BIOGRAPHICAL SKETCH

NAME Duyn, Jozef H.	POSITION TITLE Senior Investigator

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGRE	MM/YY	FIELD OF STUDY
Delft University, The Netherlands	M.Sc.	1984	Mathematics/Physics
Delft University, The Netherlands	Ph.D.	1988	Atomic Physics
University of Trento, Italy	Postdoctoral	1989	Atomic Physics
University of California	Postdoctoral	1991	MRI/MR Spectroscopy

Personal Statement:
I have been interested in MRI since its early development towards a clinical diagnostic tool during the early 1980's. During my early college years studying physics, I was shown an early MRI picture of a breast tumor, which sparked my interest in this technique and helped me decide to do my undergraduate work in this field. I was lucky to receive training in a strong MR physics group at Delft University and able to witness some of the early MRI technological developments, including Flash Imaging and shielded gradients. Although my interest in MRI was put on hold for the seconds half of the 1980's because of budget issues in the physics group, I returned to the field in 1989 when joining the Weiner lab at UCSF. It was at UCSF where my interest in neurological applications of MRI developed and where I was involved in developing the early spectroscopic tools to look at brain neurochemistry, work which continued during my subsequent postdoctoral assignments at NIH in the labs of Chrit Moonen and Joe Frank. Following my conversion to independent investigator at NIH, and my subsequent transfer to the LFMI of Alan Koretsky, my lab has continued to work on the development of MRI technology and applications, including technology to improve resolution and contrast (detectors and high field MRI systems), ways to manipulate contrast (based on tissue magnetic properties) and ways to study brain function (concurrent EEG and fMRI). This has led to novel discoveries (e.g., laminar variation of cortical iron content, spontaneous brain activity during sleep) and has catalyzed collaborations with clinical groups (e.g. multiple sclerosis and amyotropic lateral sclerosis groups) and basic science groups (e.g. primate physiology group). Many of the about 20 fellows that have trained in my group have therefore been exposed to a mixture of basic and applied science. Applications of and technology for MRI are still developing, and the lab is currently involved in exciting projects to improve MRI contrast and resolution to further reveal anatomy and function of the human brain.

Research and Professional Experience
1) Teaching Assistant, Delft University, Holland. 1982-1984.
2) Lecturer, Atomic Physics Course, Delft University, Holland. 1987-1988.
3) Visiting Associate, LDRR, OD, NIH, Bethesda, MD. 1992-1994.
4) Investigator, Section of Advanced MRI Development, OD, NIH, Bethesda, MD. 1994-2000.
5) Adjunct Faculty Member, Chemical Physics Program, University of Maryland. 1996-.
6) Senior Investigator, Section of Advanced MRI, NIH, Bethesda, MD, 2000-
7) Adjunct Faculty Member, Neuroscience Program, Georgetown University. 2014-.

Honors and Awards:
1) International Society of Magnetic Resonance in Medicine Young Investigator Award finalist. 1993.
2) NIH Director's Award. 2007.
3) General Electric MR Thought Leadership Award. 2009.
4) International Society of Magnetic Resonance in Medicine Fellow Award. 2011.

Invited Talks (last four years):

At Meetings:

1) First International Workshop on MRI phase contrast and susceptibility mapping, Dornburg, Germany. "Sources of Phase Contrast in the Human Brain" (January 14-15, 2011)
2) ISMRM Worksop on Ultra-High Field Systems & Applications, Lake Louise, Canada "Quantitative Susceptibility Imaging at Ultrahigh Field" (February 20-23, 2011)
3) ISMRM Anuual Meeting Educational Program, Montreal, Canada. "Magnetic Susceptibility Contrast" (May 7-13, 2011)
4) Workshop on Brain Function Investigation by MR, Electrophysiology, and Molecular Imaging, Erice Italy. "Study of Brain Structure with Magnetic Susceptibility Contrast" (May 25-June 1, 2011)
5) Scientific workshop fMRI-From Cortical Layers to Networks, "sources of temporal correlations in fMRI signals. Whisler-Blackcomb, B.C., Canada (Feb 26-29, 2012).
6) Third Biennial Conference on Resting State Brain Connectivity, Magdeburg, Germany (Sept 5-7, 2012)
7) Eighteenth Triennial ISMAR Conference, Rio de Janeiro, Brazil (May 14-19, 2013)
8) Second International Workshop on MRI phase contrast & Quantitative susceptibility Mapping, Ithaca, New York. "Connection between biology and tissue susceptibility" (July 25, 2013).

