BIOGRAPHICAL SKETCH

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NAME: Barnes, Patrick D.

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

POSITION TITLE: Professor of Radiology

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
University of Oklahoma, Norman OK	BA	06/1969	Letters/Premedicine – Honors PE-ET
Univ of Oklahoma College of Medicine, Oklahoma City, OK	MD	06/1973	Medicine – Honors, AOA
Univ of Oklahoma College of Medicine, Oklahoma City, OK	Residency	06/1796	Diagnostic Radiology
Children's Hospital and Harvard Med School, Boston, MA	Fellowship	06/1977	Pediatric Neuroradiology, Cardiovascular Radiology

A. Personal Statement

Our work seeks to advance neonatal care and outcomes by performing observational studies and interventional trials within a multicenter network of academic institutions. I am a professor of Radiology (Pediatric Neuroradiology) at Stanford University School of Medicine, Chief of the Section of Pediatric Radiology, and Co-Director, Pediatric MRI and CT Center at Lucile Packard Children's Hospital at Stanford. For the past two decades I have continued to dedicate my clinical, teaching, and research endeavors in pediatric neuroradiology emphasizing the design and implementation of advanced MRI technology and techniques for evaluating injury to the developing central nervous system. These endeavors focus upon children from the fetus through adolescence, including the assessment of imaging indicators or predictors of neurodevelopmental outcome. I have served as lead neuroradiologic consultant and central reader for MRI for several NICHD Neonatal Research Network studies including the Whole Body Therapeutic Hypothermia trial and the SUPPORT Neuroimaging study. These studies have yielded highly useful data regarding the ability of neuroimaging to predict outcome in term hypoxic ischemic encephalopathy as well as in extremely low birth weight infants when performed at near term. I am well suited to participate as a neuroradiology faculty collaborator and I look forward to future collaborations with the NICHD Neonatal Research Network.

B. Positions and Honors

Positions and Employment

1977-86	Associate Professor of Radiology, University of Oklahoma College of Medicine, Oklahoma City, OK
1977-86	Chief, Section of Pediatric Neuroradiology and Cardiovascular Radiology, Oklahoma Children's Memorial Hospital, Oklahoma City, OK
1986-99	Director of MRI, Department of Radiology, Children's Hospital, Boston, MA
1986-99	Director, Division of Neuroradiology, Department of Radiology, Children's Hospital, Boston, MA
1986-00	Associate Professor of Radiology, Harvard Medical School, Boston, MA
2000-07	Associate Professor of Radiology, Stanford University Medical Center, Stanford, CA
2000-	Chief, Section of Pediatric Neuroradiology and Co-Director, Pediatric MRI and CT Center,

Lucile Salter Packard Children's Hospital, Palo Alto, CA
2007- Professor of Radiology, Stanford University Medical Center, Stanford, CA
2018- Emeritus Professor of Radiology (Pediatric Radiology – Neuroradiology), Stanford University Medical Center, Stanford CA.

Other Experience and Professional Memberships

1988- Reviewer, Radiology (journal of the Radiological Society of North America)
1988- Reviewer, American Journal of Neuroradiology (journal of the American Society of Neuroradiology)
1991- Editorial Board, Reviewer, Journal of Child Neurology
1991- Reviewer, American Journal of Roentgenology (American Roentgen Ray Society)
1993- Reviewer, Neuroradiology
1993- Reviewer, Pediatrics
1993- Reviewer, Journal of Pediatrics
1994- Editorial Board, Reviewer, Pediatric Radiology (Journal of The Society for Pediatric Radiology and the European Society for Pediatric Radiology)
1995-97 Associate Editor for Pediatric Neuroradiology, International Medical Image Registry
1995- Reviewer, Journal of Computed Assisted Tomography
1997- Reviewer, Neurology
1998-99 Co-Founder, President and Chair, Program/Education Committee, American Society of Pediatric Neuroradiology
1998-99 Member, Executive Committee, Program/Education Committee, Clinical Practice Committee, Clinical Outcomes Research Committee, American Society of Neuroradiology
1999-00 Chair, Board of Directors, American Society of Pediatric Neuroradiology
2000- Chair, Standards and Guidelines Committee, American Society of Pediatric Neuroradiology
2000- Member, Child Abuse Committee, Society for Pediatric Radiology
2007 Chair, Child Abuse Task Force, Society for Pediatric Radiology
2008- Member, Child Abuse Task Force, Society for Pediatric Radiology
2008- Member, Neuroradiology Committee, Society for Pediatric Radiology

