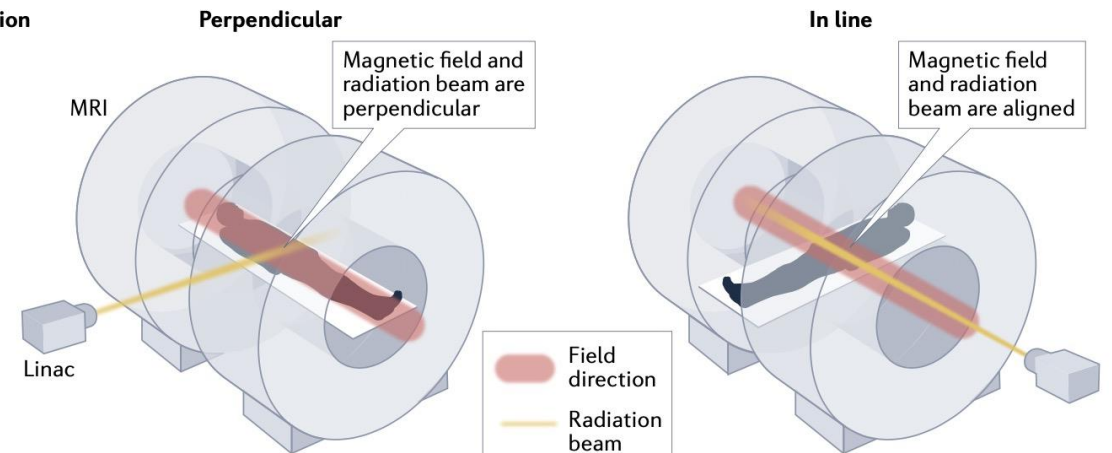
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Configuration



Increasing Accessibility of MRI

Increasing Accessibility of MRI



Not an endorsement. Demonstrating the range of products available and companies operating in the space.

Increasing Accessibility of MRI



64 mT



0.5 T

Not an endorsement. Demonstrating the range of products available and companies operating in the space.

Increasing Accessibility of MRI



1 T



66 mT



64 mT



0.5 T



0.55 T

Not an endorsement. Demonstrating the range of products available and companies operating in the space.

