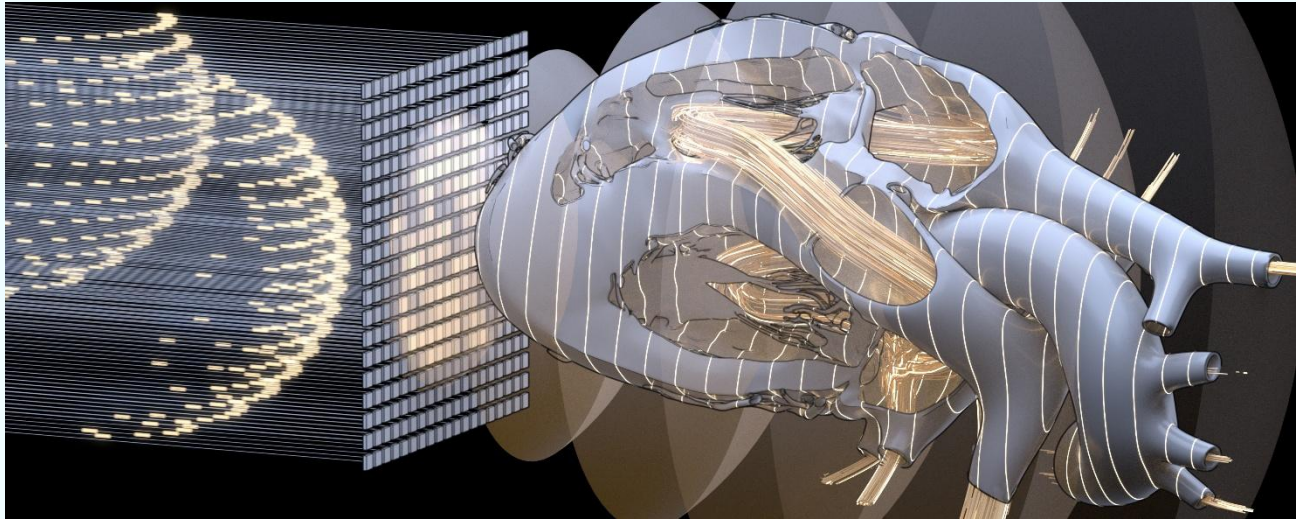


4D Ultrafast Ultrasound: the next revolution in biomedical imaging

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Abstract—Four-dimensional ultrafast ultrasound imaging is emerging as a major paradigm shift in biomedical imaging by enabling the direct visualization and quantification of dynamic physiological processes in three-dimensional space over time. This review provides a comprehensive overview of the principles, technological developments, and applications that underpin this rapidly evolving field. We first describe the foundations of volumetric ultrafast acquisition based on unfocused wave transmissions and coherent compounding, followed by key advances in volumetric beamforming, motion estimation, Doppler imaging, elastography, and ultrasound localization microscopy. Particular emphasis is placed on the hardware challenges associated with matrix array transducers, including channel count limitations, data throughput, and emerging solutions such as microbeamforming, sparse arrays, row-column addressing, and wearable probes. We further highlight the critical role of high-performance computing and artificial intelligence in enabling real-time processing and analysis of large volumetric datasets. Beyond acquisition and reconstruction, this review underscores the importance of advanced visualization and quantification strategies as essential tools for extracting meaningful information from complex 4D data. Applications ranging from in vitro validation to preclinical and early clinical studies in cardiovascular, neurovascular, and abdominal imaging demonstrate the unique capabilities of this modality. Finally, we discuss current limitations and future directions, emphasizing the need for scalable hardware, efficient data handling, and new conceptual frameworks to fully exploit the spatiotemporal richness of 4D ultrafast ultrasound.

Index Terms— 4D ultrafast ultrasound, volumetric imaging, matrix array transducers, Doppler imaging, ultrasound localization microscopy, elastography, functional ultrasound imaging, biomedical imaging

I. INTRODUCTION

PIONEERED in the late 1970s [1], the discovery of high frame rate imaging in ultrasound also referred as ultrafast

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Highlights

- **Introduces 4D ultrafast ultrasound as a paradigm shift enabling direct volumetric observation of fast physiological dynamics.**
- **Demonstrates multimodal capabilities including volumetric Doppler, elastography, and microvascular imaging from preclinical to clinical studies.**
- **Highlights the critical role of hardware innovation, visualization, and AI for translating 4D ultrasound into practical biomedical use.**

ultrasound marked a turning point in the history of medical imaging [2], [3], [4], [5]. By enabling frame rates several orders of magnitude higher than conventional ultrasound, it allowed researchers and clinicians to visualize rapid physiological phenomena in vivo with unprecedented detail, from shear wave propagation [6] and transient blood flow dynamics [7] to the tracking of individual microbubbles [8]. What initially seemed a technical advance soon revealed itself as a conceptual breakthrough: ultrafast imaging at very high frame rate was not merely a faster version of conventional ultrasound, but a fundamentally new way of observing and quantifying dynamic biological processes in slow motion. Applications such as ultrafast Doppler [7], pulse wave [9], shear wave elastography (SWE) [6], electromechanical wave [10], functional ultrasound imaging (fUS or fUSi) [11], and ultrasound localization microscopy (ULM) [8] emerged sequentially, as the community explored new possibilities and progressively translated these tools into clinical and industrial settings.

Yet, even with these advances, a critical limitation remained. Anatomy is inherently three-dimensional (3D), and the most natural and comprehensive way to evaluate biological structures is therefore through 3D imaging. Physiological phenomena themselves occur in three dimensions. Natural shear wave propagation in the heart, the complex fiber architecture of skeletal muscle, the intricate vascular flow dynamics, and the fine microvascular networks of organs cannot be fully characterized within a two-dimensional plane. More importantly, functional processes such as cerebral activation or rapidly evolving cardiac and vascular dynamics cannot simply be reconstructed by stitching sequential two-dimensional (2D) views, as the underlying biological state may evolve between acquisitions. Restricting imaging to 2D, inevitably discards crucial spatial information, leaving aspects of dynamic biology invisible despite high temporal resolution.

