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The Fourth Dimension: Development and Clinical Implementation of 4D Imaging for Real-Time Visualization of Dynamic Physiological Processes

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Abstract

Background: Traditional medical imaging modalities have historically provided static, two- or three-dimensional anatomical snapshots, limiting comprehension of inherently dynamic physiological processes. The evolution toward four-dimensional (4D) imaging—incorporating the temporal dimension—represents a paradigm shift in diagnostic medicine, enabling visualization of dynamic phenomena in real-time. **Aim:** This narrative review comprehensively examines the development, technical foundations, and expanding clinical implementation of 4D imaging techniques across major modalities, focusing on their role in capturing and quantifying physiological dynamics. **Methods:** A systematic literature search of PubMed, IEEE Xplore, and Scopus databases (2015-2025) was conducted, with emphasis on technological innovations, validation studies, and clinical outcome research. **Results:** Significant advancements in 4D ultrasound, CT, MRI, and nuclear medicine have enabled unprecedented visualization of cardiac motion, respiratory dynamics, blood flow patterns, and metabolic processes. Key applications include fetal cardiac assessment, functional neuroimaging, radiotherapy planning, and intraoperative guidance. Despite transformative potential, challenges persist in data management, standardization, and clinical integration. **Conclusion:** 4D imaging has matured from research curiosity to clinical reality, providing novel insights into physiological function and pathology. Successful implementation requires continued technological refinement, establishment of standardized protocols, and validation through prospective clinical trials to fully realize its potential in personalized medicine.

Keywords: 4D imaging, dynamic visualization, physiological processes, real-time imaging, medical imaging technology

Introduction

Medical imaging has undergone a revolutionary transformation from static anatomical representation to dynamic functional visualization. The conventional approach of capturing two-dimensional (2D) or three-dimensional (3D) snapshots of human anatomy has provided invaluable diagnostic information for over a century, yet it fundamentally fails to capture the temporal dynamics essential to understanding physiological function and pathology (Khalifa et al., 2025). The integration of time as the fourth dimension in medical imaging represents one of the most significant advancements in diagnostic radiology and biomedical engineering of the past decade. 4D imaging refers to the acquisition and reconstruction of volumetric data over time, creating cinematic representations of moving anatomical structures and dynamic physiological processes.

The conceptual foundation for 4D imaging emerged from the recognition that many clinically relevant processes—cardiac contraction, respiratory motion, blood flow dynamics, joint kinematics, and fetal development—are intrinsically temporal phenomena. Traditional static imaging could only infer function from anatomical structure, often requiring multiple acquisitions at different time points or phases (Fornacon-Wood et al., 2020). The development of 4D techniques addresses this limitation by capturing the complete spatiotemporal evolution of these processes, enabling clinicians to visualize and quantify motion patterns, flow

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characteristics, and temporal changes in tissue properties.

This review traces the technological evolution of 4D imaging across major modalities, examines the underlying engineering principles enabling these advancements, and comprehensively analyzes their expanding clinical applications. Particular emphasis is placed on the transition from research prototypes to clinically implemented systems, the validation of 4D-derived biomarkers, and the integration of these techniques into routine diagnostic and therapeutic workflows. As healthcare increasingly embraces personalized and precision medicine approaches, the ability to characterize individual variations in physiological dynamics through 4D imaging represents a critical enabling technology with profound implications for diagnosis, treatment planning, and therapeutic monitoring.

Technological Foundations of 4D Imaging

Acquisition Strategies and Reconstruction Algorithms

The implementation of 4D imaging across different modalities has followed distinct technological pathways dictated by the fundamental physics of each imaging technique. In computed tomography (CT), the primary challenge has been achieving sufficient temporal resolution to freeze physiological motion while acquiring complete volumetric data. The evolution from single-slice to multi-detector CT (MDCT) with increasing numbers of detector rows has been fundamental, with modern systems capable of capturing 320 slices simultaneously, covering up to 16 cm of anatomy in a single gantry rotation (McCollough et al., 2023). For cardiac imaging, retrospective or prospective electrocardiogram (ECG) gating allows reconstruction of multiple phases of the cardiac cycle from data acquired over multiple heartbeats. In thoracic and abdominal applications, respiratory motion compensation techniques, including phase-based sorting of acquired data according to respiratory signal (from external monitors or internal surrogates), enable the generation of 4D datasets representing the breathing cycle (Sindoni et al., 2016).

