Unlocking the Heart's Microstructure: Cardiac Diffusion MRI with Ultra-Strong Gradients

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Abstract

Diffusion MRI of the human heart provides unique insight into myocardial microstructure but has been hampered by cardiac and respiratory motion, short T2 of the heart muscle, and limited gradient strength. Recent advances in ultra-strong gradient technology not only help to overcome these technical challenges but also allow higher diffusion weighting (i.e., b-values) with clinically compatible echo times. Our recent studies demonstrate how this enabled in vivo diffusion kurtosis imaging (DKI) and q-space trajectory imaging (QTI) in the beating human heart, therefore moving beyond the Gaussian assumptions of diffusion tensor imaging (DTI). These advances may pave the way for more sensitive biomarkers of pathological changes of the myocardium and bring microstructural imaging closer to clinical application.

Key points

- Ultra-strong gradients (300 mT/m) make cardiac diffusion MRI feasible at higher b-values.
- In vivo cardiac diffusion kurtosis imaging and q-space trajectory imaging (QTI) were demonstrated with clinically compatible echo times.
- Kurtosis and QTI metrics reveal non-Gaussian diffusion, offering access to new imaging biomarkers of myocardial microstructure.
- Translation to clinical systems is within reach with new 200 mT/m gradient scanners.

Clinical motivation: The unmet need for microstructural cardiac imaging

Cardiovascular disease remains one of the leading causes of death worldwide [1]. While conventional cardiac MRI has revolutionized non-invasive assessment of cardiac anatomy, function, perfusion, and viability, it offers only indirect surrogates of myocardial microstructure [2]. Yet microstructural remodeling – including cardiomyocyte disarray, hypertrophy, fibrosis, and altered cellularity – underpins the pathogenesis of cardiomyopathies, ischemic injury, heart failure, and arrhythmias [3].

Histology provides exquisite microstructural information but is invasive, destructive, and limited to the biopsied region. Clinicians have long sought a "virtual biopsy" tool that could provide microstructural insights non-invasively and reproducibly [4]. Diffusion MRI offers precisely this promise, with sensitivity to water motion at the cellular scale [5]. However, its potential has remained largely unrealized in the heart, where motion, limited gradient performance, and low signal-to-noise ratio (SNR) have posed formidable barriers [6].

Why standard diffusion MRI falls short in the heart

T2 in the brain tissue is about 69 ms in white matter and around 99 ms in gray matter [8] (using a 3T MRI system). T2 in the heart muscle (i.e., myocardium) is ~46 ms at 3T [7], which is about two-thirds to half of the values found

in the brain. It is therefore important to achieve shorter echo times in cardiac imaging compared to brain imaging. In addition, motion-compensated diffusion gradient waveforms are needed for cardiac diffusion-weighted MRI (due to the motion of heart), which adds to the required echo time. Finally, mean diffusivity in the myocardium (~1.5 μm²/ms) [9] is higher than in brain tissue (0.93 μm²/ms in white matter [10, 11]), which causes higher signal attenuation in the heart compared to the brain for the same b-value, and hence puts further constraints on the SNR. Therefore, short TE are essential for the successful application of cardiac diffusion MRI techniques, which in turn require higher gradient performance.

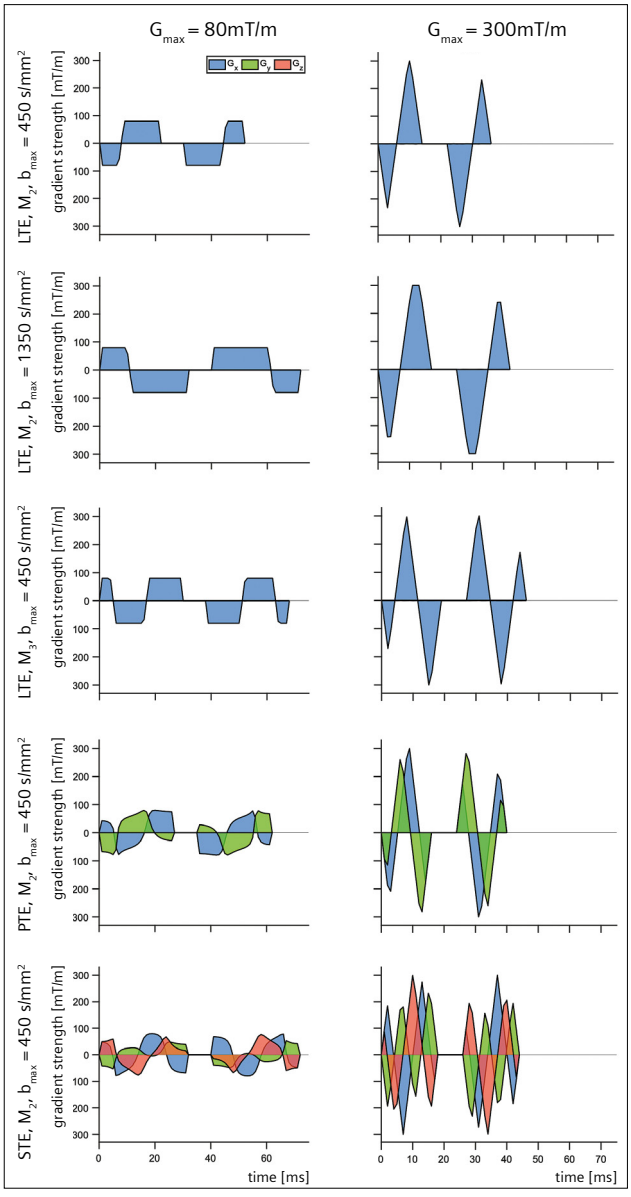
Ultra-strong gradients: A step-change for diffusion encoding