Earlier generations of 3D ultrasound could not overcome this limitation, relying on mechanically swept transducers that produced only a few volumes per second [12]. The introduction of matrix array transducers has enabled real time volumetric imaging in clinical settings, often also referred to as 4D imaging, particularly in cardiac applications. These systems achieve volumetric frame rates on the order of tens of volumes per second, depending on field of view and beam density. While this represents a major advance toward dynamic 3D imaging, they remain constrained by sequential line-by-line transmission and therefore do not reach the very high volumetric frame rates required to capture rapidly evolving wave phenomena, transient flow dynamics, or fast neurovascular events, even with ECG gating.

In contrast, by capturing the temporal evolution of structures in three dimensions, 4D ultrafast ultrasound extends high-frame rate imaging into the volumetric domain. The terms 4D

ultrafast, volumetric ultrafast, high-frame-rate volumetric, and 3D ultrafast ultrasound are often used interchangeably in the literature to describe the acquisition of three-dimensional spatial data at very high volumetric frame rates. In this review, we adopt the term 4D ultrafast ultrasound to emphasize the dual role of time. First, a fast time scale corresponds to ultrafast volumetric acquisition, typically hundreds of volumes per second or more, enabling the capture of rapid physical phenomena within each 3D dataset, such as shear wave propagation, flow motion, or microbubble trajectories, which can then be visualized in slow motion. Second, a slow time scale corresponds to the integration of these ultrafast volumes in applications such as SWE, ULM, or Doppler imaging, where maps can be displayed at lower frame rates.

The development of 4D ultrafast ultrasound has been inseparable from advances in hardware. The need for each piezoelectric element to be connected to dedicated acquisition electronics poses a major engineering challenge. Efforts range from building high-density matrix array probes with thousands of elements for improved image quality and field of view, to the design of low-channel-count solutions that are more suited for clinical and industrial translation. Innovations in probe design, electronics, and multiplexing strategies remain key challenges for the community. Equally critical are software and post-processing methods to handle the massive data streams generated by 4D ultrafast acquisitions. Here, progress has been accelerated by advances in the video game industry that led to the widespread availability of high-performance Graphics Processing Units (GPUs). More recently, artificial intelligence (AI) has emerged as a powerful enabler, offering strategies to accelerate reconstruction [13], [14], [15], enhance image quality [16], [17], and even extract new forms of information from the data [18], [19]. Image display and visualization is also crucial, as it typically precedes discovery and novel tools will be critical for transforming raw volumetric data into clinically and scientifically meaningful insights.

In this review, we first explore the fundamental principles of 4D ultrafast ultrasound imaging and the post-processing strategies that transform raw volumetric data into meaningful data. We then highlight recent hardware innovations that make high-speed, high-resolution volumetric imaging possible, and finally examine in vitro, preclinical, and clinical applications across multiple organs, illustrating both early achievements and the vast potential for discovery.

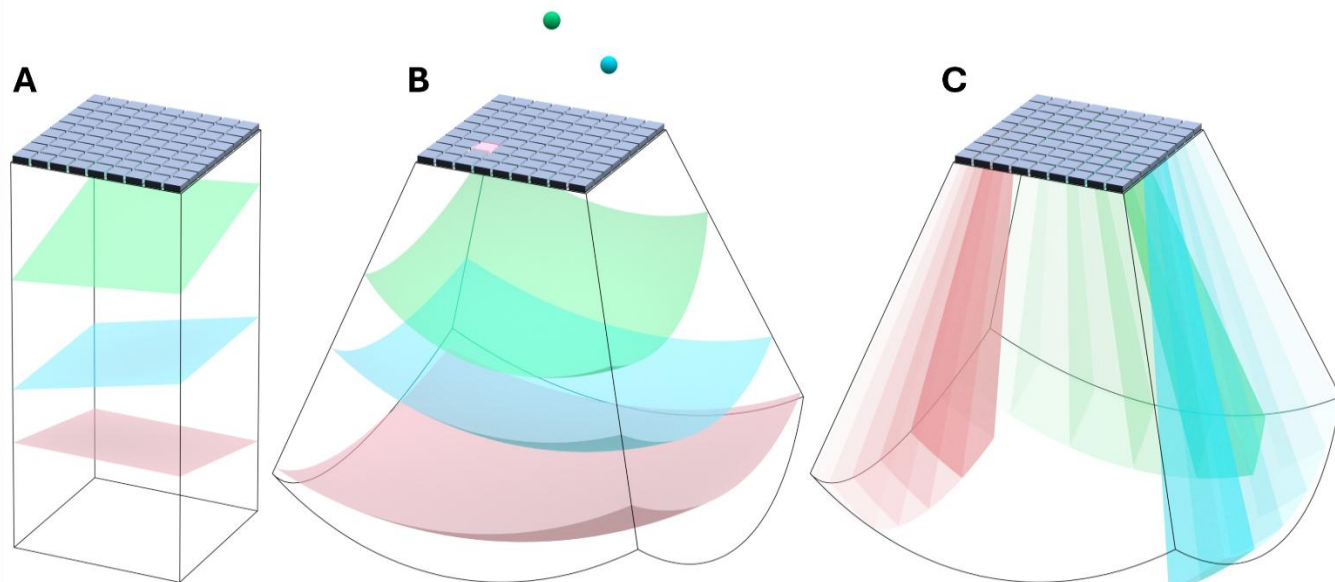


Figure 1: **Main ways to perform 4D ultrafast ultrasound.** Plane waves with tilted angles (A), diverging waves emitted from virtual source or single element (sub-synthetic aperture imaging) (B) or wide-beams (C) can be implemented to increase volume rate.

II. BASIC PRINCIPLES

A. Foundations of Real-Time 3D Imaging: Enabling 4D Ultrafast Ultrasound

Several pioneering studies performed in the 90's laid the groundwork for modern 4D ultrafast ultrasound by establishing the theoretical and practical foundations of high frame rate 4D imaging. Von Ramm and Smith (1990) [20] proposed the concept of Explososcan [21] based on a parallel processing approach. Jian-Yu Lu (1997) [2] proposed to achieve high frame rate 4D imaging by using plane wave transmission with limited diffraction-beam-based reconstruction in the frequency domain. Lockwood et al. (1998) [22] demonstrated that mechanically translating a linear array with sparse synthetic aperture beamforming could achieve volumetric acquisitions at unprecedented frame rates; in the second study of the same group [23], they provided a rigorous theoretical framework for synthetic aperture beamforming in 3D. Together, these works underscored strategies to balance spatial resolution, field of view, and acquisition speed, i.e., the key principles that enable 4D ultrafast imaging, where full volumetric datasets are captured at hundreds to thousands of volumes per second.

