**BIOGRAPHICAL SKETCH**

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NAME: **Peter C.M. van Zijl**

eRA COMMONS USER NAME (credential, e.g., agency login): **pvanzij1**

POSITION TITLE: **Professor of Radiology; Director, F.M. Kirby Research Center**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Free University, Amsterdam, The Netherlands | BS | 1977 | Chemistry |
| Free University, Amsterdam, The Netherlands | MS | 1980 | Chemistry |
| Free University, Amsterdam, The Netherlands | PhD | 1985 | Mathematics & Physics |
| Carnegie Mellon University, Pittsburgh, PA | postdoc | 1985-87 | Chemistry |
| National Cancer Institute, NIH, Bethesda, MD | postdoc | 1987-90 | MRI and MRS of cancer |

## A. Positions and honors

**Positions and Employment**

- Research Assistant Professor, Dept. of Pharmacology, Georgetown University Medical School 90-92
- Assistant Professor, Dept. of Radiology, Johns Hopkins University Medical School 4/92-8/92
- Associate Professor, Dept. of Radiology, Johns Hopkins University Medical School 9/92-9/97
- Professor, Dept. of Radiology, Johns Hopkins University Medical School 10/97-
- Founding Director, F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Research Institute 1/99 –

**Other Experience and Professional Memberships**

- **Associate Editor** Magnetic Resonance in Medicine; J. Magn. Reson.
- **Editorial Board:** NMR in Biomedicine.
- **Board of Trustees (ISMRM),** 2000-2004**; Member Executive Committee for Experimental NMR conference (ENC),** 1997-2004**; ISMAR council:** 2001- present.
- **Member of many scientific advisory boards and NIH review panels**

**Awards, Honors:**

- Laukien Award, Experimental NMR Conference 2016
  for the development of CEST imaging (shared with Robert Balaban)
- Fellow, International Society of Magnetic Resonance (ISMAR) 2016
- Distinguished Investigator, Academy of Radiology Research 2012
- Gold Medal, International Society of Magnetic Resonance in Medicine 2007
  For neuroscience contributions to fMRI techniques, diffusion imaging and MRS
- Fellow, International Society of Magnetic Resonance in Medicine (ISMRM) 2004
- Chair, Experimental NMR conference (ENC) 2003
- Established Investigator Award, American Heart Association 1995

## C. Contribution to Science (chronological order).

**C-1:** My first scientific contributions in vivo were to the fields of localized spectroscopy and spectroscopic imaging, where I designed pulse sequences that employ gradient coherence selection to achieve clean signals (i.e. without water or intracellular vs extracellular, etc.). Together with Chrit Moonen I optimized water suppression approaches and we wrote the coherence transfer theory for such optimized signal selection for both homonuclear and heteronuclear MRS. Many of the water suppression schemes based on these principles are now standard in MRS on most clinical scanners. We also published the first measurement of intracellular spectra of perfused cancer cells. Together with Ralph Hurd, we also designed pulse sequences for converting high resolution NMR approaches from being based mainly on phase cycling schemes to employing pulsed field gradients. These are now used on all high resolution NMR spectrometers and one of our papers was recognized as one of 20 influential papers in NMR published in the Journal of Magnetic Resonance in a special issue of the journal in 2011. Some of the relevant papers are:

1) Moonen CTW, Van Zijl PCM, Highly effective water suppression for in vivo proton NMR spectroscopy (DRYSTEAM), J. Magn. Reson. 1990; 88(1):28-41
2) Van Zijl PC, Moonen CT, Faustino P, Pekar J, Kaplan O, Cohen JS. Complete separation of intracellular and extracellular information in NMR spectra of perfused cells by diffusion-weighted spectroscopy. Proc Natl Acad Sci U S A. 1991 Apr 15;88(8):3228-32.
3) Ruiz-Cabello J, Vuister GW, Moonen CT, van Gelderen P, Cohen JS, van Zijl PC. Gradient-enhanced heteronuclear correlation spectroscopy: theory and experimental aspects. J. Magn. Reson. 1992; 100:282-302. Reprinted in a historical issue of about 20 papers most affecting the field during 40 years of J. Magn. Reson. : J Magn Reson. 2011 Dec;213(2):446-66
4) Duyn JH, Gillen J, Sobering G, van Zijl PC, Moonen CT. Multisection proton MR spectroscopic imaging of the brain. Radiology. 1993 Jul;188(1):277-82.

