Orientation dependency of T_2 in newborn white matter shows dipole-dipole interaction effects

Bartels L.(1,2,9), Doucette J.(1,2,9), Birkl C.(2,3,4), Zhang Y.(5,6,7,8), Weber A.(2,9), Rauscher A.(1,2,9)

(1) Dept. of Physics and Astronomy, University of British Columbia, Vancouver, BC, Canada; (2) UBC MRI Research Centre, University of British Columbia, Vancouver, BC, Canada; (3) Dept. of Neuroradiology, Medical University of Innsbruck, Innsbruck, Austria; (4) Dept. of Neurology, Medical University of Graz, Graz, Austria; (5) Department of Radiology, Children's Hospital of Chongqing Medical University, Chongqing, China; (6) Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Medical University, Chongqing, China; (7) Key Laboratory of Pediatrics in Chongqing, Chongqing Medical University, Chongqing, China; (8) Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Chongqing, China; (9) Division of Neurology, Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada

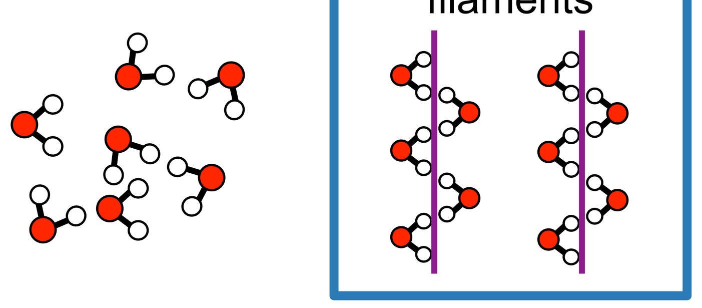
Theoretical Models

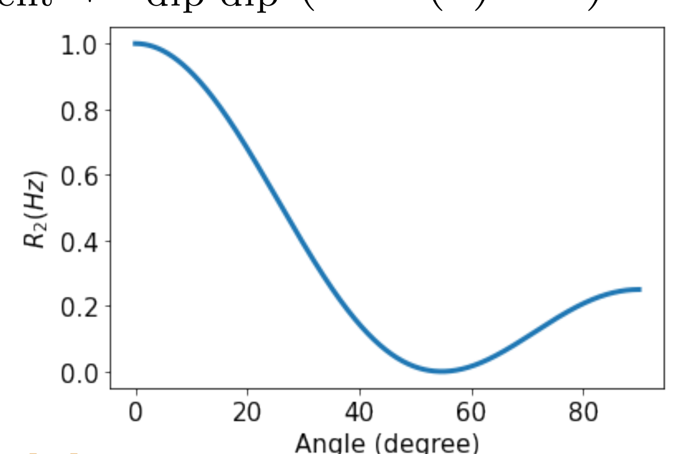
Tissue orientation effects in MRI in the transverse relaxation rate $R_2=1/T_2$ in highly organized tissues have been widely observed and studied in adult subjects and are well described by two models.

Collagen-rich tissues: The Dipole-dipole Model

Tissue orientation effects in R_2 relaxation are well known in tissues rich in collagen fibers such as tendons and cartilage.[1,2] The source of the orientation dependence in those tissues are dipole-dipole interactions between water molecules aligned along the parallel collagen filaments as shown below which can be modelled by [1]

$$R_2^{\text{dip-dip}} = c_{\text{orientation independent}} + c_{\text{dip-dip}}\,(3\cos(\theta) - 1)^2$$