B. Transmission of unfocused waves

Conventional 3D ultrasound volumes are typically formed using line-by-line focused transmissions [12]. This strategy yields high-quality volumetric images, but at the cost of very low frame rates. Such approaches are widely implemented in current clinical ultrasound systems, for instance to measure cavity volumes [24] or to quantify regurgitant flow across the aortic valve in cardiac applications [25]. Similar to 2D ultrafast imaging, 4D ultrafast ultrasound relies on the transmission of unfocused waves [2], [3], [26] (Figure 1 A, B) or wide-beams [27] (Figure 1 C). In this case, waves emitted from a 2D matrix array insonify a volume of interest in a single transmit event. This drastically increases the achievable volume rate up to tens of thousands of volumes per second [26].

In practice, however, the contrast and lateral resolution achieved by the transmission of unfocused beams are usually considered insufficient and must be improved. To achieve this, coherent compounding is performed by coherently summing echoes from a sequence of transmissions [26]. These transmissions can be conceptualized as originating from a virtual source placed behind the probe: small lateral shifts in source position correspond to angular tilts of the transmitted wave. If the virtual source is positioned at infinity, the emitted waves are plane waves. Conversely, if the virtual source is located close to the aperture, the array generates diverging waves, where the source position directly influences resolution and the formation of grating lobes. For coherent compounding, the transmit parameters can therefore be varied through the 3D position of the virtual source, corresponding to different steering angles and/or wavefront curvatures. This framework allows considerable flexibility, with transmission schemes optimized according to the target application.

The number of compounded transmissions therefore represents a direct trade-off between image quality and volume rate, for both plane- and diverging-wave imaging. For example, at 15 cm depth, the round-trip propagation time limits the pulse repetition frequency to approximately 5,000 transmissions/s. Compounding 10 or 100 transmissions would therefore yield volume rates of approximately 500 or 50 volumes/s, respectively. While a few transmissions may be sufficient when temporal resolution is prioritized, more transmissions can be used when higher image quality is required, for instance for cardiac strain imaging or speckle tracking.

C. Transmit strategies

1) Transmit Frequency

The choice of transmit frequency represents a fundamental trade-off between spatial resolution and penetration depth. Higher frequencies provide improved spatial resolution but suffer from increased tissue attenuation, whereas lower frequencies enable deeper imaging at the expense of resolution. In 2D arrays, frequency also constrains element dimensions and



pitch, with important consequences for channel count and grating-lobe formation as well as matrix array size. The optimal transmit frequency therefore strongly depends on the targeted organ, imaging depth, and array architecture.

2) Coded Excitation

Coded excitation can increase the transmitted energy without a corresponding increase in peak acoustic pressure by transmitting longer encoded waveforms followed by pulse compression on receive. This approach can improve sensitivity and penetration [28], [29], which is particularly attractive for 4D ultrafast imaging where limited transmit focusing can reduce signal-to-noise ratio. However, pulse compression may introduce range sidelobes and requires additional processing, resulting in trade-offs between sensitivity, image quality, and sequence complexity. Coded excitation can also be used to transmit multiple beams simultaneously, each encoded with a distinct waveform, thereby increasing the frame rate while maintaining acceptable image quality.

3) Tissue Harmonic imaging

Tissue harmonic imaging exploits nonlinear propagation to reconstruct images from harmonic frequency components generated within tissue. It can improve image contrast and reduce near-field clutter and sidelobe artifacts and is particularly important in challenging patients and in cardiac imaging [30]. However, harmonic generation depends on the acoustic pressure reached during propagation. Broad unfocused or diverging-wave transmissions used in ultrafast imaging distribute acoustic energy over a large volume and may therefore generate insufficient harmonic content, particularly at depth. Importantly, this nonlinear harmonic generation cannot be recovered retrospectively through coherent compounding or synthetic transmit focusing. Maintaining some degree of physical transmit focusing, for example through elevation focusing or broad transmissions generated using a distant virtual focus, may therefore provide a compromise between ultrafast volumetric coverage and sufficient harmonic generation. This trade-off is particularly relevant for cardiac 4D ultrafast imaging.

D. Data transfer and processing

The feasibility and impact of 4D ultrafast ultrasound are intimately tied to advances in computational power, algorithm design, and visualization tools. Volumetric acquisitions at high frame rates generate massive data streams, often at several gigabytes per second, necessitating optimized pipelines for beamforming, motion estimation, clutter rejection, and microbubble tracking. Beyond image formation, meaningful interpretation requires innovative visualization strategies and dedicated quantification methods to extract physiologically relevant parameters from the 4D datasets.

1) Volumetric Beamforming

The most direct approach for volumetric reconstruction is the extension of delay-and-sum (DAS) beamforming [31] to volumetric acquisitions [26]. Reconstructing thousands of volumes per second is computationally intensive, and GPU-based parallelization has been critical in enabling fast performance [26], [32], [33]. Optimization of beamforming implementation is highly recommended to reach a reasonable computation time. Volumetric beamforming has long been limited to several volumes per second, but optimized

implementation on modern GPUs can now provide real time volumetric beamforming at several hundreds of volume/s [34], [35]. To further accelerate reconstruction, advanced strategies such as sparse convolutional beamforming [36], Fourier methods [2], [3], [37], [38], [39], dual stage beamforming for Row Column Array (RCA) transducers [40], and adaptive weight-based approaches [41] have been introduced. In parallel, efforts to improve image quality and optimize beamforming have focused on exploiting spatial coherence, either through coherence-based weighting or adaptive apodization [41], [42], [43], or using multiply-and-sum [44], providing higher contrast and resolution without prohibitive computational cost. XDoppler [45], RC-FMAS [46], or spatiotemporal similarity weighting (St-SW) [47]. An interesting approach was recently proposed using diffusion models to increase spatial and temporal resolution [48].