**C-2:** I have contributed significantly to the development of diffusion tensor spectroscopy and imaging and especially the study of diffusion anisotropy in vivo and the development of diffusion tensor imaging (DTI) and fiber tracking. Early work on the tensor was in the beginning of the nineties with Chrit Moonen to use the trace of the tensor for studying brain ischemia (paper 1 below). We later used this to explain anomalies in the development of ischemia as a function of time, which was affected by the choice of orientation of the field gradients used for diffusion weighting. This led to the measurement of isotropic diffusion for the study of stroke evolution. Later, together with Susumu Mori, we contributed to the origination and application of DTI based fiber tractography in animals and humans. This was subsequently applied for the study of brain tumors, developmental disorders, and many diseases in the brain and spinal cord.
Some of the relevant papers are:

1) van Gelderen P, de Vleeschouwer MH, DesPres D, Pekar J, van Zijl PC, Moonen CT. Water diffusion and acute stroke. Magn Reson Med. 1994 Feb;31(2):154-63.
2) Mori S, van Zijl PC. Diffusion weighting by the trace of the diffusion tensor within a single scan. Magn Reson Med. 1995 Jan;33(1):41-52.
3) Mori S, Crain BJ, Chacko VP, van Zijl PC. Three-dimensional tracking of axonal projections in the brain by magnetic resonance imaging. Ann Neurol. 1999 Feb;45(2):265-9. First paper showing DTI fiber tracking.
4) Mori S, van Zijl PC. Fiber tracking: principles and strategies - a technical review. NMR Biomed. 2002 Nov-Dec;15(7-8):468-80.

**C-3:** I have contributed to the basic understanding of mechanisms underlying the BOLD effect and the signal changes based on it. These were especially BOLD mechanisms for spin echo sequences, but later also for gradient echo sequences. We developed quantitative theories for both T2 and T2* signal changes and used these to quantify the physiological parameters underlying the BOLD effects, namely oxygen extraction fraction (OEF) and the cerebral metabolic rate of oxygen metabolism (CMRO2). I also contributed to the understanding of the well-known post-stimulus undershoot following the positive signal changes during brain activation. In addition my group has developed technologies to quantify cerebral blood flow, blood volume and OEF and CMRO2. One well known approach is the vascular space occupancy technique. Many of these studies were done together with the group of Risto Kauppinen from Finland and Xavier Golay, Hanzhang Lu and Jun Hua.
Some of the relevant papers are:

1) van Zijl PC, Eleff SM, Ulatowski JA, Oja JM, Uluğ AM, Traystman RJ, Kauppinen RA. Quantitative assessment of blood flow, blood volume and blood oxygenation effects in functional magnetic resonance imaging. Nat Med. 1998 Feb;4(2):159-67.

2) Oja JM, Gillen JS, Kauppinen RA, Kraut M, van Zijl PC. Determination of oxygen extraction ratios by magnetic resonance imaging. J Cereb Blood Flow Metab. 1999 Dec;19(12):1289-95.
3) Lu H, Golay X, Pekar JJ, Van Zijl PC. Functional magnetic resonance imaging based on changes in vascular space occupancy. Magn Reson Med. 2003 Aug;50(2):263-74.
4) Lu H, Golay X, Pekar JJ, Van Zijl PC. Sustained poststimulus elevation in cerebral oxygen utilization after vascular recovery. J Cereb Blood Flow Metab. 2004 Jul;24(7):764-70.

**C-4:** I have had a long-time interest in the study of exchangeable protons, both using MR spectroscopy in the 1990s and, since the first report of the chemical exchange saturation transfer (CEST) effect by Ward and Balaban in 2000, in the use of CEST and other exchange transfer technologies to sensitively detect both contrast agents and endogenous compounds that contain exchangeable protons. Based on the amide proton spectroscopy work done in the nineties, I conceived the amide proton transfer (APT) technology that is now used in vivo in patients to grade tumors, distinguish recurrent tumor from treatment necrosis and to predict survival of glioma patients. It also can be used to noninvasively map pH using the water signal, e.g. following ischemia. We also described the origin of relayed nuclear Overhauser enhancements (NOEs) measured in CEST experiments (paper 4 below) and are now developing pulsed exchange transfer technologies that do not use transfer of saturation but coherence transfer to transfer magnetization and enhance signal. This is opening up a new field to allow translation of editing techniques typically used in high resolution NMR spectroscopy to in vivo detection of low concentration solutes in vivo using water imaging.
Some of the relevant papers are:
1) Zhou J, Payen JF, Wilson DA, Traystman RJ, van Zijl PC. Using the amide proton signals of intracellular proteins and peptides to detect pH effects in MRI. Nat Med. 2003 Aug;9(8):1085-90.
2) Gilad AA, McMahon MT, Walczak P, Winnard PT Jr, Raman V, van Laarhoven HW, Skoglund CM, Bulte JW, van Zijl PC. Artificial reporter gene providing MRI contrast based on proton exchange. Nat Biotechnol. 2007 Feb;25(2):217-9.
3) van Zijl PC, Jones CK, Ren J, Malloy CR, Sherry AD. MRI detection of glycogen in vivo by using chemical exchange saturation transfer imaging (glycoCEST). Proc Natl Acad Sci U S A. 2007 Mar 13;104(11):4359-64. PMCID: PMC1838607
4) Kim M, Gillen J, Landman BA, Zhou J, van Zijl PC. Water saturation shift referencing (WASSR) for chemical exchange saturation transfer (CEST) experiments. Magn Reson Med. 2009 Jun;61(6):1441-50. PMCID: PMC2860191

The above summary is very brief and only highlights a fraction of my work. Many papers of relevance for the current proposal could not be listed, but can be found in the citations in the proposal. My current h-factor is 105 and total number of citations is > 41,000 of which more than 20,000 since 2012. Over my career, I have published more than 350 papers.