Quantitative MRI

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Medical Physics 710
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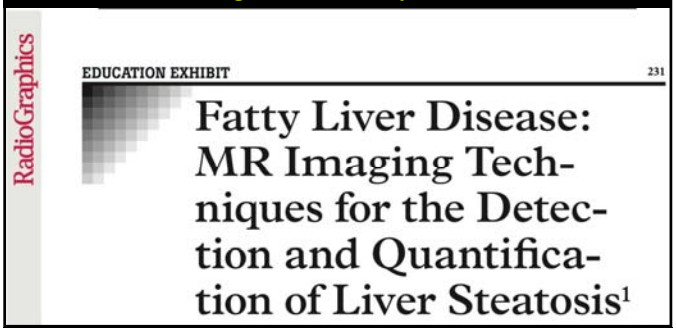
Outline

- Motivation (*Why quantitative MRI?*)
- Examples (*What can we measure?*)
- Challenges
- Development of Quantitative MRI techniques
- Current Status (*Where do we stand?*)

Diagnosis of Fatty Liver

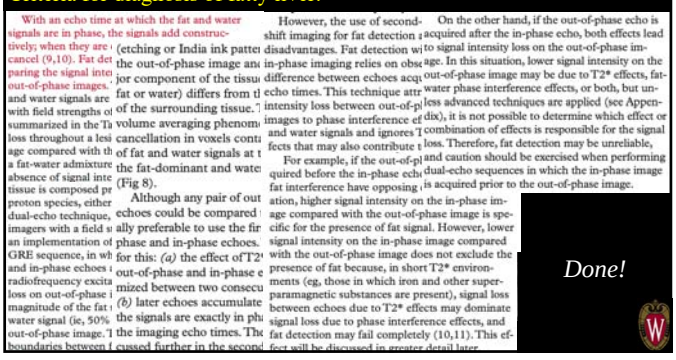

RadioGraphics

EDUCATION EXHIBIT 231

Fatty Liver Disease: MR Imaging Techniques for the Detection and Quantification of Liver Steatosis[1]

Qualitative Imaging

Criteria for diagnosis of fatty liver:


With an echo time at which the fat and water signals are in phase, the signals add constructively; when they are ... cancel (9,10). Fat det... paring the signal inte... out-of-phase images.' ... and water signals are ... with field strengths o... summarized in the Ta... loss throughout a lesi... age compared with th... a fat-water admixture ... absence of signal inte... tissue is composed pr... proton species, either ... dual-echo technique, ... imagers with a field s... an implementation of ... GRE sequence, in wh... and in-phase echoes ... radiofrequency excita... loss on out-of-phase i... magnitude of the fat ... water signal (ie, 50% ... out-of-phase image. T... boundaries between t...

However, the use of second-... shift imaging for fat detection ... disadvantages. Fat detection wi... in-phase imaging relies on obse... difference between echoes acqu... echo times. This technique attr... intensity loss between out-of-p... images to phase interference ef... and water signals and ignores t... fects that may also contribute t...

For example, if the out-of-p... quired before the in-phase echo ... fat interference have opposing ... ation, higher signal intensity on the in-phase im... age compared with the out-of-phase image is spe... cific for the presence of fat signal. However, lower signal intensity on the in-phase image compared with the out-of-phase image does not exclude the presence of fat because, in short T2* environments (eg, those in which iron and other superparamagnetic substances are present), signal loss between echoes due to T2* effects may dominate signal loss due to phase interference effects, and fat detection may fail completely (10,11). This effect will be discussed in greater detail later...

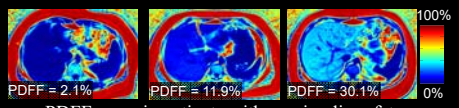
On the other hand, if the out-of-phase echo is acquired after the in-phase echo, both effects lead to signal intensity loss on the out-of-phase image. In this situation, lower signal intensity on the out-of-phase image may be due to T2* effects, fat-water phase interference effects, or both, but unless advanced techniques are applied (see Appendix), it is not possible to determine which effect or combination of effects is responsible for the signal loss. Therefore, fat detection may be unreliable, and caution should be exercised when performing dual-echo sequences in which the in-phase image is acquired prior to the out-of-phase image.

Done!