Magnetic resonance imaging (MRI) offers unparalleled soft-tissue contrast and flexibility in contrast mechanisms but faces unique challenges in 4D acquisition due to inherently longer scan times. Key innovations include parallel imaging using multi-channel receiver coils to accelerate acquisition, compressed sensing techniques that exploit sparsity in the temporal domain to reconstruct images from undersampled data, and novel k-space sampling trajectories like radial and spiral acquisitions that are inherently motion-robust (Yang et al., 2017). Cardiac cine MRI using balanced steady-state free precession (bSSFP) sequences with retrospective ECG gating remains the gold standard for assessing ventricular function and wall motion, while phase-contrast MRI can provide 4D velocity mapping of blood flow in major vessels and cardiac chambers, enabling calculation of derived hemodynamic parameters like wall shear stress (Markl & Hope, 2022).

In ultrasound, the transition to 4D imaging has been facilitated by the development of matrix array transducers containing thousands of independently addressable elements. These transducers enable electronic beam steering in both elevation and azimuth dimensions, allowing rapid acquisition of volumetric data. High-volume rate acquisition is achieved through techniques like parallel receive processing and sparse array designs, with some systems capable of capturing over 50 volumes per second for cardiac applications (Sugeng et al., 2010). For fetal imaging, automated volume acquisition with subsequent spatiotemporal image correlation (STIC) allows offline reconstruction of 4D cine loops of the fetal heart from data acquired during freehand sweeps.

Nuclear medicine techniques, particularly positron emission tomography (PET), face the dual challenges of low signal-to-noise ratio and long acquisition times. 4D-PET typically involves list-mode data acquisition, where each detected event is tagged with its time of arrival and synchronized with external respiratory and/or cardiac motion signals. The data are subsequently sorted into temporal bins representing different phases of the motion cycle, and images are reconstructed for each bin (Xin et al., 2023). The development of digital PET detectors with improved timing resolution and total-body PET systems with dramatically increased sensitivity has significantly enhanced the feasibility and quality of 4D functional imaging.

Computational Advances

The enormous data burden of 4D imaging—often comprising hundreds of volumetric timepoints—has necessitated parallel advances in computational methods for reconstruction, processing, and visualization. Iterative reconstruction algorithms have largely replaced traditional filtered back-projection in CT and PET, providing better noise performance and enabling high-quality images from lower radiation dose acquisitions or fewer detected events (Willemink et al., 2013). In MRI, model-based reconstructions incorporating physical models of motion or contrast dynamics allow dramatic acceleration of 4D acquisitions.

Post-processing and analysis represent an equally critical component of the 4D imaging pipeline. Deformable image registration algorithms enable alignment of all timepoints to a common reference frame, facilitating voxel-wise analysis of signal changes over time and compensating for residual patient motion (Fu et al., 2020). Segmentation, once a labor-intensive manual process, is increasingly performed using deep learning algorithms trained on large annotated datasets, enabling automatic delineation of moving structures like the heart chambers across all cardiac phases (Tayebi Arasteh et al., 2023). Quantitative analysis tools extract functional parameters from 4D datasets, such as regional myocardial strain from tagged MRI or tissue tracking, ventricular volume-time curves, or ventilation/perfusion maps from functional lung MRI.

Visualization of 4D data poses unique challenges in effectively conveying four-dimensional information on two-dimensional displays. Clinical workstations now routinely employ synchronized multi-planar reformatting (displaying orthogonal slices simultaneously), volume rendering with transparency and clipping planes, and endoluminal "fly-through" views for hollow structures. Cinematic loop display is standard, with tools for controlling playback speed and synchronization of multiple 4D datasets (e.g., PET/CT). Emerging virtual and augmented reality platforms offer immersive 3D visualization of 4D data, allowing clinicians to intuitively explore spatial relationships and temporal dynamics (Barteit et al., 2021).