Honors

1996 John A. Kirkpatrick Jr. Teaching Award, Pediatric Radiology Fellowship Program, Dept. of Radiology, Children's Hospital and Harvard Medical School, Boston, MA
2001 Award of Appreciation for Service & Leadership, The American Society of Pediatric Neuroradiology, American Society of Neuroradiology 39th Annual Meeting, Boston, MA, April 23, 2001.
2003 Stanford B. Rossiter Senior Faculty of the Year, Dept of Radiology, Stanford Univ Medical Center, Stanford, CA
2005 Senior Faculty of the Year, Dept of Radiology, Stanford Univ Medical Center, Stanford, CA
2006 Senior Faculty of the Year, Dept of Radiology, Stanford Univ Medical Center, Stanford, CA

C. Contribution to Science

1. **Pioneering and ongoing collaborative MRI development for pediatrics.** When I completed my pediatric neuroradiology fellowship in 1977, the existing imaging modalities were limited to ultrasound, radiography, computed tomography, myelography, angiography, and nuclear medicine. I pioneered the development of magnetic resonance imaging (MRI) for investigating the pediatric central nervous system. With researchers from the University of Oklahoma and Oral Roberts University, I showed magnetic resonance imaging (MRI) to be a reliable, non-invasive methodology to screen patients for lumbosacral dysraphism (a). With this research, we effectively replaced myelography with magnetic resonance imaging. I led the development of MRI research programs and centers throughout the country – in Oklahoma City, at Boston's Children's, and at Lucile Packard Children's Hospital Stanford. At Boston Children's we published the very first paper using MR to image vascular anomalies (b). MR replaced CT and angiography as the standard of care and allowed us to establish a multi-disciplinary approach to care. We also pioneered a faster imaging technique (c), which was especially helpful for pediatric patients as it increased access for pediatric patients, shortened imaging times, and lessened the need for prolonged anesthesia. At Stanford using software by

Roland Bammer, we developed motion-correction software thus further reducing the need for sedation and anesthesia in pediatric patients receiving MR imaging (d).

a. Barnes PD, Lester PD, Yamanashi WS, Prince JR. MRI in infants and children with spinal dysraphism. AJR Am J Roentgenol. 1986 Aug;147(2):339-46. PMID: 3524163.
b. Meyer JS, Hoffer FA, Barnes PD, Mulliken JB. Biological classification of soft-tissue vascular anomalies: MR correlation. AJR Am J Roentgenol. 1991 Sep;157(3):559-64. PMID: 1872245.
c. Ahn SS, Mantello MT, Jones KM, Mulkern RV, Melki PS, Higuchi N, Barnes PD. Rapid MR imaging of the pediatric brain using the fast spin-echo technique. AJNR Am J Neuroradiol. 1992 Jul-Aug;13(4):1169-77. PMID: 1636531.
d. Skare S, Holdsworth S, Yeom K, Barnes P, Bammer R. High-resolution motion corrected diffusion-tensor imaging (DTI) in infants. Scientific Paper Presentation Society for Pediatric Radiology Annual Meeting, Boston MA April 2010. Received the "Caffey Award Scientific Paper"
e. Yeom KW, Straka M, Iv M, Moseley ME, **Barnes PD**, Skare S, Holdsworth SJ. Intensity-Corrected Dual-Echo Echo-Planar Imaging (DE- EPI) for Improved Pediatric Brain Diffusion Imaging. PLoS One. 2015 Jun 12;10(6):e0129325. doi: 10.1371/journal.pone.0129325. eCollection 2015.