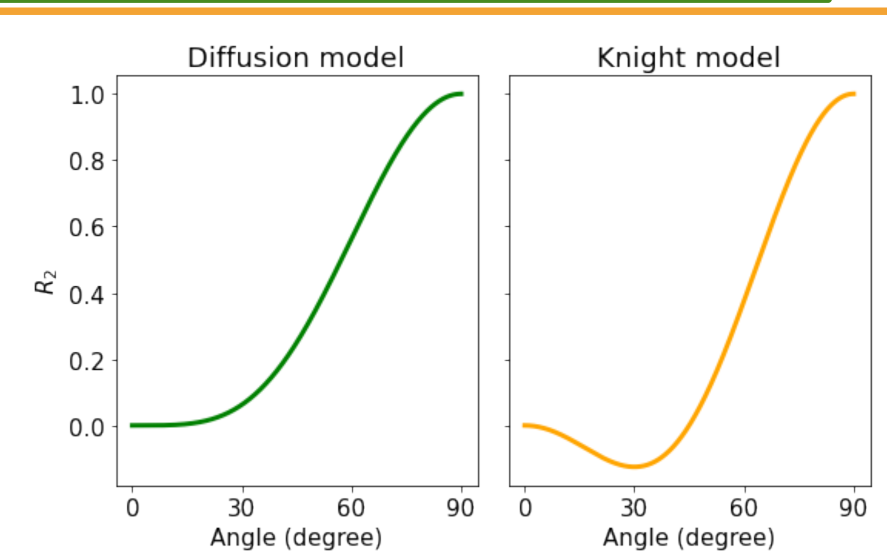




Brain White Matter - The Knight Model

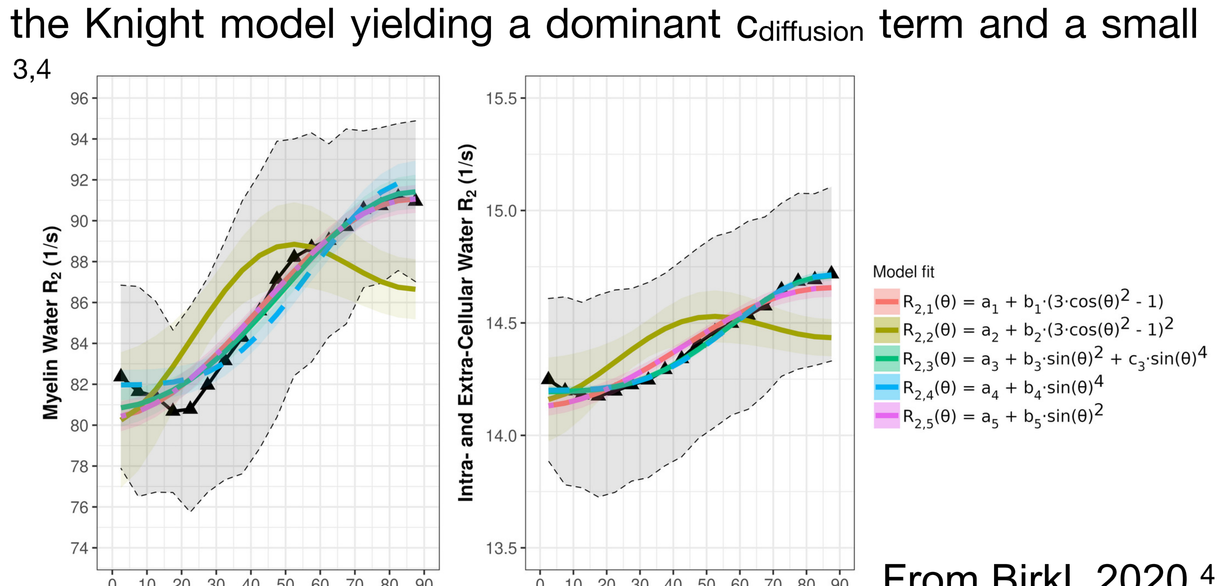
The $R_2=1/T_2$ orientation dependence in brain white matter (WM) is attributed to the diffusion of spins through local field inhomogeneities created by the axonal myelin sheaths and, to a small degree, the interaction of susceptibility related fields with applied imaging gradients.[5] This 'Knight model' is modelled by

$$R_2^{\text{Knight}} = c_{\text{orientation independent}} + c_{\text{diffusion}}\sin^4(\theta) \pm c_{\text{gradient}}\sin^2(\theta)$$



Previous Results in Adults

Studies of the orientation dependence of R_2 in adult WM have shown good agreement with the Knight model yielding a dominant $c_{\text{diffusion}}$ term and a small correction term.[3,4]



From Birkl, 2020.[4]