Clinical Implementation Across Modalities

4D Computed Tomography

The clinical adoption of 4D-CT has been most prominent in radiation oncology, where precise delineation of tumor motion during respiration is critical for accurate treatment planning, particularly for thoracic and abdominal malignancies. By capturing the entire trajectory of tumor movement, 4D-CT allows the generation of internal target volumes (ITVs) that encompass all positions of the tumor throughout the breathing cycle, enabling margin reduction compared to conventional approaches using generic population-based margins (Keall et al., 2006). This directly translates to decreased radiation exposure to surrounding healthy tissues and potential for dose escalation to the tumor. Additionally, 4D-CT data are used to program motion-compensating techniques in modern linear accelerators, such as respiratory gating (beam on only during specific breathing phases) or tumor tracking (dynamic multileaf collimator motion following the tumor in real-time).

In diagnostic radiology, 4D-CT angiography has revolutionized vascular assessment, particularly for evaluation of aortic dissection, endoleaks after endovascular repair, and vascular malformations. By capturing the transit of contrast bolus through the vasculature over time, clinicians can differentiate true lumen from false lumen, identify entry and re-entry tears in dissections, and characterize the hemodynamic significance of vascular lesions (Zhou et al., 2023). For cardiac applications, while coronary CT angiography primarily focuses on anatomical assessment of stenosis, 4D acquisitions allow evaluation of ventricular function, wall motion abnormalities, and even calculation of fractional flow reserve (CT-FFR) from computational fluid dynamics simulations based on the dynamic dataset.

Functional lung imaging using 4D-CT leverages respiratory-induced density changes to generate regional maps of ventilation. By registering inspiration and expiration phases, regional lung expansion can be calculated on a voxel-wise basis, identifying poorly ventilated regions in diseases like chronic obstructive pulmonary disease (COPD) or pulmonary fibrosis (Baschnagel et al., 2024). This functional information can guide surgical planning (identifying optimal lung regions for resection) or radiotherapy planning (avoiding dose to highly functional lung regions).

4D Magnetic Resonance Imaging

Cardiovascular MRI stands as the most mature clinical application of 4D-MRI, providing a comprehensive assessment of cardiac structure, function, flow, and tissue characterization in a single exam. Cine bSSFP sequences yield high-resolution 4D datasets of the heart throughout the cardiac cycle, enabling precise quantification of ventricular volumes, ejection fraction, and regional wall motion. When combined with late gadolinium enhancement for scar detection and T1/T2 mapping for tissue characterization, this provides an unparalleled comprehensive cardiac assessment (Petersen et al., 2016). 4D flow MRI, which encodes velocity in all three spatial directions over time, has transitioned from research to clinical practice, particularly for congenital heart disease and valvular pathology. It allows visualization of complex flow patterns (equis, vortices, wall shear stress) associated with conditions like aortic dilation, coarctation, or repaired tetralogy of Fallot, offering insights into disease progression and timing of intervention (Robinson et al., 2019).

In neuroimaging, 4D time-resolved MR angiography is standard for evaluating arteriovenous malformations (AVMs) and dural arteriovenous fistulas, precisely delineating feeding arteries, nidus, and draining veins with temporal resolution sufficient to appreciate hemodynamic alterations (Jiang et al., 2025). Dynamic contrast-enhanced (DCE) and dynamic susceptibility contrast (DSC) MRI provide 4D information on tissue perfusion and permeability, critical for brain tumor grading, differentiation of tumor recurrence from radiation necrosis, and assessment of stroke penumbra.

Body applications continue to expand, with 4D-MRI used for radiotherapy planning as a radiation-free alternative to 4D-CT, particularly advantageous for pediatric patients and for imaging soft-tissue tumors with poor CT contrast (Aljaafari et al., 2024). Dynamic pelvic floor MRI visualizes organ prolapse and functional disorders during straining and defecation, while dynamic MRI of the swallowing mechanism (MR fluoroscopy) assesses pharyngeal function without ionizing radiation.

