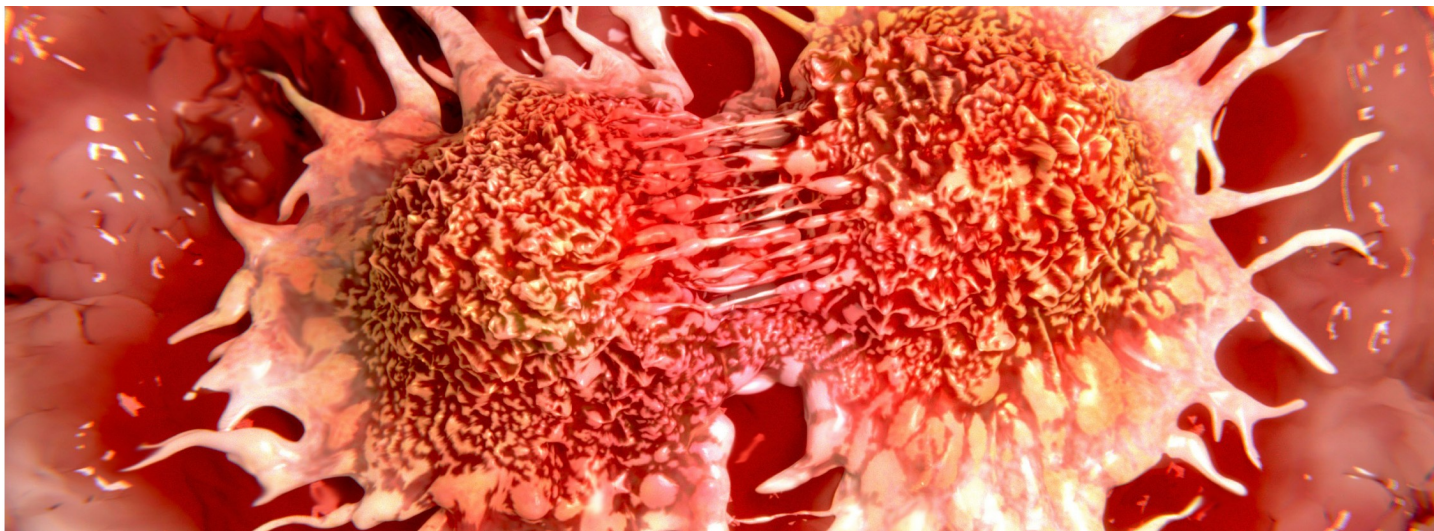


Oncologic Imaging: The Benefits of Diffusion-Weighted MRI

By Todd Tibbetts, M.D., Ph.D., Board Certified and Fellowship Trained Radiologist · Updated for 2026 by Intrinsic Imaging



Diffusion-weighted MRI (DWI) was first used to greatest advantage in stroke imaging. Advances in gradients and pulse sequences have since made it a core tool for detecting, characterizing and following malignant lesions in the chest, abdomen and pelvis. Today it is the dominant sequence for peripheral-zone prostate cancer, a foundation of whole-body MRI for bone and marrow disease, and, through the apparent diffusion coefficient (ADC), a quantitative biomarker with published repeatability standards. For sponsors, DWI offers a fast, contrast-free measure of tumor cellularity and treatment response, provided acquisition and analysis are standardized across sites.

Diffusion-Weighted MRI

Whereas conventional MRI focuses on anatomic detail, diffusion-weighted MRI measures the ability of water molecules to undergo unrestricted Brownian motion. In tissue, extracellular water moves freely, while intracellular water is limited by complex interactions with cellular components and the highly compartmentalized intracellular environment. This restricted motion, or diffusion restriction, was first exploited in stroke imaging. Brain ischemia drives water from the extracellular to the intracellular space, and the resulting increase in diffusion restriction appears on DWI as elevated signal with a decreased apparent diffusion coefficient (ADC).

Water moving into cells is not the only cause of elevated signal. If one tissue is inherently more cellular than another, it will on average contain more intracellular water and show higher signal on DWI. This is of particular interest in oncologic imaging, because tumors and metastases tend to be composed of large or tightly packed cells with limited extracellular matrix compared with surrounding normal tissue.

DWI also relies on inherent tissue contrast rather than intravenous contrast. This matters for patients with renal failure or contrast allergies, and it has gained further weight since 2017, when the FDA required a class-wide warning that gadolinium-based contrast agents can be retained in the brain and other tissues.¹ Because DWI uses fast single-shot echo-planar sequences, it adds substantial information at little cost in scan time.