Quantitative Imaging

Map of Proton-Density Fat-Fraction

(Quantitative Biomarker of Triglyceride Concentration)



PDFF maps in patients with varying liver fat

Criterion for diagnosis of fatty liver:

LS Szczepaniak et al, 2005

Qualitative vs Quantitative MRI

Qualitative
(T1-weighted)

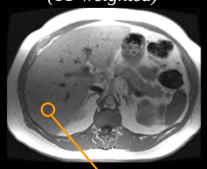


Image intensity arbitrary
(eg: dependent on coil sensitivities)

Quantitative
(Fat Fraction map)

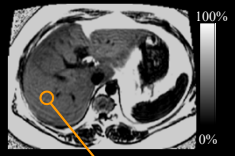
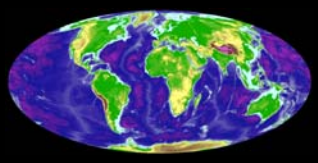


Image intensity reflects fundamental tissue property

Quantitative Imaging Biomarkers

Why Quantitative?

Standardization of diagnosis, staging and treatment monitoring



Paradigm Shift: *Qualitative vs Quantitative MRI*

Examples

T1 and T2

Tumor Detection by Nuclear Magnetic Resonance

Abstract. *Spin echo nuclear magnetic resonance measurements may be used as a method for discriminating between malignant tumors and normal tissue. Measurements of spin-lattice (T_1) and spin-spin (T_2) magnetic relaxation times were made in six normal tissues in the rat (muscle, kidney, stomach, intestine, brain, and liver) and in two malignant solid tumors, Walker sarcoma and Novikoff tissues were characterized by an increase in the motional freedom of tissue water molecules. The possibility of using magnetic relaxation methods for rapid discrimination between benign and malignant surgical specimens has also been considered. Spin-lattice relaxation times for two benign fibroadenomas were distinct from those for both malignant tissues and were the same as those of muscle.*

Relaxation times for the two malignant tumors were distinctly outside the range of values for the normal tissues studied.

Quantitative MRI?

Damadian R, Science 1971

Table 2. Spin-lattice (T_1) and spin-spin (T_2) relaxation times (in seconds) in tumors.

Rat No.	Weight (g)	T_1	T_2
	Walker sarcoma		
6	156	0.700	0.100
7	150	.750	.100
8	495	.794 (0.794)*	.100
9	233	.688	
10	255	.750	
Mean and S.E.		0.736 ± 0.022	.100
P		< .01†	
	Novikoff hepatoma		
11	155	0.798	0.120
12	160	.852	.120
13	231	.827	.115
Mean and S.E.		0.826 ± 0.013	0.118 ±
P		< .01†	0.002
	Fibroadenoma (benign)		
14		0.448	
15		.537	
Mean		.492	
	Distilled water		
		2.691	
		2.690	
		2.640	
Mean and S.E.		2.677 ± 0.021	

* Spin-lattice relaxation time after the specimen stood overnight at room temperature. † The *P* values are the probability estimates of the significance of the difference in the means of T_1 for the malignant tumor and for brain.

MR Imaging

Image Formation by Induced Local Interactions: Examples Employing Nuclear Magnetic Resonance

An image of an object may be defined as a graphical representation of the spatial distribution of one or more of its properties. Image formation usually requires that the object interact with a matter or radiation field characterized by a wavelength comparable to or smaller than the smallest features to be distinguished, so that the region of interaction may be restricted and a resolved image generated.

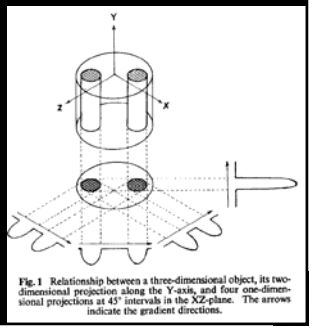
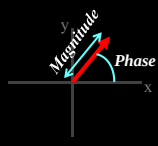


Fig. 1 Relationship between a three-dimensional object, its two-dimensional projection along the Y-axis, and four one-dimensional projections at 45° intervals in the XZ-plane. The arrows indicate the gradient directions.