4D Ultrasound

The real-time nature and portability of ultrasound have made 4D ultrasound particularly impactful in obstetric and cardiac point-of-care applications. In fetal medicine, 4D ultrasound with STIC technology allows acquisition of a volumetric cine loop of the fetal heart, which can be electronically dissected after the exam to obtain standardized diagnostic views regardless of fetal position. This has significantly improved the detection rate of congenital heart diseases in mid-trimester screening, especially in difficult imaging conditions (Zhang et al., 2024). Beyond anatomy, functional assessment includes quantification of ventricular volumes and ejection fraction, and emerging techniques measure myocardial deformation (strain) from the 4D dataset.

In cardiology, transthoracic and transesophageal 4D echocardiography provide a comprehensive assessment of cardiac chambers and valves. It enables accurate quantification of left ventricular volumes and ejection fraction without geometric assumptions, overcoming limitations of 2D methods. For valvular disease, 4D imaging allows precise planimetry of valve orifice area (particularly for aortic stenosis) and detailed assessment of mitral valve morphology in planning reparative surgery, with en face views of the valve from the atrial or ventricular perspective (Addetia et al., 2023). Intracardiac flow visualization using vector flow mapping or blood speckle tracking derived from 4D data provides insights into ventricular hemodynamics and efficiency.

Musculoskeletal applications include dynamic assessment of tendon motion, joint kinematics, and muscle contraction patterns. 4D ultrasound can capture the motion of the supraspinatus tendon under the acromion to diagnose impingement or visualize patellar tracking abnormalities in real-time during flexion-extension movements (Miller et al., 2024). In regional anesthesia, 4D ultrasound aids in needle guidance for complex nerve blocks by maintaining visualization of both needle and target structures in volumetric space during the procedure.

4D Nuclear Medicine and Hybrid Imaging

The combination of functional information from nuclear medicine with anatomical context from CT or MRI in hybrid systems is naturally extended into the temporal domain. 4D PET/CT is primarily employed for motion correction in thoracic and abdominal oncology. By synchronizing PET data acquisition with respiratory motion (via external monitors or data-driven methods), activity that is blurred over the breathing cycle in standard PET can be assigned to its correct anatomical location on the CT, improving lesion detection, quantification of standardized uptake values (SUV), and accuracy of radiation therapy targeting (Kerna et al., 2024). This is particularly crucial for radiotherapy planning in lung and liver cancers, where target volumes can be significantly reduced, sparing healthy tissue.

Beyond motion correction, dynamic PET acquisitions following tracer injection capture the pharmacokinetics of tracer uptake and washout, providing rich information about tissue metabolism, receptor density, and perfusion. Dynamic ^{18}F-FDG PET can distinguish malignant from inflammatory processes based on different uptake patterns over time, while dynamic neuroreceptor studies (e.g., for dopamine or amyloid) enable more accurate quantification of binding potential than static imaging (Tamaki et al., 2022). The recent advent of total-body PET scanners, with dramatically increased sensitivity, makes dynamic imaging with high temporal resolution feasible for the entire body, opening new possibilities for studying systemic physiological interactions (Table 1). Figure 1 illustrates the principal four-dimensional (4D) medical imaging modalities, including 4D ultrasound, 4D computed tomography (CT), 4D magnetic resonance imaging (MRI), and 4D positron emission tomography (PET).