The advent of ultra-strong gradient systems, such as the 3T MAGNETOM Connectom[1] system equipped with a 300 mT/m gradient coil, has transformed what is experimentally possible. By enabling higher b-values at shorter echo times, these systems provide a new window into tissue microstructure. Originally developed for brain imaging, the MAGNETOM Connectom has subsequently become a unique platform for translational "below-the-neck" research, including the heart.

In our recent studies, we leveraged the capability of the MAGNETOM Connectom MR system to push the boundaries of cardiac diffusion MRI. We performed, for the first time, in vivo cardiac diffusion tensor imaging (DTI) on the MAGNETOM Connectom, which enabled higher b-value and higher-order motion compensation (up to third order; diffusion gradient waveforms were designed using the NOW toolbox [12, 13], see Fig. 1) [11] with an echo time comparable to what is commonly used on clinical scanners (such as the 3T MAGNETOM Prisma) for cardiac DTI. Diffusion-weighted imaging was performed with a prototype pulse sequence[2] that enabled diffusion encoding with user-defined gradient waveforms [14, 15]. This work already hinted at non-Gaussian behavior and potentially time-dependent diffusion effects [16], and showed that the myocardium can be probed more deeply and specifically than ever before. It also demonstrated that strong gradients do not merely "improve" existing methods, but also unlock qualitatively new experimental spaces.

Building on this foundation [16], our 2025 *Magnetic Resonance in Medicine* paper [17] reported the first successful implementation of diffusion kurtosis imaging (DKI) in the human heart. DKI extends beyond the Gaussian assumption of DTI, quantifying how water diffusion deviates from it due to microstructural heterogeneity.