Innovative interventional MRI

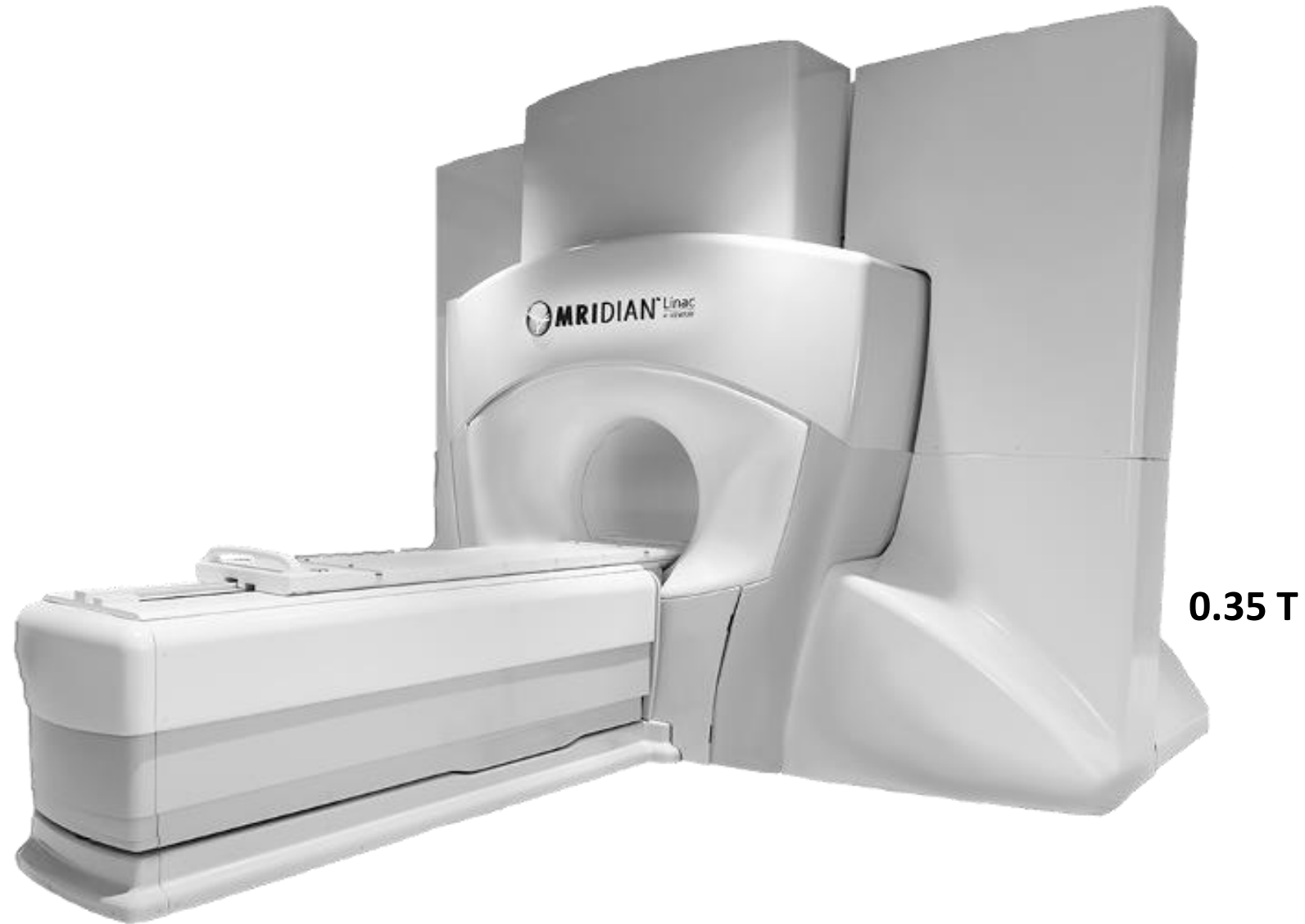


promaxo



Not an endorsement. Demonstrating the range of products available and companies operating in the space.

Innovative use of MRI



Not an endorsement. Demonstrating the range of products available and companies operating in the space.

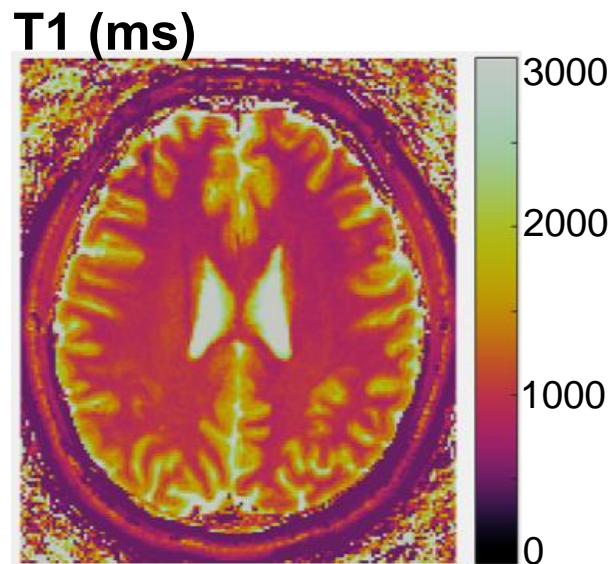
Innovative Use of MRI



**MRI is being used in new
places and new ways.**

Not an endorsement. Demonstrating the range of products available and companies operating in the space.