2. **Pioneering and ongoing collaborative advances in imaging for pediatric neuroncology.** At the Boston Children's Hospital, I collaborated with Dr. Nancy Tarbell and other leaders in the subspecialties of Pediatric Oncology (Dana Farber Cancer Institute), Radiation Oncology, and Neurosurgery to establish one of the first Pediatric Brain Tumor Working Groups eventually leading to the formation of the Pediatric Brain Tumor Consortium. This collaboration successfully developed image-guided techniques that have allowed more effective and safer therapeutic interventions with improved outcomes (a, b, c). In studying central nervous system tumors using MRI, we found the termination of the caudal sac to be highly variable among pediatric patients, indicating imaging should guide craniospinal irradiation (a). In another study of pediatric and adult patients with intracranial neoplasms we showed the overall benefits of image guided stereotactic radiation therapy, which delivered localized treatment to a target area thus providing more effective delivery of the radiation and sparing normal brain (b). The adverse outcomes seen including central endocrinopathies and impaired cognitive function were reduced. MRI proved critical in terms of distinguishing hemorrhage from tumor progression following the treatment of CNS neoplasia in pediatric patients (c). Progress in pediatric neuro-oncology continues at the Lucile Packard Children's Hospital Stanford, where we recently determined that distinctive MRI features, notably the apparent diffusion coefficient, can be used to predict medulloblastoma histologic subtypes (d).

a. Dunbar SF, Barnes PD, Tarbell NJ. Radiologic determination of the caudal border of the spinal field in cranial spinal irradiation. Int J Radiat Oncol Biol Phys. 1993 Jul 15;26(4):669-73. PMID: 8330999.
b. Dunbar SF, Tarbell NJ, Kooy HM, Alexander E 3rd, Black PM, Barnes PD, Goumnerova L, Scott RM, Pomeroy SL, La Vally B, et al. Stereotactic radiotherapy for pediatric and adult brain tumors: preliminary report. Int J Radiat Oncol Biol Phys. 1994 Oct 15;30(3):531-9. PMID: 7928483.
c. Poussaint TY, Siffert J, Barnes PD, Pomeroy SL, Goumnerova LC, Anthony DC, Sallan SE, Tarbell NJ. Hemorrhagic vasculopathy after treatment of central nervous system neoplasia in childhood: diagnosis and follow-up. AJNR Am J Neuroradiol. 1995 Apr;16(4):693-9. PMID: 7611024.
d. Yeom KW, Mobley BC, Lober RM, Andre JB, Partap S, Vogel H, Barnes PD. Distinctive MRI features of pediatric medulloblastoma subtypes. AJR Am J Roentgenol. 2013 Apr;200(4):895-903. PMID: 23521467.

3. **Pioneering and ongoing collaborative advances in fetal MRI.** While at the Boston Children's Hospital, I collaborated with Dr. Deborah Levine of the Beth Israel Deaconess Medical Center in her revolutionary work to develop fetal MRI, including for the early diagnosis of central nervous system anomalies and other abnormalities. When an ultrasound shows that a central nervous system anomaly is suspected, we found that a fetal MRI can add information to imaging findings and/or alter diagnoses. Importantly, MRI findings may decrease the ambiguity in counseling expectant parents (a, c). We observed that changes in diagnosis and maternal counseling were significantly associated with gestational age, with MRI findings more likely to impact the course of care for fetuses evaluated at older gestational ages (d). Additionally, fetal MRI also

allows for the evaluation of cortical anatomy and can identify secondarily acquired CNS injuries. It provides faster imaging and improved resolution (b). I provided leadership in neuroradiology for these studies, which contributed to the impetus for creating Fetal Medicine programs and decreased ambiguity in counseling expectant parents.