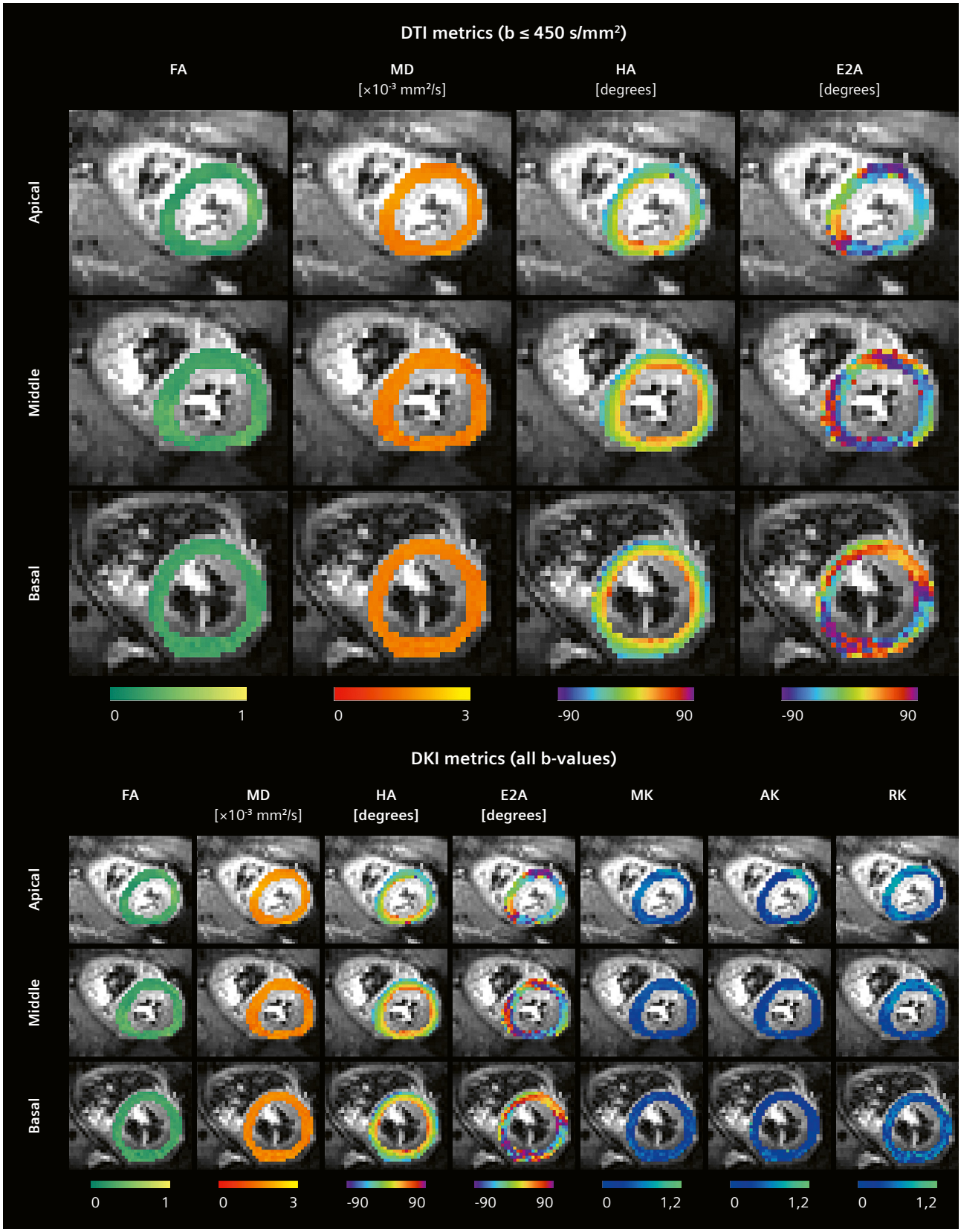
We acquired multi-shell diffusion data in healthy volunteers using 300 mT/m gradients, fitted a DKI model, and obtained parametric maps of mean, axial, and radial kurtosis (see Fig. 2). These maps revealed measurable non-Gaussian behavior in the myocardium, consistent with the tissue's known complexity.



1 Gradient performance comparison. Schematic showing the difference between 80 mT/m and 300 mT/m gradient strength for different b-values, motion compensation order, and encoding schemes (LTE, PTE, STE).

[1] *MAGNETOM Connectom is ongoing research. All data shown are acquired using a non-commercial system under institutional review board permission. Siemens Healthineers does not intend to commercialize the system.*

[2] *Work in progress. The application is currently under development and is not for sale in the U.S. and in other countries. Its future availability cannot be ensured.*



2 Example fractional anisotropy (FA), mean diffusivity (MD), helix angle (HA), and secondary eigenvector angle (E2A) maps using cardiac diffusion tensor imaging and mean, axial, and radial kurtosis maps (MK, AK, RK) using cardiac diffusion kurtosis imaging.

Together, these results provide a new set of imaging biomarkers for characterizing myocardial tissue – potentially sensitive to disease processes such as hypertrophy, fibrosis, and microstructural disarray.

Probing complex microstructure

Q-space trajectory imaging (QTI) represents a paradigm shift in (cardiac) diffusion MRI [16]. Unlike conventional DTI or DKI, which sample diffusion along a single encoding direction at a time (linear tensor encoding (LTE)), QTI explores diffusion along continuous or arbitrarily shaped trajectories in q-space, allowing direct estimation of higher-order diffusion moments and compartment-specific properties [18]. QTI can capture features such as microscopic anisotropy, isotropic and anisotropic kurtosis, heterogeneity, and orientation dispersion, providing a rich description of myocardial microstructure that is inaccessible with lower-order models.

Using an ultra-strong gradient system, we were able to acquire cardiac diffusion weighted images using advanced diffusion encoding schemes such as planar tensor encoding (PTE) and spherical tensor encoding (STE). These enable the quantification of microstructural features of the tissue such as microscopic anisotropy and isotropic and anisotropic kurtosis [19] (see Fig. 3).

