

NIST Special Publication 250 NIST SP 250-100

# Magnetic Resonance Imaging Biomarker Calibration Service: NMR Measurement of Isotropic Water Diffusion Coefficient

Michael A. Boss Kathryn E. Keenan Karl F. Stupic Nikki S. Rentz Cassandra M. Stoffer Stephen E. Russek Amanda A. Koepke Kevin J. Coakley

This publication is available free of charge from: https://doi.org/10.6028/NIST.SP.250-100

# NIST Special Publication 250 NIST SP 250-100

# Magnetic Resonance Imaging Biomarker Calibration Service: NMR Measurement of Isotropic Water Diffusion Coefficient

Michael A. Boss\* Kathryn E. Keenan Karl F. Stupic Cassandra M. Stoffer Stephen E. Russek Applied Physics Division Physical Measurement Laboratory Nikki S. Rentz Boulder Safety, Health, and Environment Division Office of Safety, Health and Environment

> Amanda A. Koepke Kevin J. Coakley Statistical Engineering Division

\*Former NIST employee; all work for this publication was done while at NIST.

This publication is available free of charge from: https://doi.org/10.6028/NIST.SP.250-100

March 2023



U.S. Department of Commerce Gina M. Raimondo, Secretary

National Institute of Standards and Technology Laurie E. Locascio, NIST Director and Under Secretary of Commerce for Standards and Technology NIST SP 250-100 March 2023

Certain commercial entities, equipment, or materials may be identified in this document in order to describe an experimental procedure or concept adequately. Such identification is not intended to imply recommendation or endorsement by the National Institute of Standards and Technology, nor is it intended to imply that the entities, materials, or equipment are necessarily the best available for the purpose.

#### **NIST Technical Series Policies**

Copyright, Fair Use, and Licensing Statements NIST Technical Series Publication Identifier Syntax

#### **Publication History**

Approved by the NIST Editorial Review Board on 2022-11-19

#### How to Cite this NIST Technical Series Publication

Boss MA, Keenan KE, Stupic KF, Rentz NS, Stoffer CM, Koepke A, Coakley KJ, Russek SE (2023) Magnetic Resonance Imaging Biomarker Calibration Service: NMR Measurement of Isotropic Water Diffusion Coefficient. (National Institute of Standards and Technology, Boulder, CO), Special Publication (SP) NIST SP 250-100. https://doi.org/10.6028/NIST.SP.250-100

#### NIST Author ORCID iDs

M. Boss: 0000-0002-9492-767X K. Keenan: 0000-0001-9070-5255 K. Stupic: 0000-0001-8356-1660 N. Rentz: 0000-0002-7328-5639 C Stoffer: 0000-0003-2619-546X S. Russek: 0000-0002-8788-2442 K. Coakley: 0000-0003-3787-2577 A Koepke: 0000-0001-9515-0383

#### **Contact Information**

stephen.russek@nist.gov

NIST SP 250-100 March 2023

### Abstract

This document describes a calibration service to measure the water diffusion coefficient, or diffusivity, in reference materials and tissue mimics using nuclear magnetic resonance (NMR) techniques. This calibration is restricted to materials which exhibit isotropic Gaussian water diffusion. The measurement uses the water proton spin as a tag and standard NMR gradient techniques to measure diffusion of the proton magnetization, which, in low viscosity fluids, is largely determined by the physical motion of water molecules. The calibrated materials are meant to be used in phantoms (calibration devices) to verify the accuracy of magnetic resonance imaging (MRI)-based water diffusion measurements. The local diffusion coefficient (often referred to as the apparent diffusion coefficient in complex materials) and other associated parameters, are used as image-based biomarkers to assess the state of tissue cellular density, detect tissue anomalies, characterize tumor type, evaluate treatment efficacy, and assess neural connectivity and neural tissue degeneration. A biomarker, as defined by the U.S. Food and Drug Administration, is "a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or biological responses to a therapeutic intervention." (1) Diffusion coefficients, which describe the rate that water protons move due to random thermal motion, are phenomenological parameters that must be carefully defined and measured to enable rigorous quantification and their use as biomarkers for clinical decision making. Diffusion parameters, in addition to being dependent on local material properties, are dependent on environmental parameters such as temperature, which must be controlled and precisely and accurately measured.

### Keywords

Biomarker; magnetic resonance imaging; MRI; MRI phantoms; NMR; nuclear magnetic resonance; proton magnetization diffusion; water diffusion.

## **Table of Contents**

1.		roduction	
2.		libration Service Summary	
3.	The	eory of Measurement	3
3.	1.	Diffusion Model and Measurement Equations	3
3.	2.	Pulsed Gradient Spin Echo Sequence	6
4.	Sai	mple Geometry and Measurement System	10
4.		NMR system	
	4.1.	.1 Magnetic Field Ramp and Shimming	12
	4.1.	.2 NMR time base verification:	12
	4.1.	.3 Probe tuning:	12
	4.1.	.4 NMR radiofrequency (RF) power calibration:	14
	4.1.	.5 NMR instrument linewidth and peak integration:	17
	4.1	.6 Triaxial gradient system:	18
4.	2	Sample cells	21
4.	3	Fiber optic temperature probe and temperature control system	24
4.	4	Gradient Calibrations	
4.	5	PGSE Robustness Tests	29
4	4.5.1	I Gradient recovery and eddy current compensation	30
4	4.5.2	2 Gradient pulse shape and spacing	31
4	4.5.3	3 Computed vs. measured <i>b</i> -values	
4.5.4		t <b>180</b> Test	34
2	4.5.5	5 Water calibration	35
5. Standard Operating Procedures			
5.	1	Diffusion Measurement Protocol	
5.	2	System Startup and Calibration	
5.	3	Prerun calibrations	
5.	4	Data Acquisition	
5.	5	Data Analysis	
6.	Un	certainty Evaluation	41
6.	1 Int	troduction	41
6.	2	Overview of Measurement System Uncertainties	43
6.	3 No	on-Ideal Pulse Sequence (NPS)	46
6.	4	Local Environment Variation (LE)	46
6.	5	Non-ideal material properties (NM)	49
6.	6	Data Analysis (DA)	50