At Universities:

1) Colloquium, Neurophysiics Section, Max Planck Institute, Leipzig. "MRI studies of brain tissue microstructure" (Feb 17, 2014).

Contributions to Science

Development of MRI

Since MRI started to have clinical impact around 1980, major advances have been made in technology for signal acquisition, contrast generation and image reconstruction. As a result, image resolution has improved at least ten-fold, and the breadth of application has grown dramatically. My lab has been involved in various aspects of this development, including practical approaches to obtaining metabolic information (1), the early development of detector arrays for signal reception, including the first demonstration of improved sensitivity throughout the brain (2), the first application of accelerated fMRI with EPI (3), and the first demonstration imaging tissue susceptibility in human brain (4).

1) Duyn JH, Gillen J, Sobering G, van Zijl PCM, and Moonen CTW. Multislice Proton Spectroscopic Imaging of Human Brain. Radiology 188: 277-282 (1993)
2) de Zwart JA, Ledden PJ, Kellman P, van Gelderen P, Duyn JH. Design of a SENSE-optimized high-sensitivity MRI receive coil for brain imaging. Magn Reson Med. 2002 Jun;47(6):1218-27.
3) De Zwart JA, Van Gelderen P, Kellman P, Duyn JH. Application of sensitivity-encoded echo-planar imaging for blood oxygen level-dependent functional brain imaging. Magn Reson Med. 2002 Dec;48(6):1011-20.
4) Schmueli K, de Zwart JA, van Gelderen P, Li TQ, Dodd SJ, Duyn JH. Magnetic susceptibility mapping of brain tissue in vivo using MRI phase data. Magn Reson Med. 2009 Oct 26. [Epub ahead of print].

Study of brain structure using magnetic susceptibility contrast

MRI has seen a continuous increase in magnetic field strength, and this has led to increased sensitivity to the magnetic properties of brain tissue. The leadership of NIH in pushing MRI field strength and acquiring a human 7 T system has given my lab the unique opportunity to study susceptibility variations in human brain and exploit these to study anatomy (1), iron and myelin content (2,3), and cellular organization in white matter (4).

This led us to demonstrate iron variations across cortical layers, and describe the magnetic properties of myelin, including its anisotropic susceptibility (3,4).

1) Duyn, JH, van Gelderen P, Li Tie-Qiang, de Zwart JA, Koretsky A, Fukunaga M, High-field MRI of brain cortical substructure based on signal phase. Proc. Nat. Acad. Sci. 2007.
2) Fukunaga M, Li TQ, van Gelderen P, de Zwart JA, Shmueli K, Yao B, Lee J,Maric D, Aronova MA, Zhang G, Leapman RD, Schenck JF, Merkle H, Duyn JH. Layer-specific variation of iron content in cerebral cortex as a source of MRI contrast. Proc Natl Acad Sci U S A. 2010;107(8):3834-9.
3) Lee J, Shmueli K, Fukunaga M, van Gelderen P, Merkle H, Silva AC, Duyn JH.Sensitivity of MRI resonance frequency to the orientation of brain tissue microstructure. Proc Natl Acad Sci U S A. 2010;107(11):5130-5.
4) Sati P, van Gelderen P, Silva AC, Reich DS, Merkle H, de Zwart JA, Duyn JH. Micro-compartment specific T_2* relaxation in the brain. Neuroimage. 2013, 77: 268-78.

Study of spontaneous brain activity with fMRI

fMRI signal fluctuations unrelated to overt behavior are an intriguing phenomenon that, to the extent that it reflects neuronal activity, can be used to study the brain's functional networks. My lab's first contribution tot this field was to establish that this neuronal activity does not relate to conscious activity, as it remains present during sleep (1), although with a reduced involvement of the frontal cortex (2). More recently, we have discovered that this acitivity occurs in brief (~seconds) bouts of activity in distinct networks (3), and confirmed its neurophysiological correlate with ECoG data from primates from the Fujii lab (RIKEN) (4).