Broad Applicability

Liver. DWI is now part of the routine liver MRI and is the most sensitive non-contrast sequence for detecting focal liver lesions. Low b-value diffusion sequences are significantly more sensitive than conventional T2-weighted fat-saturated images, and for some tumors, such as small carcinoid metastases, DWI may be the only sequence on which lesions are reliably seen. It also aids detection of infiltrative, hypoenhancing tumors such as cholangiocarcinoma. ADC values, while not completely specific, help characterize lesions as benign or malignant, because malignant lesions tend toward lower ADC. ADC also decreases with collagen deposition in hepatic fibrosis. The same effect, how-

ever, raises background signal in the cirrhotic liver and can obscure small lesions, which limits DWI as a stand-alone screening tool for hepatocellular carcinoma in cirrhosis.

Pancreas. Pancreatic adenocarcinoma is often difficult to detect and delineate because it is infiltrative and enhances poorly. Because these tumors are densely cellular, surrounded by tumor-induced fibrosis, or both, DWI provides important additional data for detection, characterization and measurement of the tumor mass.

Breast. Malignant breast lesions show lower ADC values than benign lesions, aiding characterization, and tumor ADC rises measurably as tumors respond to chemotherapy. The multicenter ACRIN 6698 trial, conducted within I-SPY 2 across 10 institutions, confirmed that the change in tumor ADC after 12 weeks of neoadjuvant therapy predicts pathologic complete response, with the strongest performance in hormone receptor-positive, HER2-negative tumors.²

Prostate. DWI has moved from a useful adjunct to the center of prostate MRI. Under PI-RADS version 2.1, DWI is the dominant sequence for assessing the peripheral zone, with dynamic contrast enhancement relegated to a secondary role.³ In 2025, the international PRIME trial of 490 biopsy-naïve men found that biparametric MRI, using T2-weighted imaging and DWI without contrast, was noninferior to multiparametric MRI, detecting clinically significant cancer in 29.2% versus 29.6% of men.⁴

Pelvis and whole body. Other established uses include cervical cancer, lymph node evaluation and restaging of rectal cancer after neoadjuvant therapy. Whole-body DWI now has its own reporting standards, MET-RADS-P for advanced prostate cancer and MY-RADS for multiple myeloma, for staging and response assessment in bone and marrow disease that CT and RECIST measure poorly.⁵

ADC as a Quantitative Endpoint

For clinical trials, the most important development is standardization. The Quantitative Imaging Biomarkers Alliance (QIBA) DWI Profile defines the change in ADC that indicates a true change with 95% confidence: 11% for brain, 26% for liver, 47% for prostate and 13% for breast lesions, when its acquisition and analysis requirements are met.⁶ In 2024, QIBA advanced

the profile to the "clinically feasible" stage and proposed updated thresholds, including 27% for prostate.⁷ These figures give sponsors a defensible basis for sample-size calculations and response definitions.

Guidance for Sponsors

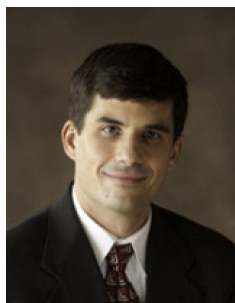
Using DWI in an oncology trial

- **Standardize acquisition.** Fix b-values, slice thickness and fat suppression in the imaging charter, and qualify every scanner, using a diffusion phantom where possible.⁶
- **Define the ADC endpoint in advance.** Specify region-of-interest method, whole-lesion or single-slice measurement, and the threshold for response, based on published repeatability.^{6,7}
- **Time the scans to the biology.** ADC change can precede change in size; build early on-treatment time points into the schedule.²
- **Use DWI where contrast is a concern.** Biparametric protocols reduce gadolinium exposure and scan time without compromising detection in suitable indications.⁴
- **Account for known limitations.** Plan reads for low-cellularity, necrotic or hemorrhagic tumors, motion and susceptibility artifacts, and the cirrhotic liver.
- **Read centrally.** Independent, blinded central review by subspecialty radiologists reduces site-to-site variability in qualitative and quantitative DWI assessment.

Summary

Diffusion-weighted MRI has limitations. Tumors with low cellularity often do not show restricted diffusion, hemorrhagic or necrotic tumors may not either, and motion and susceptibility artifacts remain technical challenges. Yet DWI has become an essential tool in oncologic imaging outside the central nervous system. With validated reporting systems, randomized evidence in prostate cancer and published repeatability standards for ADC, it now offers sponsors a fast, contrast-free and quantitative window on tumor cellularity and treatment response.

About the Author



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About Intrinsic Imaging, LLC

Headquartered in Bolton, Massachusetts, Intrinsic Imaging is an imaging CRO and core lab supporting Phase I–IV drug trials, medical device studies and AI/CAD validation studies. The company has completed three FDA Bioresearch Monitoring Program inspections, each with zero Form FDA 483 observations, and holds five BSI certifications: ISO 9001, ISO 13485, ISO 22301, ISO/IEC 27001 and ISO/IEC 27018. Its network of more than 1,000 board-certified, fellowship-trained physicians has supported trials at more than 4,000 sites in 64 countries.



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