Lauterbur P, Nature 1973

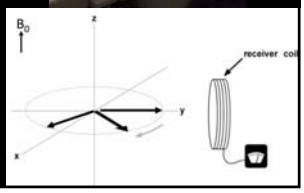
MRI Magnitude and Phase

Measured signal at single voxel



MR signal is complex (magnitude and phase)

- *Usually only magnitude displayed*
- *Phase important in some applications*



MRI Magnitude and Phase

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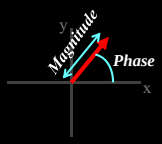

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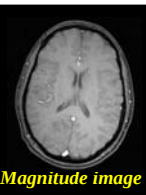


Magnitude image

Phase image

Today: Contrast in MRI

- MR image ***magnitude and phase*** depend on:
  - **Proton density**
  - **T1**
  - **T2**
  - **T2***
  - **Diffusion**
  - **Flow**
  - **Magnetic susceptibility**
  - **Chemical composition of tissue**
  - **…**

Quantitative Imaging Examples

- Size measurements
- Relaxation parameters
- Blood flow
- Concentrations of different materials
- Electromagnetic properties of tissue
- Mechanical properties of tissue
- Molecular diffusion

Techniques

From Contrast to Quantification

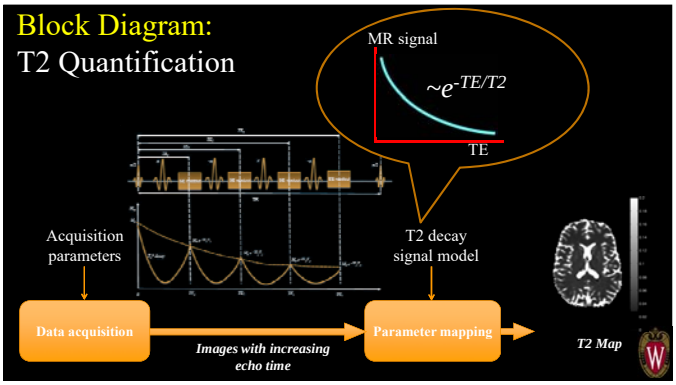
- MR signals (magnitude and phase) depend on a large number of contrast mechanisms
  - Proton density
  - Tissue-specific MR relaxation parameters (T1, T2, T2*,…)
  - Chemical species present
  - Flow, diffusion
  - Oxygenation, etc…
- We can probe the desired contrast mechanism
  - Image with different acquisition parameters
- Physical models describe signal
  - In terms of tissue properties and acquisition parameters

MR Signal: *Depends on Many Tissue Parameters*

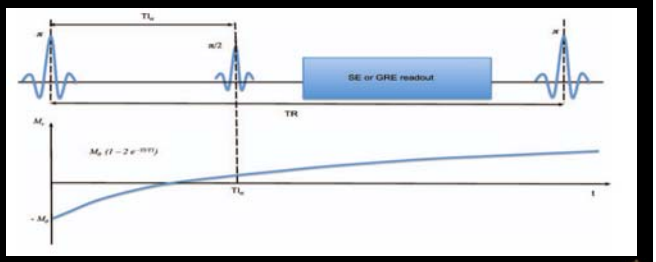
$$\frac{d\mathbf{M}}{dt} = \gamma(\mathbf{M} \times \mathbf{B_0})$$

Bloch-Torrey equation accounting for T1 and T2 relaxation, and molecular self-diffusion

Block Diagram: T2 Quantification



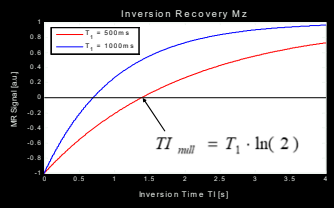
T1 Mapping: Inversion Recovery



Cheng et al. JMRI 36:805–824 (2012)

10/6/2018 SA Hurley

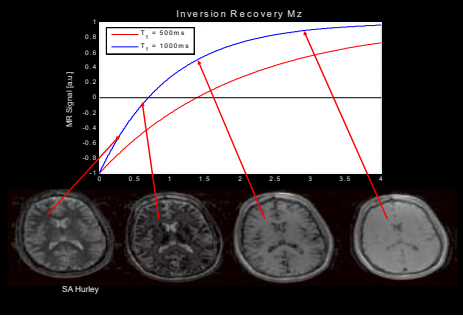
Inversion Recovery T_1



$$M_z = M_0 \cdot \left(1 - 2e^{-TI/T_1}\right)$$

10/6/2018 SA Hurley

Inversion Recovery T_1



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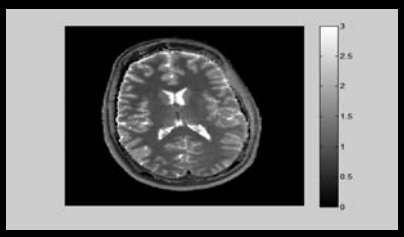


What Makes a QIB Valid?