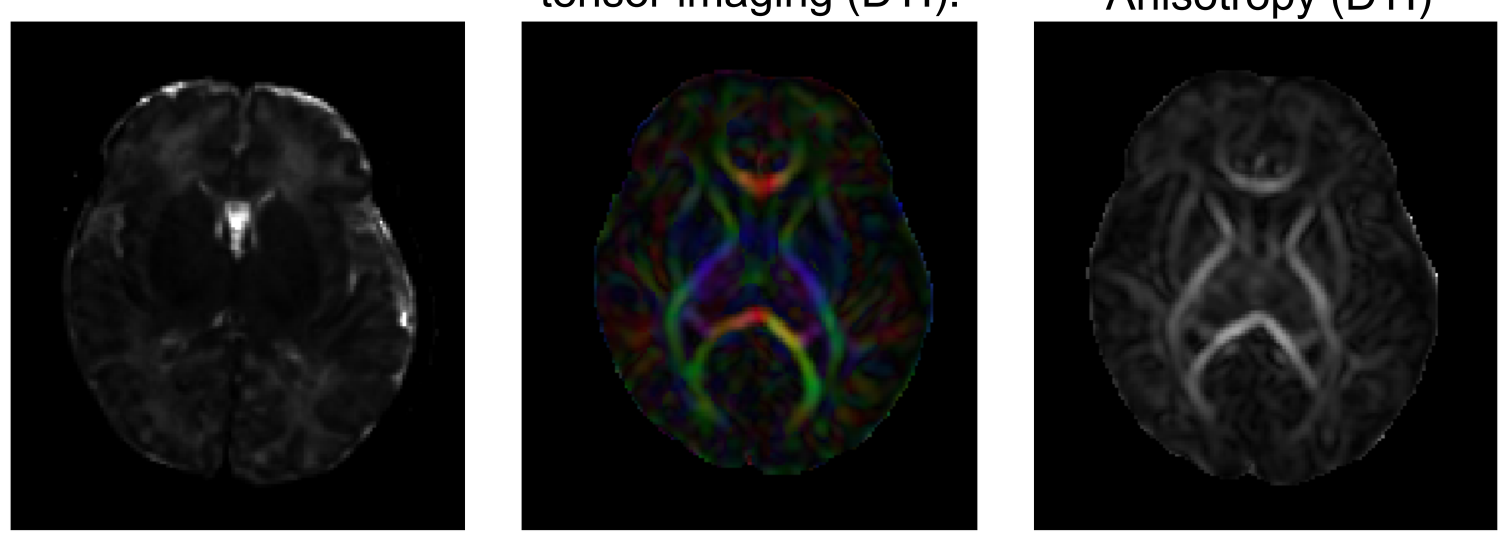
Research Question

Understanding and quantifying R_2 orientation dependency has important implications for T_2-based imaging techniques such as myelin water imaging.
It is not clear whether dipole-dipole interaction effects are absent in brain tissue or overshadowed by the magnetic susceptibility effects.[1] To address this question we measured the orientation dependency in the unmyelinated human newborn brain in vivo. In the absence of myelin and therefore the absence of significant local differences in magnetic susceptibility.

Methods

Eight healthy newborns were scanned on 3T Philips Achieva scanner.

T_2 data were acquired with a GRASE sequence. | Fiber orientation was mapped with diffusion tensor imaging (DTI). | WM masks were created by thresholding Fractional Anisotropy (DTI)