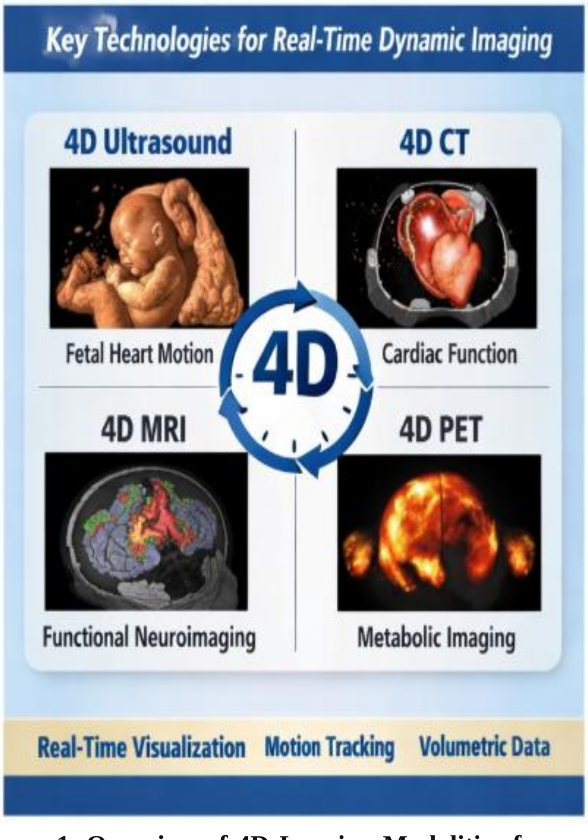

Figure 1. Overview of 4D Imaging Modalities for Dynamic Physiological Visualization

Table 1: Comparison of Major 4D Imaging Modalities

Modality	Temporal Resolution	Key Strengths	Primary Clinical Applications	Major Limitations
4D Ultrasound	20-50 volumes/sec	Real-time, portable, no ionizing radiation	Fetal cardiac screening, echocardiography, musculoskeletal dynamics	Limited field of view, operator dependence, poor penetration in obese patients
4D Computed Tomography	0.2-0.5 sec/volume	Excellent spatial resolution, fast acquisition	Radiotherapy planning, vascular dynamics, functional lung imaging	Ionizing radiation dose, poor soft-tissue contrast without contrast
4D Magnetic Resonance Imaging	0.03-0.05 sec/slice (cine), ~20 min/4D flow	Superior soft-tissue contrast, no radiation, multiple contrast mechanisms	Cardiac function & flow, dynamic pelvic floor, tumor perfusion	Long acquisition times, sensitivity to motion, contraindications (certain implants)
4D PET/CT	5-60 sec/frame (dynamic), respiratory phase bins	Quantitative molecular/ metabolic information	Motion-corrected oncology, pharmacokinetic modeling, total-body physiology	High radiation dose (PET+CT), low spatial resolution, long acquisition times

Quantitative Biomarkers and Radiomics

The transition from qualitative visualization to quantitative analysis represents a major frontier in 4D imaging. By capturing the complete temporal evolution of imaging signals, 4D techniques enable the extraction of novel biomarkers that characterize the dynamics of physiological and pathological processes. In cardiology, myocardial strain analysis—measuring the deformation of heart muscle during contraction—has emerged as a more sensitive indicator of systolic function than ejection fraction. While originally derived from speckle-tracking echocardiography, similar parameters can now be extracted from 4D MRI using tissue tagging or feature tracking, and even from 4D CT using deformable registration (Voigt & Cvijic, 2019). These strain patterns can identify regional dysfunction before global ejection fraction declines, crucial in the early detection of cardiotoxicity from chemotherapy or infiltrative diseases.

In oncology, the temporal dimension adds a new axis to radiomic analysis—the extraction of quantitative features from medical images. "Radiomics," typically applied to static 3D images, can be extended to "4D-radiomics" or "dynamic radiomics," capturing how texture, shape, and intensity features evolve (Forghani, 2020). For example, in DCE-MRI or PET, the shape of the time-activity curve (wash-in rate, peak intensity, wash-out pattern) provides information about tissue vascularity, permeability, and metabolism that may predict tumor grade, genetic mutations, or treatment response more accurately than single timepoint measurements. Early studies in lung cancer have shown that features describing tumor motion heterogeneity from 4D-CT are associated with worse outcomes, possibly reflecting more invasive behavior or local tissue constraints (Fave et al., 2017).