- *Correlation/bias*
  - High correlation, low bias compared to an accepted reference (phantom, animal, tissue)
- *Precision*
  - *Repeatability*
    - Repeatability within subjects (low variability)
    - Critically important for longitudinal studies
  - *Reproducibility*
    - Insensitive to platform and scan parameters
    - Low variability across sites and platforms
    - Critically important for multi-center studies

**Clinical Accuracy – ability to diagnose, grade and/or stage disease*

Challenges

General Challenges in MR Quantification

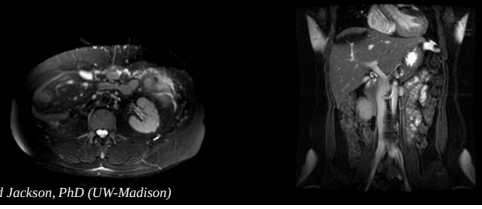
Arbitrary (and spatially- / temporally-dependent) signal intensity units

- Magnitude and homogeneity of B_o
- Magnetic field gradient nonlinearity and/or miscalibration
- RF coil dependency: RF coil type, B_1 sensitivity profiles, subject positioning within the coil
- Slice profile variations (with RF pulse shape, flip angle, *etc.*)
- System stability issues (RF & gradient subsystems, B_o, RF coils, *etc.*)

Courtesy of Ed Jackson, PhD (UW-Madison)

B_o Homogeneity

- In general: Larger B_0 => higher signal-to-noise
- B_0 inhomogeneity yields spatially variant signal intensities in general and spatially variant fat suppression when chemically selective saturation methods are utilized.



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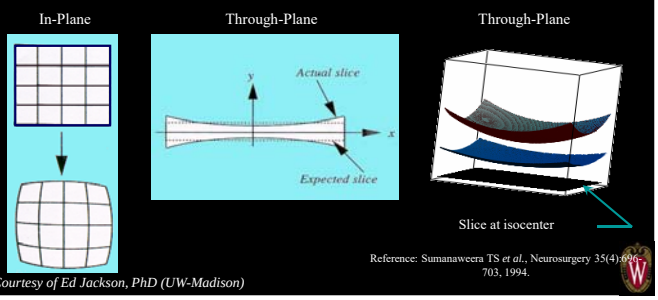
Gradient Field Nonlinearity Effects



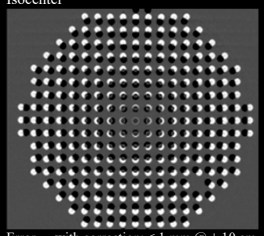
Reference: Sumanaweera TS *et al.*, Neurosurgery 35(4):696-703, 1994.

Courtesy of Ed Jackson, PhD (UW-Madison)

Gradient Field Nonlinearity Effects

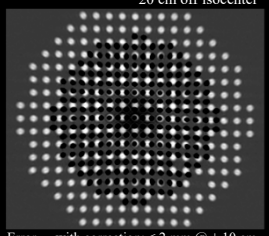
20 cm FOV, white: w/correction, black: w/o correction

Isocenter



$Error_{max}$ with correction: < 1 mm @ ± 10 cm
$Error_{max}$ w/o correction: ~ 4.5mm @ ± 10 cm

20 cm off isocenter



$Error_{max}$ with correction: < 2 mm @ ± 10 cm
$Error_{max}$ w/o correction: ~ 5.5cm @ ± 10 cm

Courtesy of Ed Jackson, PhD (UW-Madison)

General Challenges in MR Quantification

Arbitrary (and spatially- / temporally dependent) signal intensity units

- Magnitude and homogeneity of B_o
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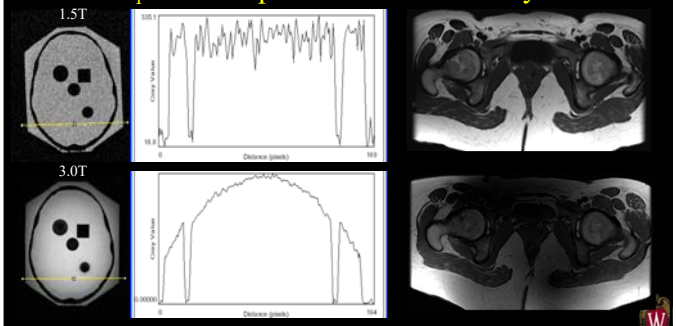
Courtesy of Ed Jackson, PhD (UW-Madison)