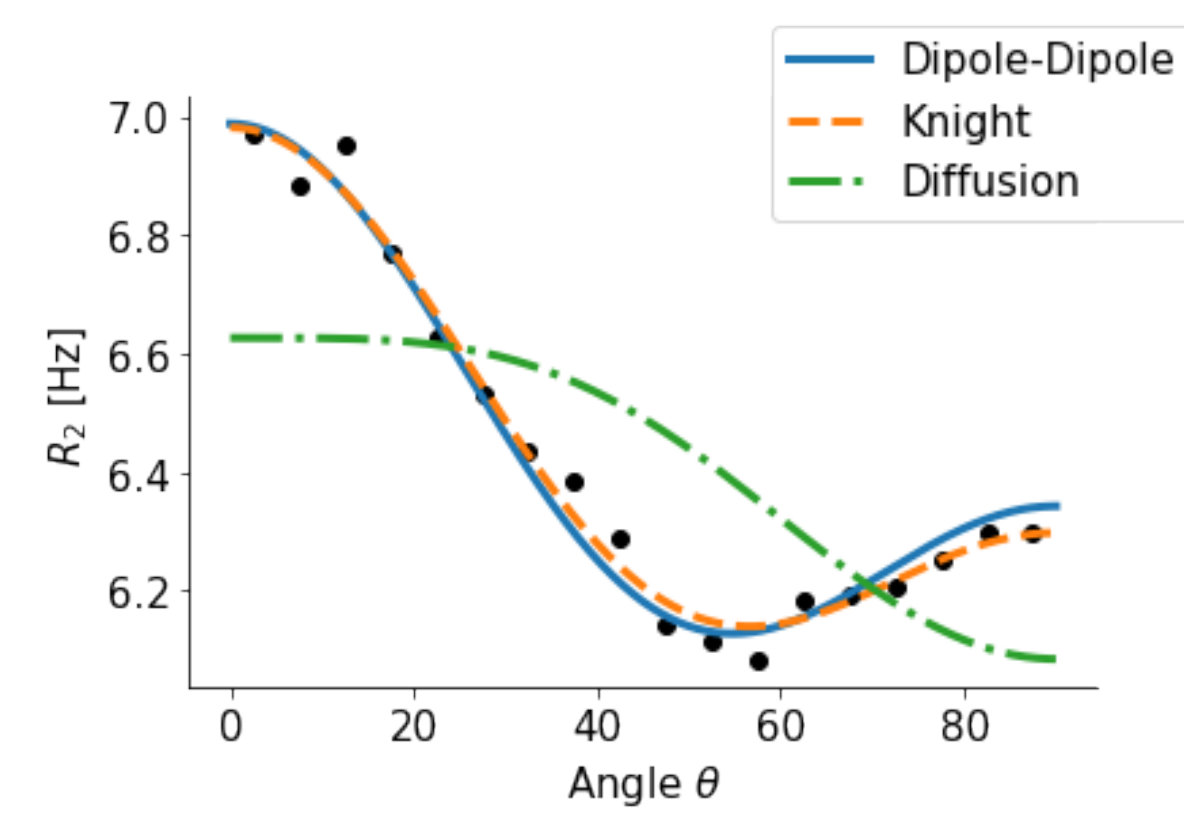


Geometric mean T_2 | Principal diffusion direction | FA

The spin echo data were analyzed using DECAES[6] and T_2 was computed as the geometric mean T_2. R_2 was plotted as a function of fiber angle pooling voxels according to their orientation in 5° intervals. Models of dipole-dipole interaction, diffusion related dephasing and the model of diffusion and field gradients [Knight] were fitted to $R_2(\theta)$.

Results

The average myelin water fraction of the neonate subjects is in the expected low range for newborns with 1.7%.



	Dipole-dipole Model		Knight Model		
	$c_{\text{or indep}}$	$c_{\text{dip-dip}}$	$c_{\text{or indep}}$	$c_{\text{diffusion}}$	c_{grad}
Best fit	6.12	0.22	6.98	1.73	-2.41
MAE	0.0353		0.0301		
Adj. R^2	0.965		0.976		
AICc	-53.5		-57.6		

Discussion

Both the dipole-dipole interaction model and the model by Knight (diffusion plus effects of imaging gradients) fit the observed data well as indicated by the low MAE and high adjusted R^2 values. However, the model by Knight assumes the presence of magnetic susceptibility differences in myelin sheaths and it only fits the data with a large coefficient for the imaging gradient term, which is not realistic. Furthermore, the simpler model of dipole-dipole interaction which only has a single orientation dependent term, fits the data almost as well as the more flexible Knight's model. For these reasons we suggest that the orientation dependency of R_2 in the newborn brain is due to dipole-dipole interaction. This interpretation is consistent with the absence of myelin in newborns and it implies the alignment of water molecules with elongated structures. Two primary candidates for hydrated filaments that might be associated with such structured water in human WM are the microtubules and neurofilaments within the axon.

Conclusion

The orientation dependence of R_2 in neonate WM is very different from that found in adults and is best described by a model of dipole-dipole interaction. In the absence of myelin, this finding suggests the alignment of water with neurofilaments or microtubuli.

References

1. Oh S.-H. et al. Origin of B_0 orientation dependent R_2^* ($= 1/T_2^*$) in white matter. NeuroImage. 2013;73:71–79.
2. Bydder M, et al. The Magic Angle Effect: A Source of Artifact, Determinant of Image Contrast, and Technique for Imaging. Journal of MRI. 2007;25:290–300.
3. Knight M, et al. Anisotropy of spin-echo T_2 relaxation by magnetic resonance imaging in the human brain in vivo. Biomedical Spectroscopy and Imaging. 2015;4:299–310.
4. Birkl C, et al. Myelin water imaging depends on white matter fiber orientation in the human brain, Magn Res Med. 2020;00:1–11.
5. Knight M, et al. Magnetic Resonance Relaxation Anisotropy: Physical Principles and Uses in Microstructure Imaging. Biophysical Journal. 2017;112:1517–1528.
6. Doucette J, et al. DECAES – DEcomposition and Component Analysis of Exponential Signals. Z Med Phys. 2020;30(4):271–278.

BC Children's Hospital
Provincial Health Services Authority

UBC MRI Research Centre

THE UNIVERSITY OF BRITISH COLUMBIA