a. Levine D, Barnes PD, Madsen JR, Li W, Edelman RR. Fetal central nervous system anomalies: MR imaging augments sonographic diagnosis. Radiology. 1997 Sep;204(3):635-42. PMID: 9280237.
b. Levine D, Barnes PD, Madsen JR, Abbott J, Wong GP, Hulka C, Mehta T, Li W, Edelman RR. Fetal CNS anomalies revealed on ultrafast MR imaging. AJR Am J Roentgenol. 1999 Mar;172(3):813-8. PMID: 10063888.
c. Levine D, Barnes PD, Madsen JR, Abbott J, Mehta T, Edelman RR. Central nervous system abnormalities assessed with prenatal magnetic resonance imaging. Obstet Gynecol. 1999 Dec;94(6):1011-9. PMID: 10576192.
d. Levine D, Barnes PD, Robertson RR, Wong G, Mehta TS. Fast MR imaging of fetal central nervous system abnormalities. Radiology. 2003 Oct;229(1):51-61. PMID: 12920177.
e. Katz J, Chock V, Davis A, Blumenfeld Y, Hahn J, Barnes P, Barth R, Rubesova E, Hintz, S. Utility of prenatal MRI in the evaluation and management of fetal ventriculomegaly. J. Perinatology, In press 2018.

4. **Pioneering and ongoing collaborative advances in neonatal neuroimaging.** Prior to the use of diffusion-weighted imaging, T1- and T2-weighted MR imaging was often normal in the first few hours after an ischemic insult. This early period overlaps with the narrow and finite “therapeutic window” during which neuroprotective therapies can be effective. In collaboration with Dr. Joseph Volpe’s neonatal neurology team we showed that differences in line-scan diffusion imaging (LSDI) of symmetric/diffuse and focal/multifocal lesions reflect differences in pathophysiology or timing of the injury (a). Neonates with brain ischemia were observed to develop either symmetric/diffuse injury or focal/multifocal injury. At Stanford, I have focused on neonatal neuroimaging, one project was to compare the utility of serial cranial ultrasound with a single near term MRI to predict cerebral palsy (b). Early cranial US is the usual practice. We found that MR was superior however both demonstrated high specificity. I have continued this important work with Dr. Susan Hintz and the NICHD Neonatal Research Network (NRN) (c). We prospectively evaluated MRI white matter abnormalities and cerebellar lesions and serial CUS findings as predictors of outcomes at 18-22 months corrected age in 480 infants. We found that both late CUS and MRI were associated with outcomes independent of early CUS and other factors underscoring the prognostic value of near-term neuroimaging. This study is the largest of its kind and the findings are likely to significantly impact the practices and recommendations for neuroimaging in preterm infants. In a second collaboration with the NICHD NRN, we investigated the relationship between brain injury on MRI and outcome within a randomized controlled trial of whole body cooling for neonatal hypoxic-ischemic encephalopathy (d). Fewer areas of infarction and a trend towards more normal scans were noted following whole body hypothermia. We were able to use MRI scans to categorize all areas of brain injury, including hemispheric devastation, and show the NRN pattern of brain injury is strongly associated with death or disability at 18-22 months no matter the treatment modality. This may prove beneficial when counseling parents. I served as the sole pediatric neuroradiology collaborator on these investigations.

a. Robertson RL, Maier SE, Robson CD, Mulkern RV, Karas PM, Barnes PD. MR line scan diffusion imaging of the brain in children. AJNR Am J Neuroradiol. 1999 Mar;20(3):419-25. PMID: 10219407. Derek Harwood-Nash for Outstanding Pediatric Neuroradiology Paper: presented at the ASNR/ASPNR Annual Meeting, San Diego, CA, 1999.
b. Mirmiran M, Barnes PD, Keller K, Constantinou JC, Fleisher BE, Hintz SR, Ariagno RL. Neonatal brain magnetic resonance imaging before discharge is better than serial cranial ultrasound in predicting cerebral palsy in very low birth weight preterm infants. Pediatrics. 2004 Oct;114(4):992-8. PMID: 15466096.
c. Hintz SR, Barnes PD, Bulas D, Slovis TL, Finer NN, Wrage LA, Das A, Tyson JE, Stevenson DK, Carlo WA, Walsh MC, Laptook AR, Yoder BA, Van Meurs KP, Faix RG, Rich W, Newman NS, Cheng H, Heyne RJ, Vohr BR, Acarregui MJ, Vaucher YE, Pappas A, Peralta-Carcelen M, Wilson-Costello DE, Evans PW, Goldstein RF, Myers GJ, Poindexter BB, McGowan EC, Adams-Chapman I, Fuller J, Higgins RD; SUPPORT Study Group of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network.