B_1 Coil Response Non-Uniformity



Courtesy of Ed Jackson, PhD (UW-Madison)

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  - High correlation, low bias compared to an accepted reference (phantom, animal, tissue)
- *Precision*
  - *Repeatability*
    - Repeatability within subjects (low variability)
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  - *Reproducibility*
    - Insensitive to platform and scan parameters
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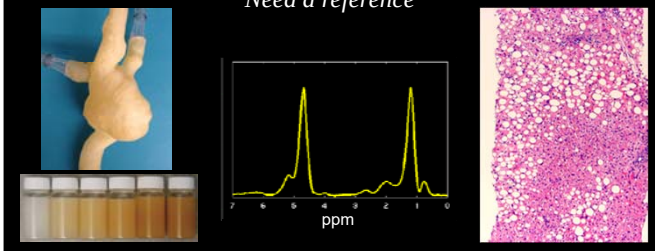
Validate Correlation/Bias

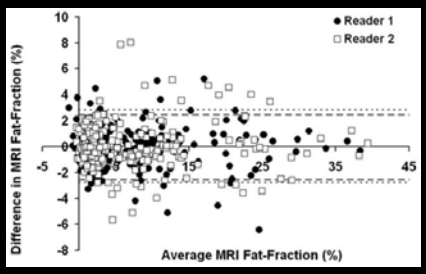
Need a reference



Phantom *MR Spectroscopy* *Biopsy*

Validate Precision (Repeatability)

Test-retest



Hines et al, JMRI 2011

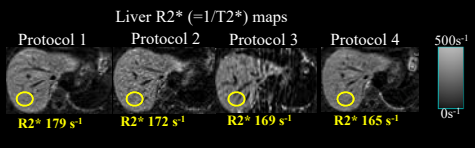
Validate Reproducibility

Insensitivity to varying imaging conditions

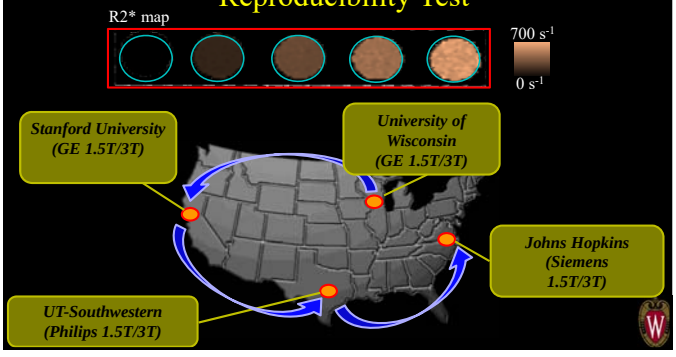
Example: scan same patient with varying imaging parameters (protocols):

- *Spatial resolution*
- *Echo times*
- *Imaging orientation, etc*

Do we get the same measurement?

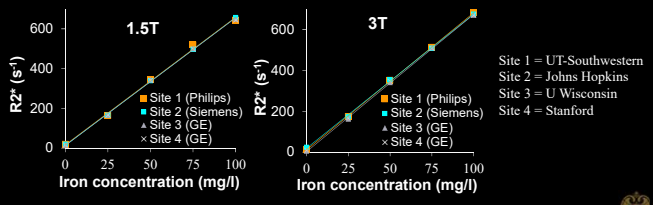


Reproducibility Test



Validate Reproducibility

SPIO phantom test at different sites



Excellent reproducibility on phantoms. How about in patients?