2) 3D Motion and Doppler processing

Extending 2D methods to three dimensions allows estimation of axial tissue velocity across entire volumes. Volume-to-volume cross-correlation using Doppler estimators can compute displacements and velocities along the axial dimension, enabling the assessment of transient mechanical events, such as shear [26] or natural waves [49], and the computation of incremental axial strain or strain rate maps [50]. Other methods to assess 3D Doppler flow include vector Doppler, transverse oscillations [51], [52], and speckle tracking [27], [53], [54]. Based on motion estimation, motion correction can also be added [55].

For blood-flow imaging, separation of tissue and blood signals represents a critical processing step. Singular value decomposition (SVD), widely used for clutter filtering in 2D ultrafast Doppler, was extended to volumetric datasets with only minor adaptations [56], [57]. However, performing SVD on blocks of hundreds of large volumes substantially increases computational and memory requirements. Although GPU implementations have considerably accelerated this processing [58], memory transfer and computational load remain important challenges, and real-time implementations require efficient approximate algorithms [59]. Following clutter filtering, 3D power Doppler can be obtained by integrating the Doppler signal energy within each voxel, yielding volumetric maps of blood volume or flow intensity [56]. Flow-optimized strategies have also been introduced for RCA probes, including XDoppler [45], which exploits directional filtering and multi-angle processing to improve sensitivity to multidirectional and tortuous flows while reducing blooming artifacts.

3) 4D Shear Wave Elastography processing

4D ultrafast acquisitions enable shear-wave propagation to be captured throughout a volume rather than within a single imaging plane. Volumetric motion estimation is first used to recover tissue displacement or velocity induced by the propagating shear wave [26]. The resulting 3D wave field can then be analyzed to estimate local shear-wave velocity and derive volumetric stiffness maps [176]. Beyond isotropic stiffness estimation, 4D acquisitions can also characterize direction-dependent wave propagation and provide access to mechanical anisotropy and local elastic tensor properties [60]. This is particularly relevant in structurally anisotropic tissues such as skeletal and cardiac muscle.

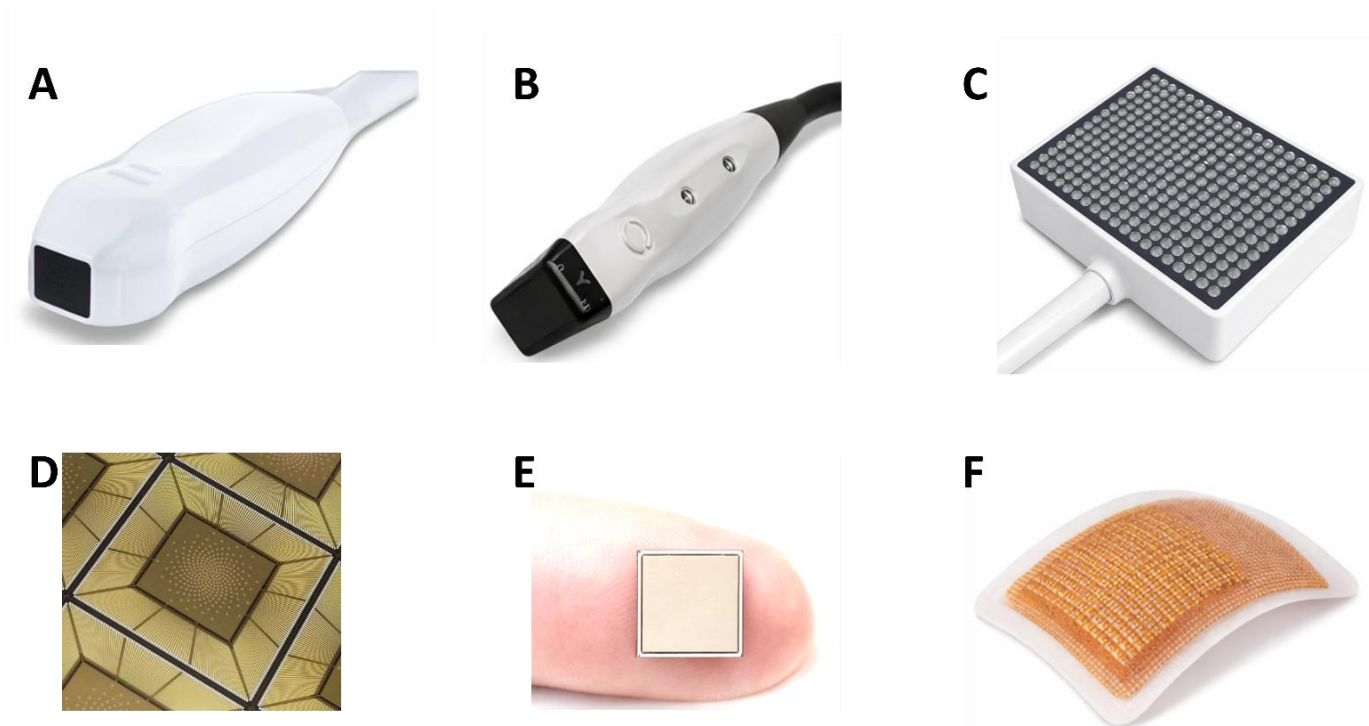


Figure 2: Representative matrix array transducer architectures for 4D ultrafast ultrasound imaging. Illustrated are (A) a fully populated matrix array with 1,024 individually addressed elements (Vernon, France), and several alternative designs aimed at reducing channel count and data throughput: (B) microbeamformed matrix arrays (Odelft, Netherlands), (C) multi-lens architectures (Haidour et al, 2025), (D) sparse arrays (CMUT 256-element density-tapered spiral array, courtesy of A. Savoia, University Roma TRE, Italy), (E) row-column addressed arrays (Blancquart et al, 2025) and (F) wearable patch-based matrix arrays.

4) 4D Functional Ultrasound processing

4D functional ultrasound imaging extends ultrafast power Doppler to volumetric mapping of cerebral hemodynamic activity. After clutter filtering, the power Doppler signal provides a surrogate of cerebral blood volume whose temporal variations can be analyzed throughout the volume [28]. These volumetric time series can subsequently be correlated with stimuli, behavior, or spontaneous activity to generate 3D activation and functional connectivity maps. By combining whole-brain coverage with sub-second temporal resolution, 4D fUSi enables the investigation of brain-wide functional networks and the propagation of dynamic events such as epileptiform activity [28].