Neurological applications include quantification of cerebrospinal fluid (CSF) flow dynamics in the cerebral aqueduct using phase-contrast MRI, which is altered in normal pressure hydrocephalus and may help predict shunt responsiveness (Rivera-Rivera et al., 2024). Dynamic connectivity analysis from functional MRI (fMRI) data examines how connections between brain regions fluctuate over time, offering insights into brain states and disorders like epilepsy or Alzheimer's disease that may not be apparent from static connectivity measures (Table 2). Figure 2 demonstrates key clinical applications of 4D imaging across multiple medical specialties.

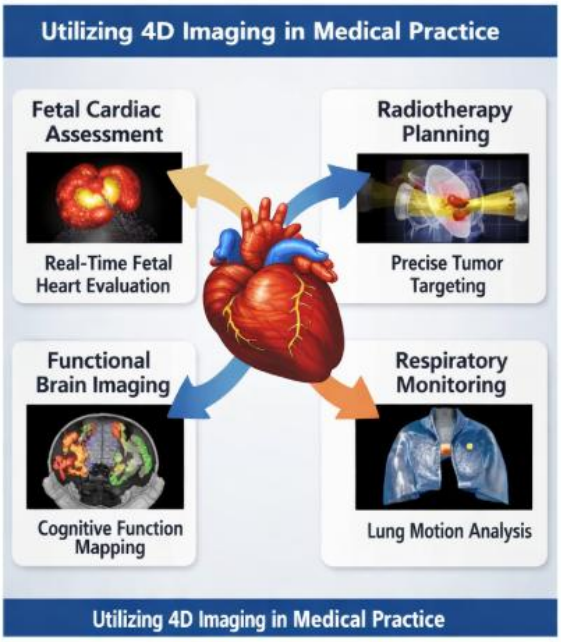

Figure 2. Clinical Applications of 4D Imaging in Contemporary Medical Practice

Table 2: Validated Clinical Applications of 4D Imaging Biomarkers

Biomarker	Modality	Clinical Application	Interpretation	Evidence Level
Left Ventricular Global Longitudinal Strain (GLS)	4D Echo, Cardiac MRI	Cardiotoxicity monitoring, early heart failure detection	Reduction >15% from baseline indicates significant dysfunction	Guideline-supported (ASE/EACVI)
Tumor Motion Amplitude & Heterogeneity	4D-CT	Radiotherapy planning for lung/liver cancers	>5 mm motion requires motion management; heterogeneity predicts worse local control	Established in clinical protocols
4D Flow Wall Shear Stress	4D Flow MRI	Aortic dilation risk stratification	Focal areas of low/oscillatory shear stress predict progression	Multiple large cohort studies
Dynamic PET Patlak Ki	Dynamic ^{18}F-FDG PET	Differentiation tumor vs. inflammation	High Ki indicates malignant hypermetabolism; inflammatory lesions show different kinetics	Validation in multicenter trials
CSF Flow Stroke Volume	Phase-contrast MRI	Normal pressure hydrocephalus diagnosis	>42 µL/cycle suggests shunt-responsive NPH	Meta-analysis supporting diagnostic accuracy

Interventional and Surgical Guidance

The real-time nature of some 4D imaging modalities, particularly ultrasound, has enabled transformative applications in image-guided interventions. In radiation therapy, 4D imaging is no longer confined to the planning stage. Many modern linear accelerators are equipped with on-board 4D cone-beam CT (CBCT) or respiratory-correlated kilovoltage imaging, allowing verification of tumor position immediately before or during treatment delivery (Grimbergen et al., 2023). Real-time tracking systems using implanted electromagnetic transponders or surface monitoring create a continuous 4D representation of tumor motion, enabling gated delivery or dynamic multileaf collimator tracking that follows the tumor's trajectory, maximizing dose to the target while minimizing exposure to surrounding organs-at-risk.