Reproducibility of Dynamic Contrast-enhanced MR Imaging
Part I. Perfusion Characteristics in the Female Pelvis by Using Multiple Computer-aided Diagnosis Perfusion Analysis Solutions[1]

Tobias Heye, MD
Matthew S. Davenport, MD
Jeffrey J. Horvath, MD
Sebastian Feuerlein, MD
Steven R. Breault, MD
Mustafa R. Bashir, MD
Elmar M. Merkle, MD
Daniel T. Boll, MD

Radiology

- *Compared 4 different FDA approved perfusion quantification algorithms*
- *Used same underlying data to calculate standard kinetic parameters*
- *Poor agreement between methods*

Conclusion: A considerable variability for DCE MR imaging pharmacokinetic parameters (K^{trans}, k_{ep}, v_e, iAUGC) was found among commercially available perfusion analysis solutions. Therefore, clinical comparability across perfusion analysis solutions is currently not warranted. Agreement on a postprocessing standard is paramount prior to establishing DCE MR imaging as a widely incorporated biomarker.

Heye et al Radiology March 2013

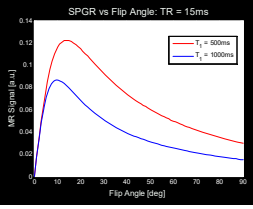
If Quantitative Imaging is so Great, why isn't all MRI Quantitative?

- ***Challenging to develop and validate***
  - Confounding factors
- ***Slower***
  - Typically need to acquire multiple images

Accelerating Quantitative MRI

Using Faster Pulse Sequences: T_1

- Standard: Inversion Recovery with TR>>T_1 (Slow!)
- Accelerated: Spoiled Gradient Echo with variable flip angles
  - Challenge: B1 inhomogeneity dependence (flip angle errors)



$$S_i = M_0 \frac{1 - E_1}{1 - E_1 \cos(\alpha_i)} \sin(\alpha_i)$$

$$E_1 = e^{-TR/T_1}$$

Using Faster Pulse Sequences: T_2

- Standard: Spin Echo (slow!)
- Accelerated: SSFP with variable flip angles
  - Requires T1 map
- Challenge: more complex signal model (more confounders!)
  - B1 dependence

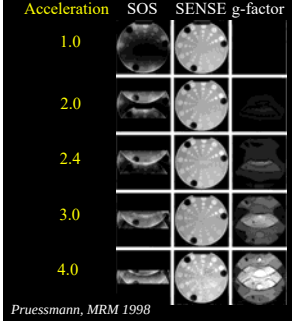
$$S_{SSFP} = \frac{M_o(1 - E_1)\sin(\alpha)}{1 - E_1E_2 - (E_1 - E_2)\cos(\alpha)}$$

$$E_1 = \exp(-TR/T_1)$$

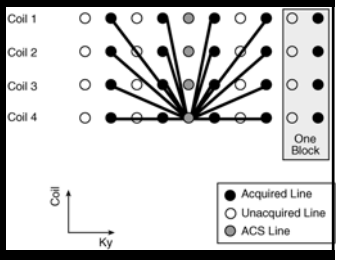
$$E_2 = \exp(-TR/T_2)$$

Deoni SCL MRM 2003

Parallel Imaging Acceleration



Pruessmann, MRM 1998



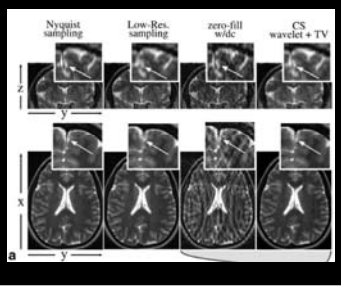
Griswold, MRM 2002

Compressed Sensing

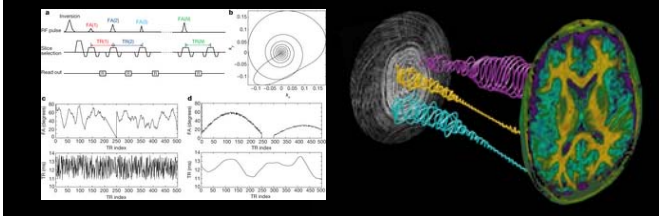
Sparse MRI: The Application of Compressed Sensing for Rapid MR Imaging

Michael Lustig,[1]* David Donoho,[2] and John M. Pauly[1]

$$\begin{aligned} &\text{minimize} \quad \|\Psi m\|_1 + \alpha TV(m) \\ &s.t. \quad \|\mathcal{F}_u m - y\|_2 < \epsilon, \end{aligned}$$



MR Fingerprinting



Ma et al, Nature 2015

MR Fingerprinting

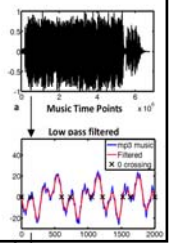
Using Gradient Waveforms Derived from Music in MR Fingerprinting (MRF) to Increase Patient Comfort in MRI