5) 3D ULM post-processing

The transition from 2D to 3D ULM was demonstrated [61] without introducing fundamental methodological barriers. The pipeline, including microbubble localization, tracking, and volumetric reconstruction, builds on established 2D principles, though it requires increased and intensive computational resources and must be adapted to the probe geometries. 3D ULM is arguably the most computationally demanding, owing to the combination of high volumetric frame rates, large channel counts inherent to matrix arrays, and the need for sub-wavelength localization and tracking over extended acquisition times. The simultaneous requirements in data throughput, memory footprint, and reconstruction time considerably exceed those of other 4D ultrafast modalities such as volumetric Doppler or elastography. While this core pipeline is now well-established and published [62], further optimization, particularly in processing time, scalability and hardware efficiency, remains necessary to fully realize its potential for

widespread application in other fields. In this context, approaches aimed at reducing the number of receive channels, based on RCA probes, sparse arrays, or multi-lens architectures, represent promising avenues to alleviate data throughput and storage constraints without fundamentally altering the 4D ULM workflow.

6) Visualization Tools and quantification strategies

Visualizing 4D ultrafast ultrasound data (rapidly changing 3D volumes acquired at hundreds to thousands of volumes per second) poses challenges that go far beyond conventional volume rendering. Unlike static 3D datasets, 4D ultrafast acquisitions combine high spatial dimensionality, high temporal resolution, and often vectorial information (e.g., velocity fields, displacement fields, or microbubble trajectories). Therefore, effective visualization requires tools capable of handling large data throughput, interactive rendering of time-resolved volumes, vector-field representation, and scalable quantitative interrogation without collapsing the data into oversimplified projections.

Standard multiplanar reconstructions and basic volume rendering are insufficient to capture fast volumetric dynamics or complex flow topology. As a result, a range of visualization environments has been adopted or specifically developed within the community. Commercial and academic platforms such as VolumeViewer (MATLAB), Amira used by [26], 3D slicer used by [63] have been used for volumetric rendering and segmentation. In parallel, several laboratories have developed custom visualization pipelines, enabling tailored rendering of 4D data.

More recently, visual effects engines such as Houdini have been leveraged to generate interactive 2D and 3D renderings of



complex ultrasound datasets [64], demonstrating the potential of borrowing tools from computer graphics and cinematic simulation to explore dense spatiotemporal data. These environments support advanced representations such as streamlines, pathlines, and vorticity-based color encoding for 3D Doppler, as well as graph-based vascular reconstructions and network analysis for ULM [65]. Such approaches have enabled intuitive visualization of 4D cerebrovascular dynamics, including complex vascular territories such as the circle of Willis in primates [66].

Beyond screen-based rendering, emerging augmented and immersive visualization strategies offer additional perspectives for interacting with volumetric ultrafast data. Augmented reality and virtual reality environments allow depth perception, interactive clipping, and spatial navigation within dense vascular or myocardial datasets, potentially facilitating both research interpretation and clinical translation [67]. 4D ultrafast ultrasound also provides unique opportunities for quantitative assessment across scales. Volumetric flow rates, velocity vector fields, and vorticity maps can be extracted from 4D Doppler data [68], while graph-based vascular metrics can characterize complex microvascular networks reconstructed using ULM [65]. In the myocardium, volumetric backscatter tensor imaging combined with fiber-tracking algorithms can reveal myocardial fiber orientation in vivo [69].

Together, these developments illustrate that advanced visualization is not merely a display problem but a methodological necessity. When quantitative outputs consist of time-resolved vector fields, tensors, connectivity graphs, or whole-brain functional volumes, appropriate rendering, interaction, and dimensionality-reduction strategies become essential to avoid collapsing intrinsically 4D information into static or oversimplified 2D representations.

7) AI-based tools for 4D Ultrafast Ultrasound analysis

The large amount and high dimensionality of data generated by 4D ultrafast ultrasound create specific challenges in reconstruction, processing, and interpretation. AI-based approaches could help reduce computational burden, improve volumetric image reconstruction and quality, and extract relevant information from complex spatiotemporal datasets. Deep learning has already been investigated for several ultrasound processing tasks, including beamforming [70], [71], [72], [73], image reconstruction and enhancement [74], [75] and could naturally be extended to volumetric ultrafast datasets. Beyond image formation, machine-learning approaches can provide dimensionality reduction in ULM [76], [77] and identify spatiotemporal patterns within large 4D datasets, as already explored in functional ultrasound neuroimaging [78], [79]. AI therefore represents a promising tool for handling the increasing computational and analytical complexity of 4D ultrafast ultrasound, although its application specifically to 4D imaging remains an emerging field [80], [81].

III. HARDWARE INNOVATIONS IN 4D ULTRAFAST ULTRASOUND

A. Historical foundations: Matrix arrays for commercial system

A comprehensive review of different strategies adopted to move from 2D to 4D ultrasound was published recently [82]. The earliest systems relied on mechanically sweeping a 1D array to reconstruct volumes, producing high-quality static images but at the cost of very low volume rates and high motion artifacts. Their use was limited to applications such as obstetrics or anatomical assessment. Freehand scanning with position sensors offered more flexibility, but reproducibility and temporal resolution remained poor. A decisive step came in the 1990s with the introduction of dedicated 2D matrix arrays, pioneered by Smith and colleagues at Duke University [83], [84], [85]. Building sensitive, high-performance matrices was challenging, but the real bottleneck lay in the electronics: a fully populated 128x128 element array involves more than 16,000 individual piezoelectric elements, each wired to its own channel. The resulting bulk of coaxial cabling and computing hardware made such systems extremely complex and cost-prohibitive. An additional constraint arises for high-frequency probes (e.g., 15 MHz), where the piezoelectric elements must be miniaturized. As their dimensions shrink, their electrical impedance increases significantly, making impedance matching more difficult. This leads to reduced energy transfer efficiency and ultimately degrades element sensitivity.