1) Fukunaga M, Horovitz SG, van Gelderen P, de Zwart JA, Jansma JM, Ikonomidou VN, Chu R, Deckers RH, Leopold DA, Duyn JH. Large-amplitude, spatially correlated fluctuations in BOLD fMRI signals during extended rest and early sleep stages. Magn Reson Imaging. 2006 Oct;24(8):979-92.
2) Horovitz SG, Braun AR, Carr WS, Picchioni D, Balkin TJ, Fukunaga M, Duyn JH. Decoupling of the brain's default mode network during deep sleep. Proc Natl Acad Sci U S A. 2009 Jul 7;106(27):11376-81. Epub 2009 Jun 19.
3) Liu X, Duyn JH. Time-varying functional network information extracted from brief instances of spontaneous brain activity. Proc Natl Acad Sci U S A. 2013; 110(11):4392-7.
4) Liu X, Yanagawa T, Leopold DA, Fujii N, Duyn JH. Robust Long-Range Coordination of Spontaneous Neural Activity in Waking, Sleep and Anesthesia. Cer Cortex 2015, 25:2929.

Neurophysiological correlate of the fMRI signal

Over the years, it has become accepted that the fMRI signal not only results from neuronal activity, but generally also has significant contribution of confounding processes, such as variations in the cardiac and respiratory cycles. Our lab was the first to identify a contribution from cardiac rate variations (1), and, for the first time, establish the contribution of a metabolic process (2) attributed to neuronal activity. In collaboration with the Leopold lab, we went on to demonstrate, in pimates, a neuro-electrical contributions as well (3), which was further confirmed with MEG data obtained in human (4).

1) Shmueli K, van Gelderen P, de Zwart JA, Horovitz SG, Fukunaga M, Jansma JM, Duyn JH. Low-frequency fluctuations in the cardiac rate as a source of variance in the resting-state BOLD fMRI signal. Neuroimage 2007, 38: 306-320.
2) Fukunaga M, Horovitz SG, de Zwart JA, van Gelderen P, Balkin TJ, Braun AR, Duyn JH. Metabolic origin of BOLD signal fluctuations in the absence of stimuli. J Cereb Blood Flow Metab. 2008 Jul;28(7):1377-87.
3) Schölvinck ML, Maier A, Ye FQ, Duyn JH, Leopold DA. Neural basis of globalresting-state fMRI activity. Proc Natl Acad Sci U S A. 2010;107(22):10238-43.
4) Liu Z, Fukunaga M, de Zwart JA, Duyn JH. Large-scale spontaneous fluctuations and correlations in brain electrical activity observed with magnetoencephalography. Neuroimage. 2010 51:102-111.

Brain Iron and myelin changes in disease

The unique sensitivity of high field MRI to susceptibility variations was exploited to perform exploratory studies of tissue iron abnormalities in MS (1-2) and ALS (3). Focal iron depositis were demonstrated in lesions and the motor cortex respectively by combining MRI with post-mortem histology. We also discovered that MS lesions are nearly always perivenular. The unique magnetic properties of iron and myelin will make it possible to distinguish them and quantify their individual changes with disease (4).

1) Bagnato F, Hametner S, Yao B, van Gelderen P, Merkle H, Cantor FK, Lassmann H, Duyn JH. Tracking iron in multiple sclerosis: a combined imaging and histopathological study at 7 Tesla. Brain. 2011;134(Pt 12):3602-15.
2) Yao B, Bagnato F, Matsuura E, Merkle H, van Gelderen P, Cantor FK, Duyn JH (2012). Chronic multiple sclerosis lesions: characterization with high-field-strength MR imaging. Radiology, 262(1), 206-15.
3) Kwan JY, Jeong, SY, van Gelderen P, Deng H-X, Quezado MM, Dnaielian LE, Butman JA, Chen L, Bayat E, Russell J, Siddique T, Duyn JH, Rouault TA, Floeter MK. Iron accumulation in deep cortical layers accounts for MRI signal abnormalities in ALS: Correlating 7 Tesla MRI with pathology. 2012, PLOS One 7(4): e35241.
4) Ward RJ, Zucca FA, Duyn JH, Crichton RR, Zecca L. The role of iron in brain ageing and neurodegenerative disorders. Lancet Neurology 2014, 13:1045..