Dan Ma[1], Vikas Gulani[1,2], and Mark Griswold[1,2]

[1]*Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH, United States,* [2]*Radiology, Case Western Reserve University, Cleveland, OH, United States*

Purpose: Acoustic noise during the operation of an MR scanner causes discomfort for both patients and technicians. On the other hand, people routinely pay money to hear live music concerts that are significantly louder than an MRI scan. Thus it is largely the unpleasant "banging" sound that is the problem, and not necessarily the volume. The goal of this study is take advantage of the additional degrees of freedom provided by the new concept of Magnetic Resonance Fingerprinting (MRF) to directly convert digitized music into encoding gradients [1]. Unlike previous methods that interspersed music and readouts (e.g. ALOHA [2]), this MRF-based method uses these music-derived waveforms for encoding during readout, thus maximizing efficiency. In this study, we demonstrate that mp3 encoded music can be converted and optimized to arbitrary encoding gradients, including factors such as gradient moment nulling for SSFP readouts. Afterwards these gradient waveforms are used in combination with variable FAs and TRs to simultaneously quantify four tissue properties (T_1, T_2, M_0, and off-resonant frequency).

Methods: Gradients Design: As shown in Figure 1a, b, the music was first low pass filtered to 2kHz in order to remove the high frequency oscillations that cannot be replicated by a gradient. In order to match the gradient output raster time, the optimized gradients were then resampled to 100kHz. Since we will use an SSFP-based MRF sequence, each arbitrary gradient in each TR of the MRF sequence was designed to start and end at the center of the k-space. Therefore, zero crossings of the music segments were first located. The odd numbered music segments were used for RF excitation and slice selection gradients (Z) and have zero amplitude in both phase (Y) and frequency (X) encoding directions. The even numbered music segments were used as k-space encoding gradients. An optimization algorithm was applied as shown in Figure 1b to solve for each encoding gradient in order to 1) satisfy the scanner constraints of the maximum gradient



AuntMinnie.com

Deep learning can enable quantitative MRI for arthritis

By Erik L. Ridley, AuntMinnie staff writer

Quantitative MRI-Driven Deep Learning for Detection of Clinical Significant Prostate Cancer

q-Space Deep Learning: Twelve-Fold Shorter and Model-Free Diffusion MRI Scans

Predicting brain age with deep learning from raw imaging data results in a reliable and heritable biomarker

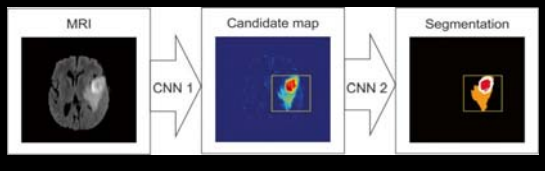
James H Cole[1], Rudra PK Poudel[2], Dimosthenis Tsagkrasoulis[3], Matthan WA Caan[4], Claire Steves[5], Tim D Spector[5], Giovanni Montana[2,3*]

Fingerprinting: A
Predicting Quantita
from T

Vacancy

PhD candidate 'Deep learning for MRI Diagnosis'

CNNs for Segmentation



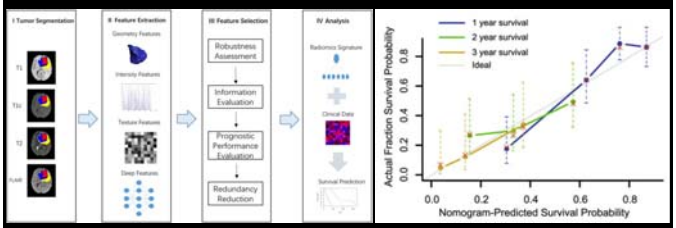
Deep Learning for Brain MRI Segmentation: State of the Art and Future Directions

Zeynettin Akkus, Alfia Galimzianova, [...], and Bradley J. Erickson

A Deep Learning-Based Radiomics Model for Prediction of Survival in Glioblastoma Multiforme