In minimally invasive surgery, the integration of pre-operative 4D imaging with intraoperative navigation systems creates dynamic roadmaps for the surgeon. For liver tumor ablation, pre-procedural 4D-CT or MRI depicting respiratory motion can be registered to intraoperative ultrasound, and the navigation system predicts the tumor's position in real-time based on the respiratory phase detected by external monitors (Zhang et al., 2015). This compensates for the liver's significant movement during breathing, improving targeting accuracy. Similarly, in cardiac electrophysiology procedures for arrhythmia ablation, systems that merge pre-acquired 4D cardiac CT or MRI with real-time electroanatomical mapping provide a detailed dynamic model of the heart chambers, aiding in catheter navigation and identification of critical structures.

Interventional radiology benefits from the fusion of live 2D fluoroscopy with pre-procedural 4D vascular datasets (from CTA or MRA). The system can overlay the dynamic vascular tree onto the live X-ray image, adjusting for respiratory motion and patient positioning, effectively providing roadmapping in multiple dimensions for complex embolization procedures or transjugular intrahepatic portosystemic shunt (TIPS) creation (Lin et al., 2022).

Challenges and Future Directions

Despite remarkable progress, the widespread clinical implementation of 4D imaging faces significant hurdles. The immense data burden—a single 4D cardiac MRI exam can exceed 10 GB—strains hospital networks, storage infrastructures, and picture archiving and communication systems (PACS) designed for 2D images (O'Connor et al., 2023). Efficient compression algorithms and cloud-based solutions are being developed, but data management remains a practical challenge. Standardization of acquisition protocols, post-processing methods, and reference values for quantitative parameters is lacking, hindering multi-center comparisons and large-scale research. Regulatory approval for quantitative biomarkers derived from 4D imaging as clinical endpoints requires robust validation studies that are often costly and time-consuming.

Future technological directions are poised to address many current limitations. Artificial intelligence (AI) and deep learning are revolutionizing every step of the 4D imaging pipeline. AI-based reconstruction can generate high-quality 4D images from vastly undersampled data, dramatically reducing acquisition times in MRI or radiation dose in CT (Hyun et al., 2018). Machine learning models can predict physiological motion patterns from partial data, enabling real-time adaptive systems. The integration of 4D imaging with other data streams—genomics, proteomics, clinical history—through multimodal AI analytics promises more holistic diagnostic and prognostic models.

Novel imaging hardware will further expand capabilities. Photon-counting CT detectors offer improved spatial resolution and spectral separation, enabling 4D imaging with material decomposition (e.g., simultaneous iodine and calcium mapping over time) (van der Bie et al., 2023). Ultra-high field (7T and above) MRI provides signal-to-noise gains that can be traded for higher spatial or temporal resolution in 4D acquisitions. Wearable and miniaturized ultrasound probes enabling continuous 4D monitoring represent a frontier in personalized longitudinal assessment.

Conclusion

The development and implementation of 4D imaging techniques represent a fundamental advancement in medical imaging, transforming our ability to visualize, quantify, and understand dynamic physiological processes. From capturing the intricate choreography of the fetal heart to mapping the complex hemodynamics of aortic flow, these technologies have moved beyond research curiosities to become essential tools in modern diagnostic and therapeutic medicine. The integration of the temporal dimension has unveiled a new layer of functional information, enabling more precise diagnoses, personalized treatment planning, and objective monitoring of therapeutic response.

The successful clinical translation of 4D imaging has been underpinned by parallel advances in acquisition hardware, reconstruction algorithms, computational analysis, and visualization platforms. Each modality—ultrasound, CT, MRI, and nuclear medicine—has followed its own evolutionary path, leveraging unique strengths to address specific clinical questions. The common thread is the enrichment of anatomical data with functional dynamics, providing a more complete representation of living systems.

Looking forward, the convergence of 4D imaging with artificial intelligence, novel detector technologies, and immersive visualization promises to further accelerate its impact. Challenges in data management, standardization, and validation must be systematically addressed through collaborative efforts across academia, industry, and clinical practice. As these barriers are overcome, 4D imaging will increasingly become the standard of care for assessing dynamic pathologies, fundamentally enhancing our ability to practice personalized, precision medicine tailored to the unique temporal characteristics of each patient's physiology and disease.

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