To address this, the idea of performing a first stage of beamforming inside the probe, often referred to as microbeamforming or sub-array beamforming, emerged in the late 1990s [86], and reached clinical translation around 2010 with commercial systems such as the Philips X6-1 xMatrix, GE 4Vc, and Siemens 4Z1c. In this approach, the matrix is divided into sub-apertures controlled by an Application-Specific Integrated Circuit (ASIC) integrated directly into the probe head. These chips carry out a preliminary beamforming step locally, reducing the number of signals that need to be digitized. Microbeamforming made high-element 2D arrays clinically feasible, bringing real-time 3D imaging (or 4D imaging) into routine practice. Its main limitation, however, lies in the architectural trade-off between channel reduction and beamforming flexibility. In particular, as highlighted in the literature [87], plane-wave or diverging-wave compounding becomes challenging due to the mismatch in receive focusing between the subaperture beamformer and the global beamformer. Maintaining coherence frequently requires limiting the transmit angle, which constrains the wide-angle insonification essential for ultrafast imaging. Although, in principle, most microbeamforming arrays may allow access to the raw element signals, this typically requires multiple transmissions (as many as the elements within each subarray) because the underlying channel data must be reconstructed sequentially. In practice, however, this possibility remains largely inaccessible to researchers. Commercial ultrasound systems typically rely on closed, proprietary architectures, and detailed information on how these devices implement microbeamforming or manage internal data routing is rarely disclosed. As a result, the mechanisms governing raw-channel

access—and the associated data-access limitations—are effectively hidden from users.

B. Matrix arrays for 4D ultrafast ultrasound

After first attempts based on linear array probes, a major breakthrough for 4D ultrafast ultrasound came with the availability of a commercial matrix array probe [26], [88]. This probe, manufactured by Vermon (Vernon, Tours, France) comprised 1,024 elements arranged in a 32×32 grid, roughly half the element count of a conventional 64-element cardiac phased array per dimension. The first-generation probe operated at a central frequency of 3 MHz [26], while a second version, later developed at 8 MHz [28], enabled higher-resolution volumetric imaging.

This probe (i.e. Figure 2 A) presented a formidable engineering challenge: at the time, commercial research ultrasound systems could handle only 256 independent channels. The first large-scale experimental system, SARUS, was developed in 2013 for synthetic aperture imaging, addressing channel-count limitations through a modular architecture composed of 64 boards with 16 channels each [89]. In 2014, the Physics for Medicine Paris group further overcame hardware constraints by synchronizing four independent 256-channel ultrafast ultrasound systems, effectively creating a 1,024-channel platform capable of true volumetric ultrafast imaging in vivo [26]. In parallel, other research groups have explored strategies to increase channel count to drive large probes [90], [91]. Nowadays, several companies (Verasonics, OpenSonics and others) offer integrated hardware solutions capable of driving such large arrays, representing a significant step toward broader accessibility of high-channel-count systems for both research and translational applications. However, this scaling strategy faces fundamental practical limits. Increasing the channel count beyond ~1,000–2,000 channels rapidly leads to prohibitive system complexity, cost, power consumption, and data throughput requirements. As a result, future developments may rely on more efficient front-end architectures—such as multiplexing schemes or microbeamforming (Figure 2 B)—to reduce the number of independent channels while maintaining acceptable imaging performance. To date, however, no system has exceeded the 1,024-channel limit, primarily due to the technical complexity, cost, power consumption, and physical bulk associated with scaling beyond this threshold. Probe integration and cabling density also become major constraints, particularly for matrix arrays where element pitch must remain small while maintaining manageable interconnect routing and thermal dissipation. These hardware limitations extend beyond the front-end electronics to data transfer bandwidth and real-time processing requirements, which scale unfavorably with channel count. Nevertheless, given the rapid pace of innovation in probe design, electronics, and data handling, it is reasonable to anticipate that systems with even higher channel counts or alternative architectures achieving equivalent spatial sampling, will emerge soon.

C. Electronic strategies to reduce the number of channels and innovations in probe technology

4D ultrafast ultrasound has followed a similar path as commercial 3D/4D imaging in seeking to reduce the number of

active hardware channels without compromising performance. As said above, an effective approach is the integration of custom microbeamforming ASICs, designed specifically for matrix arrays. These chips locally combine signals from groups of elements, enabling control of arrays ranging from 960 [92], 1,024 [87], [93], [27], 3,072 elements [94], [95], up to impressive 65,000 elements for high-end commercial systems (Philips XL14-3 xMATRIX). In parallel, capacitive micromachined ultrasonic transducer (CMUT) technologies have emerged as an alternative route toward large-scale 2D arrays with integrated front-end electronics. Recent CMUT-based implementations demonstrate tight co-integration of transducer elements and ASIC beamforming electronics, enabling high channel-count architectures with improved scalability and reduced interconnect complexity [96], [97]. Such approaches are particularly attractive for 4D ultrafast ultrasound, where minimizing cabling and power consumption is critical when pushing toward very large aperture sizes and volumetric frame rates. However, microbeamforming inherently performs partial receive beamforming within sub-apertures prior to digitization and transmission to the backend. This architecture limits the implementation of pixel-oriented beamforming and full synthetic aperture reconstruction, which are central to coherent compounding strategies in ultrafast imaging. Moreover, the increased effective element pitch can introduce receive grating lobes, particularly at large steering angles [87], [98]. While microbeamforming remains highly efficient for conventional focused imaging, it can therefore constrain the full potential of ultrafast 4D approaches that rely on flexible, element-wise delay-and-sum reconstruction.

Another complementary strategy is electronic multiplexing, which allows a large number of elements to be driven using a smaller number of channels. For instance, methods have been demonstrated to drive a 1,024-element array with only 256 channels [99], [100], [101], [102], [103], [104], [105], and arrays exceeding 3,000 elements using 1,024 channels [106]. These approaches effectively “virtualize” the channel count, balancing frame rate, image quality, system complexity, and cost. However, multiplexing requires switching between sub-apertures or element groups, which can markedly reduce volumetric frame rate. This effect is amplified in coherent compounding, where multiple beams per volume necessitate repeated switching cycles, multiplying temporal delays. While multiplexing reduces hardware complexity and enables large apertures, it can limit the effective volume rate in ultrafast 4D imaging, especially when many beams are needed to preserve image quality and contrast.