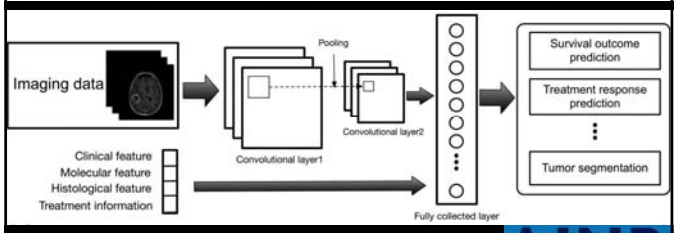
Jiangwei Lao, Yinsheng Chen, Zhi-Cheng Li, Qihua Li, Ji Zhang, Jing Liu & Guangtao Zhai

SCIENTIFIC REPORTS



Radiomics in Brain Tumor: Image Assessment, Quantitative Feature Descriptors, and Machine-Learning Approaches

M. Zhou, J. Scott, B. Chaudhury, L. Hall, D. Goldgof, K.W. Yeom, M. Iv, Y. Ou, J. Kalpathy-Cramer, S. Napel, R. Gillies, O. Gevaert and R. Gatenby



AJNR AMERICAN JOURNAL OF NEURORADIOLOGY

Who is Interested?

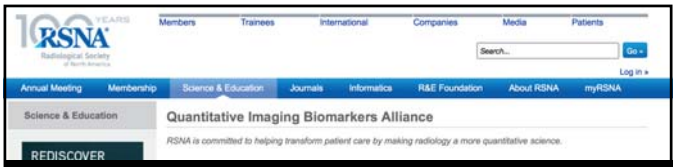
Quantitative Imaging Biomarkers – Who's Interested?

NIST USMS Workshop 2006

Representative Agencies / Organizations

RSNA · PhRMA · FDA Centennial · NIST National Institute of Standards and Technology · National Institutes of Health · The International Society for Optical Engineering · DICOM · CDRH · National Cancer Institute · National Center for Research Resources · NIBIB · NEMA · ISMRM · ACR American College of Radiology · CDER · NIAMS · National Institute of General Medical Sciences · snm · National Institute on Aging

Courtesy of Ed Jackson, PhD (UW-Madison)



- *Perfusion, Diffusion and Flow-MRI Biomarker Ctte (Roster)*
- *fMRI Biomarker Ctte (Roster)*
- *PDFF Biomarker Ctte (proposed) (Roster)*
- *MRE Biomarker Ctte (Roster)*
- *PET Amyloid Biomarker Ctte (Roster)*
- *FDG-PET Biomarker Ctte (Roster)*
- *SPECT Biomarker Ctte (Roster)*
- *CT Volumetry Biomarker Ctte (Roster)*
- *Lung Density Biomarker Ctte (Roster)*
- *Ultrasound SWS Biomarker Ctte (Roster)*
- *AIUM/QIBA Ultrasound Volume Blood Flow Biomarker Ctte (Roster)*

https://www.rsna.org/QIBA.aspx

NIST
National Institute of Standards and Technology
Technology Administration
U.S. Department of Commerce

July 2014

Workshop on Standards for Quantitative MRI

Agenda:

1. Activities at ISMRM, QIBA, MITA, FDA, NCI, ACR, IAC, ACRIN, NIST & PTB
2. How *well* do we measure fundamental MR parameters?
3. Standards for diffusion and angiography
4. Standards for dynamic contrast and susceptibility
5. Areas in need of standards
6. Apples & Oranges: Standards for data transfer and processing
7. Standards for computation and virtual phantoms
8. Emerging technologies in MRI

Plus two 1.5 hour discussion sessions to identify 'what is needed and who should do it'

Quantitative MR Study Group

ISMRM ONE COMMUNITY FOR CLINICIANS AND SCIENTISTS

Mission

To promulgate documentary and measurement standards for quantitative magnetic resonance imaging in collaboration with national metrology institutes (NMIs), academic and clinical MR sites, and through collaboration with existing study groups.

Where do the Manufacturers Stand?

- Development of quantitative techniques?
  - Cutting edge
  - New business
  - *Very appealing*
- Reproducibility across manufacturers?

Messages

- Quantitative imaging: standardization
  - Better clinical trials
  - Improved patient care
- Tremendous growth in recent years
- Making MRI quantitative is challenging
  - Accuracy, precision, ***reproducibility***
- Opportunities for research
- Technical / clinical / industrial collaborations essential

dhernando@wisc.edu

Questions?

Slides courtesy of
Scott Reeder
Alejandro Roldán
Claude Sirlin
Oliver Wieben
Ed Jackson
Sam Hurley