Quantifying the local tissue volume and composition in individual brains with magnetic resonance imaging

Aviv Mezer¹, Jason D Yeatman¹, Nikola Stikov², Kendrick N Kay¹, Nam-Joon Cho³,⁴, Robert F Dougherty⁵, Michael L Perry¹, Josef Parvizi⁶, Le H Hua⁶, Kim Butts-Pauly⁷ & Brian A Wandell¹,⁵

MRI Quantification of Local Tissue Volume and Composition

Nikola Stikov, PhD
January 27, 2014
Quantifying the local tissue volume and composition in individual brains with magnetic resonance imaging

Aviv Mezer\textsuperscript{1}, Jason D Yeatman\textsuperscript{1}, Nikola Stikov\textsuperscript{2}, Kendrick N Kay\textsuperscript{1}, Nam-Joon Cho\textsuperscript{3,4}, Robert F Dougherty\textsuperscript{5}, Michael L Perry\textsuperscript{1}, Josef Parvizi\textsuperscript{6}, Le H Hua\textsuperscript{6}, Kim Butts-Pauly\textsuperscript{7} & Brian A Wandell\textsuperscript{1,5}

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On 3 Facebook pages
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Reviews

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- in the 98 percentile of a sample of 9,995 of the 72,188 tracked articles of a similar age in all journals
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• The Problem with quantitative MRI

• Calibrating qMRI Measurements

• Myelin Imaging Applications

• In vivo histology ?

• Conclusions
• The Problem with quantitative MRI

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Conventional and quantitative magnetic resonance

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<thead>
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Cheng, Stikov et al. (JMRI 2012)

T₁ weighted
IR T1 mapping equations

\[ M_z(TI) = c(1 - 2e^{-T_1/T_1}) \]

(1) The simplest IR fitting formula, but assumes TR>>T1

\[ M_z(TI) = c(1 - 2e^{-T_1/T_1} + e^{-T_R/T_1}) \]

(2) Accounts for TR finite, but assumes perfect flip angles

\[ M_z(TI) = c(1 - [1 - \cos \theta_1]e^{-T_1/T_1} + e^{-T_R/T_1}) \]

(3) Accounts for inversion pulse \( \theta_1 \), but not for excitation \( \theta_2 \).

\[ M_z(TI) \propto M_0(1 - \cos \theta_1 \cos \theta_2 e^{-T_R/T_1}) \]

(4) Which can be simplified to:

Barral et al. MRM 2010
Protocol standardization

Barral et al. (MRM 2010)

Stikov et al. (MRM in press)
Explaining the $T_1$ discrepancy

Stikov et al. (MRM in press)
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Getting $T_1$ Right

Mezer, Yeatman, Stikov et al. (Nature Medicine 2013)
Relating T1 to tissue content

Water Volume Fraction (WVF)

PD(tissue)/PD(CSF)

$$S(\alpha) = M_0 \sin(\alpha) \left( \frac{e^{-\frac{TR}{T_1}}}{1 - \cos(\alpha) e^{-\frac{TR}{T_1}}} \right)$$

$$M_0 = g \times PD \times e^{-\frac{TE}{T_2}} = g \times PD$$

Macromolecular Tissue Volume

$$MTVF = 1 - WVF$$

Mezer, Yeatman, Stikov et al. (Nature Medicine 2013)
Relating MTVF and T1
Processing pipeline

https://github.com/mezera/mrQ

An example data set can be found at http://purl.stanford.edu/qh816pc3429.
Processing pipeline

\[ \frac{1}{T1} = FIWP \left( \frac{1}{T1_C} + (1 - FIWP) \frac{1}{T1_f} \right) \]

\[ T1_C = a_1 L + a_2 \]

\[ VIP = FIWP(1 - MTVF)V \]

\[ SIR = VIP / MTV \]

https://github.com/mezera/mrQ

An example data set can be found at http://purl.stanford.edu/qh816pc3429.
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Myelin Imaging

Free protons - water

Bound protons - macromolecules

Fractional Pool Size (F) =

sphyngomyelin

Quantitative magnetization transfer (qMT)

MTVF Correlates with F

MTVF complements FA

MTVF drops in MS
For all the fibers in the brain...

... assign a mean F score ...

... isolate the top F fibers
(95th percentile)
Top F Fibers

Stikov et al.  
(Neuroimage 2011)
Five Subjects - Top F Fibers

Stikov et al. (Neuroimage 2011)
Tractometry in Multiple Sclerosis

Top 5% MTR fibers

Bottom 5% MTR fibers
Is it thickness or density?