Another dimension of innovation to reduce ultrasound device complexity lies in probe design. The demand for 4D ultrafast imaging, combined with the burden of probe complexity and the high cost and cumbersomeness of hardware, has pushed researchers to rethink matrix arrays, proposing new strategies rooted both in physical concepts and technological breakthroughs. In this context, our review does not restrict itself strictly to matrix probes already applied in 4D ultrafast imaging, but also considers developments in matrix probes with lower volume rates as they can be adapted in the future.

One strategy is the use of sparse arrays (Figure 2 D), first introduced in the 1990s [107], [108], [109], [110] and revisited in several recent applications [111], [112], [113], [53], [114], [115], [116], [117], [43], [118], [119], [120], [121]. A sparse array consists of a sparse distribution of elements over a 2-D aperture. By distributing these elements in random or aperiodic patterns, grating lobes can be mitigated. This design substantially reduces the number of active channels, hardware complexity, and cost. In practice, this can be achieved either by selecting an optimized 256-element subset from a 1,024-element matrix [122] or by fabricating dedicated sparse probes that enlarge the field of view while keeping the channel count limited [123]. The main trade-off lies in reduced transmit energy, receive sensitivity and image contrast compared with fully sampled arrays, but these approaches remain highly attractive for enabling practical 4D ultrafast systems. A promising concept to increase transmit energy and sensitivity in receive is the use of acoustic lenses in front of large elements [124], [125] (Figure 2 C). Diverging lenses can preserve both high energy and low directivity required for wide volumetric coverage at ultrafast volume rate. These large elements may be arranged either uniformly [126] or with randomized distributions [127], [128], providing probe design flexibility. Both sparse arrays and large-element/lens approaches reduce hardware complexity and channel count, but the larger effective element pitch increases grating lobes limiting ultrafast 4D imaging performance. AI-based approaches have also been proposed to mitigate the limitations of sparse arrays. Yoon et al. used a CNN to produce interpolated RF signals from sub-sampled RF data [13], [129]. In another study, end-to-end image reconstruction from sub-sampled raw data was achieved using deep learning [130]. Mamistalov et al used an encoder-decoder architecture to produce high quality images from sub-Nyquist channel data using minimum-variance beamformed data as a reference. With advances in the field of deep learning, sparsity or under-sampling of ultrasound data can be expected to become less of a limitation.

Another innovative way is using encoding aperture masks to distort the ultrasound wavefront and reconstruct volumes via matrix inversion [131]. This concept was developed for matrix arrays [132] and called computational ultrasound imaging (cUSi). It consists in attaching a plastic distortion mask to a coarse matrix probe, scrambling the transmit and receive fields to increase k -space sampling. This improves lateral resolution, though it increases side lobes. Instead of complex hardware, cUSi relies on model-based reconstruction, calibrated with a one-time measurement of the system's volumetric impulse response. cUSi's potential was demonstrated by imaging brain hemodynamics in mice, resolving microvasculature and flow dynamics. Though challenges like side lobes, sensitivity and effective Doppler volume rate persist, this approach could shift ultrasound imaging toward computationally efficient, low-cost, increased aperture size and wearable arrays.

One very promising alternative is the use of RCAs [133], [134], [135], [136], [137] also referred as Top-orthogonal-to-bottom-electrode [138], [139]. RCA probes are built from orthogonal rows and columns of elongated elements (Figure 2 E). By alternatively transmitting along the rows and receiving along the columns, an effective "virtual element" is created at

their intersection. This design drastically reduces the required number of independent channels, from N^2 for a fully addressed $N \times N$ matrix down to only $2N$. RCA architectures provide several advantages: they simplify probe fabrication, reduce hardware complexity, and are inherently compatible with large apertures, making them well-suited for wide-field volumetric assessment. With minimal on-probe microelectronics, these probes tolerate high-voltage excitation and are highly effective for acoustic radiation force transmission and shear wave elastography. Their large acoustic aperture further enhances this capability [140]. Despite high grating lobes and field of view limitations, RCAs have shown remarkable promise in vitro [42], [51], [138], [141], [142], [143], [144], [145], [146], [147], in preclinical studies at high frequency [148], [149], [150], [151], [152], [153], low frequency [150], [154], [155], [156], and in humans [157], [158], [140], [159], [160], [46], offering a practical balance between performance, scalability, and cost. Their combination with ultrafast imaging strategies such as synthetic aperture [136], orthogonal plane waves compounding [157], XDoppler (Bertolo et al 2021) or others opens the way toward portable and clinically viable 4D ultrafast ultrasound systems and even miniaturized device for embedded sensors as they are inherently well adapted for implementation on CMUT masks [160], [161], [162]. Researchers have been looking into ways to increase the field of view beside the probe aperture using curved arrays [163] or diverging lens [146], [164], [165] and using CMUT or electrostrictive piezoelectric switching bias to selectively activate rows and columns [142] to improve the focusing RCA capabilities with hybrid sequences.

Another promising and complementary approach is the development of conformal patch arrays for volumetric monitoring [166], [167] (Figure 2 F). Here, a soft, wearable patch is combined with a 2D matrix array. By employing diverging-wave transmissions and optimized acoustic coupling, such device enables high-frame-rate volumetric cerebral blood flow imaging through the skull, while maintaining patient comfort and stability for extended monitoring sessions. This work illustrates how innovative probe geometries and integration strategies can overcome the limitations of rigid or cumbersome arrays, opening the door to practical, real-time 4D ultrafast ultrasound applications in challenging clinical contexts such as brain and cardiac monitoring.

In addition to matrix arrays developed for external volumetric imaging, miniaturized 2D arrays have been developed for intracardiac and intravascular applications. Catheter-based 2D piezoelectric arrays were demonstrated early for real-time three-dimensional intracardiac echocardiography, enabling volumetric imaging from within the cardiac chambers despite the strong constraints imposed by catheter dimensions [168]. CMUT [169] and Piezoelectric micromachined ultrasonic transducers (PMUTs) [170], have emerged as attractive technologies for highly integrated 2D arrays. These technologies therefore represent promising alternatives to conventional bulk piezoelectric matrix arrays, particularly when probe miniaturization and integration are primary constraints.