Neuroimaging and neurodevelopmental outcome in extremely preterm infants. Pediatrics. 2015 Jan;135(1):e32-42. PMID: 25554820; PMCID: PMC4279063.

d. Shankaran S, Barnes PD, Hintz SR, Laptook AR, Zaterka-Baxter KM, McDonald SA, Ehrenkranz RA, Walsh MC, Tyson JE, Donovan EF, Goldberg RN, Bara R, Das A, Finer NN, Sanchez PJ, Poindexter BB, Van Meurs KP, Carlo WA, Stoll BJ, Duara S, Guillet R, Higgins RD; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Brain injury following trial of hypothermia for neonatal hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed. 2012 Nov;97(6):F398-404. Erratum in: Arch Dis Child Fetal Neonatal Ed. 2014 Mar;99(3):301. PMID: 23080477; PMCID: PMC3722585.

e. Shankaran S, McDonald SA, Laptook AR, Hintz SR, Barnes PD, Das A, Pappas A, Higgins RD; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Neonatal Magnetic Resonance Imaging Pattern of Brain Injury as a Biomarker of Childhood Outcomes following a Trial of Hypothermia for Neonatal Hypoxic-Ischemic Encephalopathy. J Pediatr. 2015 Nov;167(5):98793.e3. doi:10.1016/ j.jpeds. 2015.08.013. Epub 2015 Sep 16. PMID:26387012

f. Shankaran S, Laptook A, McDonald S, Hintz S, Barnes P, Das A, Higgins R. Eunice Kennedy Shriver National Institute of Child Health, and Human Development Neonatal Research Network. Acute perinatal sentinel events, neonatal brain injury pattern, and outcome of infants undergoing a trial of hypothermia for neonatal hypoxic-ischemic encephalopathy. J Pediatr. 2017 Jan;180:275-278.e2. doi:10.1016/j.jpeds.2016.09.026.

g. Barnes P. Neuroimaging in the evaluation of pattern and timing of fetal and neonatal brain abnormalities. Stevenson DK, Benitz WE, Sunshine P, Hintz SR, Druzin ML, eds. *Fetal and Neonatal Brain Injury*. 5th ed. Cambridge: Cambridge University Press; 2018:283-311; doi:10.1017/9781316275498.

h. Hintz S, Vohr B, Bsnn C, Taylor H, Das A, Gustafson K, Yolton K, Watson V, Lowe J, DeAnda M, Ball M, Finer N, Van Meurs, K, Shankara, S, Pappas, A, Barnes P, Bulas D, Newman J, Wilson-Costello D, Heyne R, Harmon H, Peralta-Carcelen, M, Adams-Chapman I, Duncan A, Fuller J, Vaucher Y, Colaizy T, Winter S, McGowan e, Goldstein R, Higgins, R. Eunice Kennedy Shriver National Institute of Child Health and Human Development, Pregnancy and Perinatology Branch. Preterm neuroimaging and school-age cognitive outcomes. Pediatrics 2018;142:e20174058.

i. Laptook A, Shankaran S, Barnes P, Rollins N, et al. Limitations of conventional MRI as predictor of death or disability following neonatal hypoxic-ischemic encephalopathy in the late hypothermia trial. J Pediatr 2021; 230:106-111.

5. **Imaging of infant and child trauma, including child abuse and the mimics.** Having served as a pediatric radiologist and pediatric neuroradiologist consultant and member of child protection teams at Oklahoma Children's Memorial Hospital and Boston Children's Hospital, I then co-founded the Child Abuse SCAN team at Lucile Packard Children's Hospital Stanford in 2008. I have also collaborated with leaders in medicine and law in recognizing the "mimics" of child abuse which has led to more comprehensive and compassionate management strategies (a-d). I review case histories in the literature and find that there is no evidence base for reliably distinguishing non-accidental injury (NAI) from accidental injury from medical mimics. Radiologists must provide a detailed report of their findings and differential diagnosis, and communicate any concern for NAI. Considering a case series of rickets versus abuse, we often found severe maternal vitamin D deficiencies. This led us to claim that the diagnosis and treatment of vitamin D deficiency is most important in improving the health of pregnant women and infants (a, b). Laboratory studies showed that rickets does occur that's linked to maternal health and when observed in the fetus, it can mimic the symptoms of abuse. Our findings influenced the American Congress of Obstetricians and Gynecologists and the American Academy of Pediatrics to raise the level of vitamin D supplementation recommended for pregnant mothers and neonatal breastfed babies. We found that findings of subdural hemorrhage, retinal hemorrhage and encephalopathy cannot reliably identify abuse or the timing of such (d). I was the lead neuroradiologist on these studies.

