NON-INVASIVE IN VIVO MRI METHOD TO IMAGE SALIENT FEATURES OF AXONS AND NERVES

SUMMARY (1024-CHARACTER LIMIT)

Scientists from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) have developed a novel diffusion Magnetic Resonance Imaging (MRI) experimental and modeling framework to measure new and useful microanatomical features of white matter (and gray matter), which are closely related to the function of the central nervous system (CNS) or peripheral nervous system (PNS). This invention is available for licensing or co-development partners.

NIH REFERENCE NUMBER

E-079-2003

PRODUCT TYPE

- Diagnostics

KEYWORDS

- Diffusion Magnetic Resonance Imaging, MRI, MRI Modeling Framework, Central Nervous System, CNS, Peripheral Nervous System, PNS, Composite, Axon, Nerve, Intra-Axonal, Axon Diameter, CHARMED, AxCaliber, Basser

COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

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STATUS

Active

DESCRIPTION OF TECHNOLOGY

The invention from Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) provides a non-invasive, painless means for measuring microanatomical features of Nerve and Axon Diameter Distribution (ADD) to image the Central and Peripheral Nervous Systems (CNS and PNS). ADD is altered in abnormal development (e.g., autism), in neurodegenerative processes (e.g., aging,

alcoholism, Alzheimer's disease) and diseases such as ALS (Lou Gehrig's disease).

U.S. patent 7,643,863, related to this invention, consists of a novel diffusion Magnetic Resonance Imaging (MRI) experiment and modeling framework, termed Composite Hindered and Restricted Model of Diffusion (CHARMED). It characterizes hindered and restricted anisotropic diffusion in brain white matter by marrying Diffusion Tensor MRI (DTI) and q-space MRI. DTI provides information primarily about how water diffuses in the extracellular compartment of tissues, where water mobility is hindered (i.e., where water diffuses freely but encounters barriers from which it is reflected). However, DTI does not provide a complete characterization of diffusion in the intracellular compartment of some cells – particularly myelinated axons – where water mobility is restricted by impermeable membranes. Using CHARMED, diffusion within axons is modeled as 'hindered diffusion' parallel to the axis of the axon, and 'restricted diffusion' perpendicular to the axis. Diffusion exterior to axons is modeled as hindered diffusion with differing diffusivities parallel and perpendicular to the nerve or axonal axis. Improved angular resolution of fiber tract orientation can be obtained for tractography studies and more microstructural information can be gleaned for both diagnostic and therapeutic purposes than from conventional DTI. CHARMED improves characterization and measurement of tissue and cell microstructure in neuronal tissue. This technology promises to advance the diagnosis of neurological conditions and, potentially, cognitive and behavioral disorders – as well as monitoring normal development and aging.

An improvement and continuation of the CHARMED MRI framework was also developed and named, AxCaliber MRI, disclosed in U.S. patent 8,380,280. It enables the ADD measurement of axon bundles (fascicles) and nerves in the CNS and PNS, respectively. The invention combines CHARMED MRI and an improvement of a Nuclear Magnetic Resonance (NMR) method. Using CHARMED, axons or nerve fascicles are modeled as having a hindered extracellular compartment and a restricted intracellular or intra-axonal compartment. Using AxCaliber MRI, fascicles are modeled as a bundle of impermeable cylinders having a distribution of internal or intra-axonal diameters.

The significance of this invention is that it provides measurements of new and useful microanatomical features of white and gray matter closely related to the function of the CNS and PNS. Previously, the data provided by this non-invasive MR imaging method was only available using invasive and laborious histological means requiring tissue biopsy and optical or electron microscopic analysis of tissue slides showing only small regions of tissue. With CHARMED and AxCaliber MRI, whole-brain analysis of white matter microstructure is now possible.

POTENTIAL COMMERCIAL APPLICATIONS

- Clinical diagnostic Magnetic Resonance Imaging (MRI) including neuroradiological assessment of brain and spinal cord pathology
- Measurement of microanatomical features of nerves and white matter pathways enabling early detection and monitoring of CNS and PNS diseases
- Could provide useful information for neuropsychological and cognitive assessment
- Neurologic conditions (e.g., stroke, Muscular Sclerosis, Alzheimer's disease); and

- Cognitive and behavioral disorders (e.g., schizophrenia, autism)

COMPETITIVE ADVANTAGES

- Non-invasive, painless, in vivo measurement of microanatomical features of nerves and axons
- Possible applications to study skeletal muscle and other fibrous tissues
- No contrast agents required
- Modest data requirements allow for scans to be performed in a clinically feasible time-frame

INVENTOR(S)

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DEVELOPMENT STAGE

- Pre-clinical (in vivo)

PUBLICATIONS

Assaf Y, et al. A New Modeling and Experimental Framework to Characterize Hindered and Restricted Water Diffusion in Brain White Matter. [PMID 15508168]

Assaf Y, et al. Combining DT and q-space MRI: a new model of white matter in the brain. Proc. Intl. Soc. Mag. Reson. Med. 11 [https://cds.ismrm.org/ismrm-2003/0588.pdf]

Assaf Y, et al. Composite hindered and restricted model of diffusion (CHARMED) MR imaging of the human brain. [PMID 15979342]

Sen PN, et al. Modeling diffusion in white matter in the brain: A composite porous medium. [PMID 15833615]

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Avram L, et al. Three-dimensional water diffusion in impermeable cylindrical tubes: theory versus experiments. [PMID 18574856]

Bar-Shir A, et al. Experimental Parameters and Diffraction Patterns at High q Diffusion MR: Experiments and Theoretical Simulations. DOI 10.1.1.192.3563

PATENT STATUS

- **U.S. Patent Filed:** U.S. Patent Application Number 8,380,280 , Filed 02 May 2008
- **U.S. Patent Filed:** U.S. Patent Application Number 7,643,863 , Filed 08 Jul 2004
- **U.S. Patent Filed:** U.S. Patent Application Number PCT/US2004/22027 , Filed 08 Jul 2004
- **U.S. Provisional:** U.S. Provisional Patent Application Number 60/571,064 , Filed 14 May 2004
- **U.S. Provisional:** U.S. Provisional Patent Application Number 60/485,658 , Filed 08 Jul 2003

RELATED TECHNOLOGIES

- E-276-2008
- E-226-2010 - Quantitative In Vivo Methods for Measuring Brain Networks

THERAPEUTIC AREA

- Central Nervous System