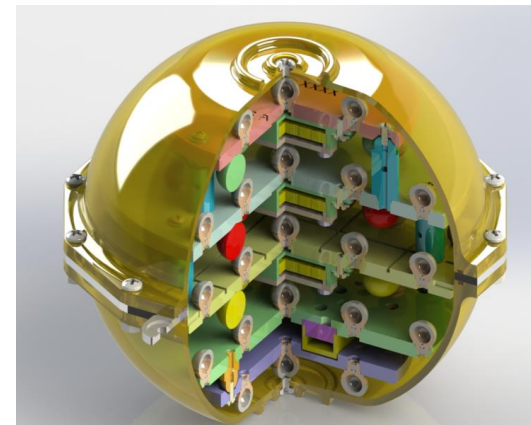
Innovations in Cancer Imaging



More than a picture

**MRI systems
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**There is bias across
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**How to implement
quantitative MRI?**

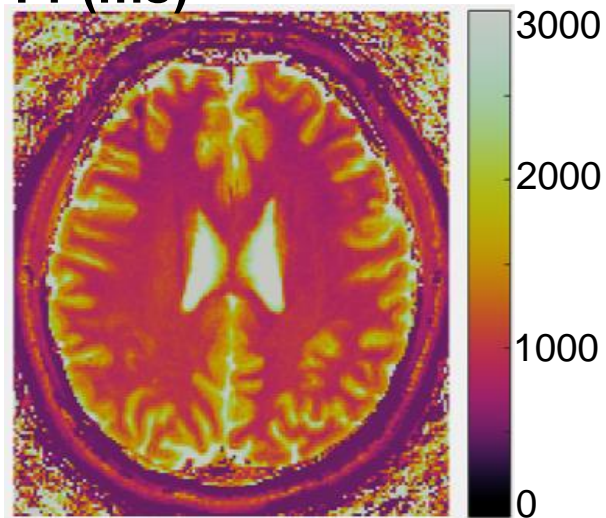
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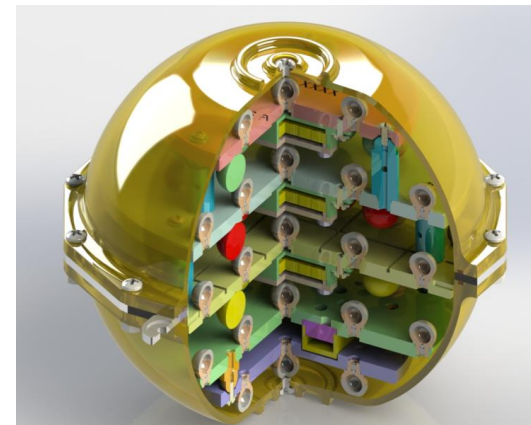
**We can implement the
same pipeline across
sites.**

Innovations in Cancer Imaging

T1 (ms)



More than a picture



**How to implement
quantitative MRI?**



Expanding the use of MRI

Thanks to all who contributed

NIST

Magnetic Imaging Group

Dan Gruber

Mark Ferris

Kalina Jordanova

Mikail Kraft

John Lundstrom

Michele Martin

Sam Oberdick

Stephen Ogier

Stephen Russek

Cassie Stoffer

Karl Stupic

Gary Zabow



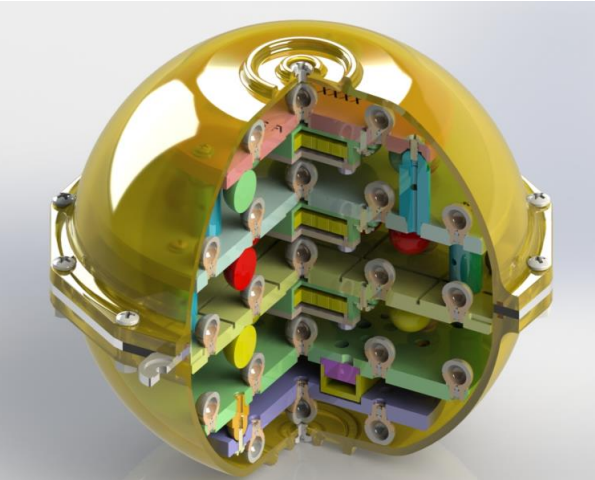
@katykeenan

kathryn.keenan@nist.gov




NIST in Boulder, CO

NIST's efforts in quantitative MRI



rosenlab.org



 @katykeenan
kathryn.keenan@nist.gov

nist.gov/pml/applied-physics-division/magnetic-imaging