   a. Keller KA, Barnes PD. Rickets vs. abuse: a national and international epidemic. Pediatr Radiol. 2008 Nov;38(11):1210-6. PMID: 18810424.

   b. Keller K, Barnes P. Rickets vs. Abuse–the evidence: Reply. Pediatr Radiol. 2009; 39:1130.

c. Barnes PD. Imaging of nonaccidental injury and the mimics: issues and controversies in the era of evidence-based medicine. Radiol Clin North Am. 2011 Jan;49(1):205-29. PMID: 21111136.
d. Findley KA, Barnes PD, Moran DA, Squier W. Shaken baby syndrome, abusive head trauma, and actual innocence: getting it right. *Legal Studies Research Paper Series,* Paper No. 1195. Houston J Health Policy. Social Science Research Network Electronic Paper Collection, 2012 http://ssrn.com/abstract=2048374 .
e. Miller D, Barnes P**,** Miller M.The significance of macrocephaly or enlarging head circumference in infants with the triad: further evidence of mimics of shaken baby syndrome. Am J Forensic Med Pathol. 2015 Jun;36(2):111-20. doi: 10.1097/PAF.0000000000000152.
f. Findley K, Risinger D, Barnes P, Mack J, Moran D, Scheck B, Bohan T. Feigned Consensus: Usurping the Law in shaken baby syndrome / abusive head trauma prosecutions. University of Wisconsin Law School. Legal Studies Research Paper Series Paper No. 1461, 2019. https://ssrn.com/abstract=3328996

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1HAaHrFq9I59/bibliography/47853117/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support
None

Completed Research Support

2U HD 27880-16 Van Meurs (PI). Project period: 04/01/06–03/31/11 NIH/NICHD
Multicenter Network of Neonatal Intensive Care Unit Intervention Trial of Hypothermia for Term Hypoxic Ischemic Encephalopathy.
Role: Central MRI reader/Neuroimaging consultant

2U HD 27880-16 Van Meurs (PI). Project period: 04/01/06–03/31/18 NIH/NICHD
Multicenter Network of Neonatal Intensive Care Units Neuroimaging and Neurodevelopmental Outcome, SUPPORT Multi-Center Project This project investigates the value of brain magnetic imaging (MRI) in predicting neurodevelopmental outcome in extremely low birthweight (ELBW) infants.
Role: Central MRI reader / Neuroimaging consultant

NIH 1R01 EB008706 Bammer (PI) 09/01/2008–08/31/2013
Short Axis Epi For Diffusion Tensor Mri At High Field
The main objective of the project is to create significant improvements in Diffusion Tensor Imaging (DTI) at high field (i.e. 3T and 7T) via novel acquisition/reconstruction techniques so that improved pediatric and adult high-field DTI is enabled. This will assist in building the basic methodological framework at high field for further clinically focused studies and basic neuroscience research
Role: Collaborator

NIH 1R01 MH083972 Hardan (PI) 03/01/2009–12/31/2013
A Neuroimaging Study of Twin Pairs with Autism
The goal of this study is to develop a better understanding of linkages among clinical features and neurobiological measures in individuals affected by autism. High resolution anatomical, diffusion tensor and proton spectroscopy scans will be obtained from 80 same-sex autism twin pairs, with at least one twin with autism, as well as 40 typically developing same-sex twin pair controls, in order to better identify clinical or biological endophenotypes associated with autism.
Role: Collaborator