~ age 1 year
(dense but thin)

~ age 15 years
(sparse but thick)

The myelin g-ratio

\[ g = \frac{r}{R} \approx 0.6-0.8 \]

- associated with gender differences in brain development
  
  Paus and Toro (2009), Front Neuroanat 14(3): 1-7
  Perrin et al. (2009), Neuroimage 45(4): 1055-1066

- g-ratio variations reported in schizophrenia
  
  Uranova et al. (2001), Brain Res Bul 55(5): 597-610

- evaluating remyelination in Multiple Sclerosis

Rushton (1951) J Physio, 115(1):101-122
Brain Tissue Model

\[ g = \frac{r}{R} \]
\[ r = Rg \]

Myelin Volume Fraction = (MVF)
Fiber Volume Fraction = (FVF)

\[ \Sigma_i \pi R_i^2 - \Sigma_i \pi r_i^2 \]
\[ \Sigma_i \pi R_i^2 \]
\[ g^2 \]

\[ \text{MVF/FVF} = 1 - g^2 \]
\[ g = \sqrt{1 - \text{MVF/FVF}} \]

Szafer et al. (1995) MRM 33(5): 697-712
Hall and Alexander (2009) IEEE Trans Med Im 28(9): 1354-1364
g-ratio imaging: what are we measuring?

\[ g = \sqrt{1 - \frac{MVF}{FVF}} \]
**g-ratio imaging: what are we measuring?**

\[ g = \sqrt{1 - \frac{MVF}{FVF}} \]

\[ r(\theta) / R(\theta) = \text{const} = g \]
g-ratio imaging: what are we measuring?

\[ g = \sqrt{1 - \frac{MVF}{FVF}} \]

\[ r(\theta)/R(\theta) = const = g \]
g-ratio imaging: what are we measuring?

\[ g = \sqrt{1 - \frac{MVF}{FVF}} \]

fiber caliber affects the measurement
g-ratio imaging: what are we measuring?

\[ g = \sqrt{1 - \frac{MVF}{FVF}} \]

Average g-ratio = 0.5
g-ratio imaging: what are we measuring?

\[ g = \sqrt{1 - \frac{MVF}{FVF}} \]

\( g \)-ratio we measure = 0.7
$g$-ratio imaging: what are we measuring?

$$g = \sqrt{1 - \frac{MVF}{FVF}}$$

$MVF \sim F, MTV...$

$FVF \sim ?$

$g$-ratio suggested $0.7$
Simulating Diffusion in the Corpus Callosum

Aboitiz et al. (1993)
FVF $\sim$ FA

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Graph showing the relationship between fractional anisotropy and fiber count (fibers/μm²).}
\end{figure}
NODDI: Neurite orientation dispersion and density imaging

intra-axonal: anisotropically restricted

extracellular: hindered

CSF: not restricted or hindered

Zhang et al. NeuroImage 2012
NODDI: Neurite orientation dispersion and density imaging

- a model of cellular structure that allows for complex subvoxel fiber geometry (splay, curvature)
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g-ratio in human Corpus Callosum

\[ g = \sqrt{1 - \frac{MVF}{FVF}} \]

Lamantia and Rakic 1990

Stikov et al. (Neuroimage 2011)
g-ratio in non-human primates

FVF

MVF

g-ratio

0.7x0.7x3mm

Lamantia and Rakic

genu

splenium

21 µm

21 µm
### Comparison with histology

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<th>Histology</th>
<th>Genu (1)</th>
<th>(2)</th>
<th>(3)</th>
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<th>Splenium (8)</th>
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<td>.71 (.06)</td>
<td>.60 (.05)</td>
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20µm
g-ratio histological validation

MRI

EM

\( r = 0.7951 \) \( p = 0.018337 \)
Whole-brain g-ratio
**Figure 4:** Hyperintense MS lesions (arrows) are identified on the FLAIR image. While both the MVF and the AVF are significantly decreased at the lesion locations, the g-ratio map indicates that one of the lesions has significantly higher g-ratio (> .85) compared to the rest.
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Aboitiz et al. (1993)

Genu
FVF = 0.45
g = 0.55

Ant. Body
FVF = 0.44
g = 0.58

Mid Body
FVF = 0.45
g = 0.62

Post. Body
FVF = 0.46
g = 0.64

Spleniunm
FVF = 0.60
g = 0.72
In vivo histology?

McNab et al. ISMRM 2012

<table>
<thead>
<tr>
<th>Region</th>
<th>FVF</th>
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Conclusions

qMRI can be calibrated

Combining qMRI biomarkers leads to in vivo histology

Histological validation is essential

\[ \begin{array}{cccccccc}
\text{Histology} & \text{Histology} & \text{Histology} & \text{Histology} & \text{Histology} & \text{Histology} & \text{Histology} & \text{Histology} \\
.72 & .69 & .67 & .74 & .69 & .72 & .57 & .85 \\
\end{array} \]
Thank you

- BIC MRI Lab
- Aviv Mezer and VISTA lab
- Stroh, Bedell and Petrides labs
- MNI CECR Fellowship
Contact

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