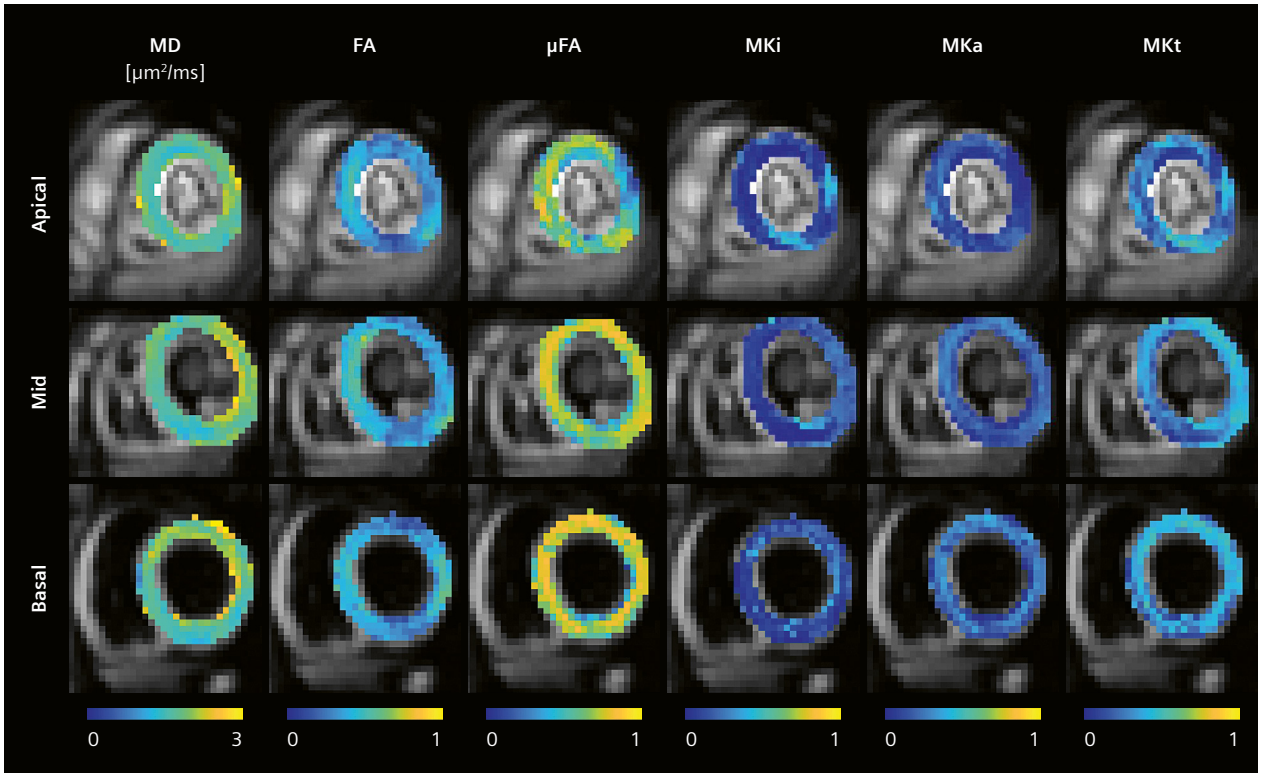
Bridging to clinical translation

While the MAGNETOM Connectom system is unique (there are only four scanners of this kind worldwide), its insights are not destined to remain restricted to these highly specialized scanners. The emergence of new clinical systems with significantly improved gradient performance, such as the 3T MAGNETOM Cima.X system equipped with a 200 mT/m gradient coil, brings these advances closer to patients.

The implications could be profound:

- Microstructural biomarkers such as kurtosis could enrich clinical MRI protocols for cardiomyopathies and heart failure.
- Higher b-value DTI may improve sensitivity to remodeling processes, better guide therapies, and benefit prognosis.
- Motion-compensated encoding and novel readouts (e.g., spiral) should allow integration into clinically feasible scan times.

By demonstrating feasibility at the high gradient strengths, our work provides a roadmap for translating cardiac microstructural imaging to the new generation of clinical scanners.



3 Example q-space trajectory imaging (QTI) metrics, microscopic fractional anisotropy (μFA), and isotropic (MKi), anisotropic (MKa), and total mean kurtosis (MKt).

Towards a virtual microscope for the heart

The ability to non-invasively probe myocardial microstructure represents a paradigm shift for cardiovascular imaging. With ultra-strong gradients, cardiac diffusion MRI is evolving from an experimental tool into a powerful research and diagnostic tool.

Future directions may include:

- Extending cardiac diffusion kurtosis imaging to patient populations with hypertrophic and dilated cardiomyopathy, ischemic heart disease, and arrhythmogenic disorders.
- Combining diffusion with relaxation dimensions, creating multidimensional "fingerprints" of cardiac tissue.
- Developing robust, motion-compensated sequences and advanced reconstruction strategies.
- Standardizing acquisition and analysis across centers, paving the way for multi-site clinical studies.

In essence, we are moving closer to a "virtual microscope" for the heart – a tool that could reveal the tissue-level signatures of disease, guide personalized treatment, and reduce reliance on invasive biopsies.

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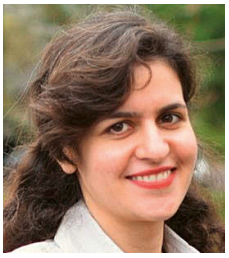

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