IV. VALIDATION METHODS AND APPLICATIONS

A. Simulation

or in vivo validation. Simulation is also increasingly used to optimize probe design for 4D Doppler and ULM applications

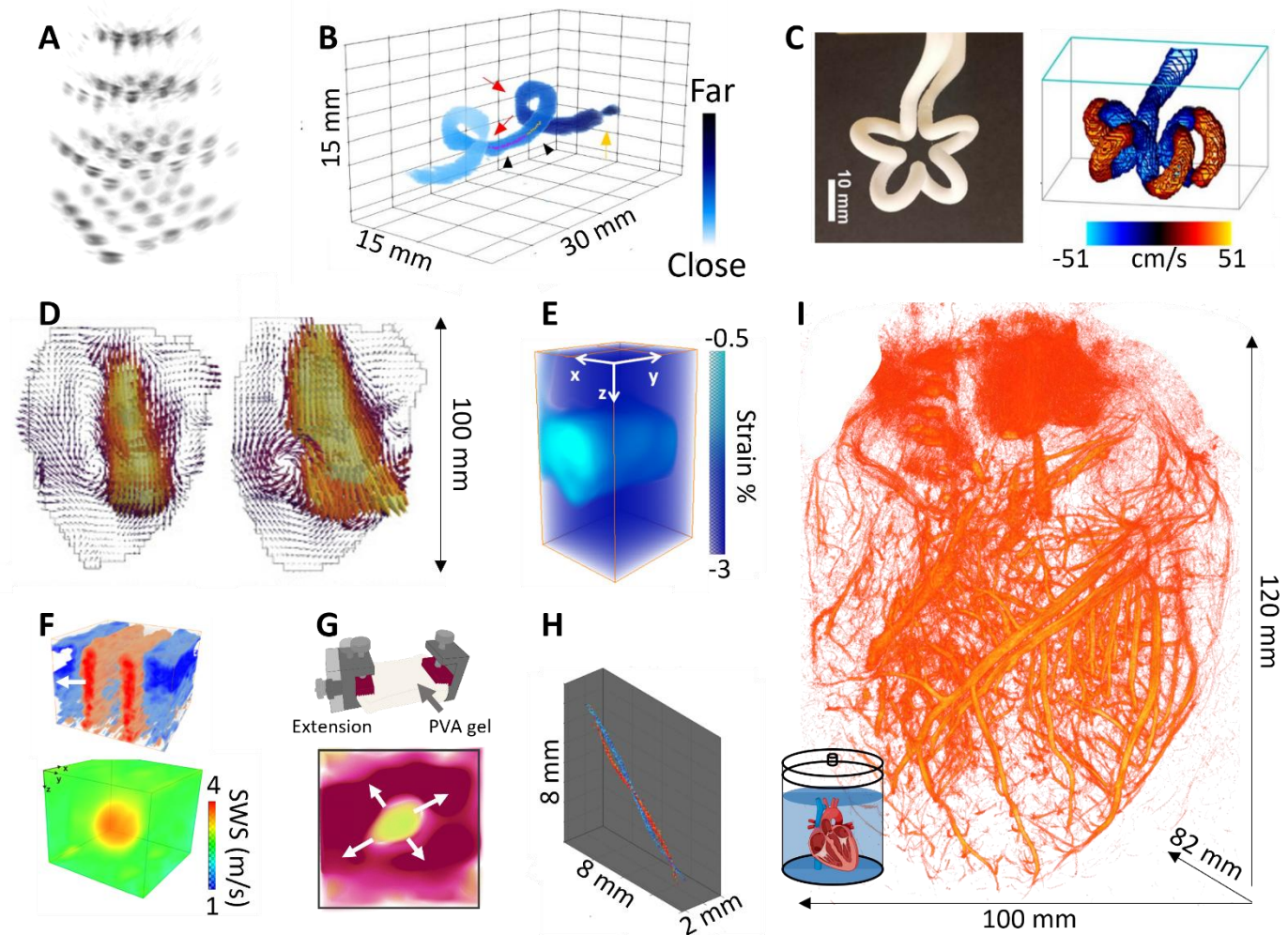


Figure 3: In vitro strategies for evaluating 4D ultrafast ultrasound modalities. Point targets (beads or needle tips) enable volumetric PSF characterization (A) (Provost et al., 2014). Flow phantoms using torsaded wires in simple (B) (Wei et al., 2021) or complex flower-like shapes (C) (Chee et al., 2021) assess 4D UF Doppler. Realistic cardiac phantoms reveal complex intracavitary vector flow (D) (Voorneveld et al., 2020). Elastography is evaluated using stiff cylinders (E) (Papadacci et al., 2017), inclusions (F) (Dong et al., 2024), or PVA gels with stiff fibers (G) (Meki et al., 2025), enabling volumetric strain and 3D shear wave stiffness assessment. Thin torsaded tubes assess ULM spatial accuracy (H) (Harput et al., 2020), while perfused ex vivo hearts provide realistic vascular networks for 3D ULM validation (I) (Haidour et al., 2025).

Simulation has played a crucial role in the development of 4D ultrafast ultrasound, particularly in the early days, when hardware and probes were not yet available. Before the first prototypes existed, researchers relied on simulation platforms to design and evaluate candidate arrays as well as transmit schemes for 4D ultrasound imaging [171], [122], [172]. Tools such as Field II [173], k-wave [174], SIMUS-3 [175] and MUST [176] provided the ability to model acoustic propagation, array geometry, and beamforming strategies, enabling feasibility studies that guided experimental development.

As the field has advanced, simulation has become even more central. Recent efforts have extended these frameworks to emulate complex modalities such as volumetric ULM [177], [178], [179], [180], [181] offering realistic environments to test localization and tracking algorithms before moving to in vitro

[180], [181]. Pushing this direction further is essential: advanced simulations not only accelerate innovation by lowering experimental costs and risks but also allow researchers to explore bold ideas and unconventional probe architectures long before they can be fabricated. In many ways, simulation serves as the incubator of 4D ultrafast ultrasound, turning conceptual advances into testable designs and seeding the next generation of experimental breakthroughs.

B. In vitro studies

The first demonstrations of 4D ultrafast ultrasound were conducted in vitro, primarily to establish feasibility and evaluate image quality under controlled conditions. Imaging phantoms provided a simple yet robust framework to test contrast, resolution, and frame rate, and to confirm that the same physical principles driving 2D ultrafast imaging could be extended to 4D. For instance, coherent compounding with

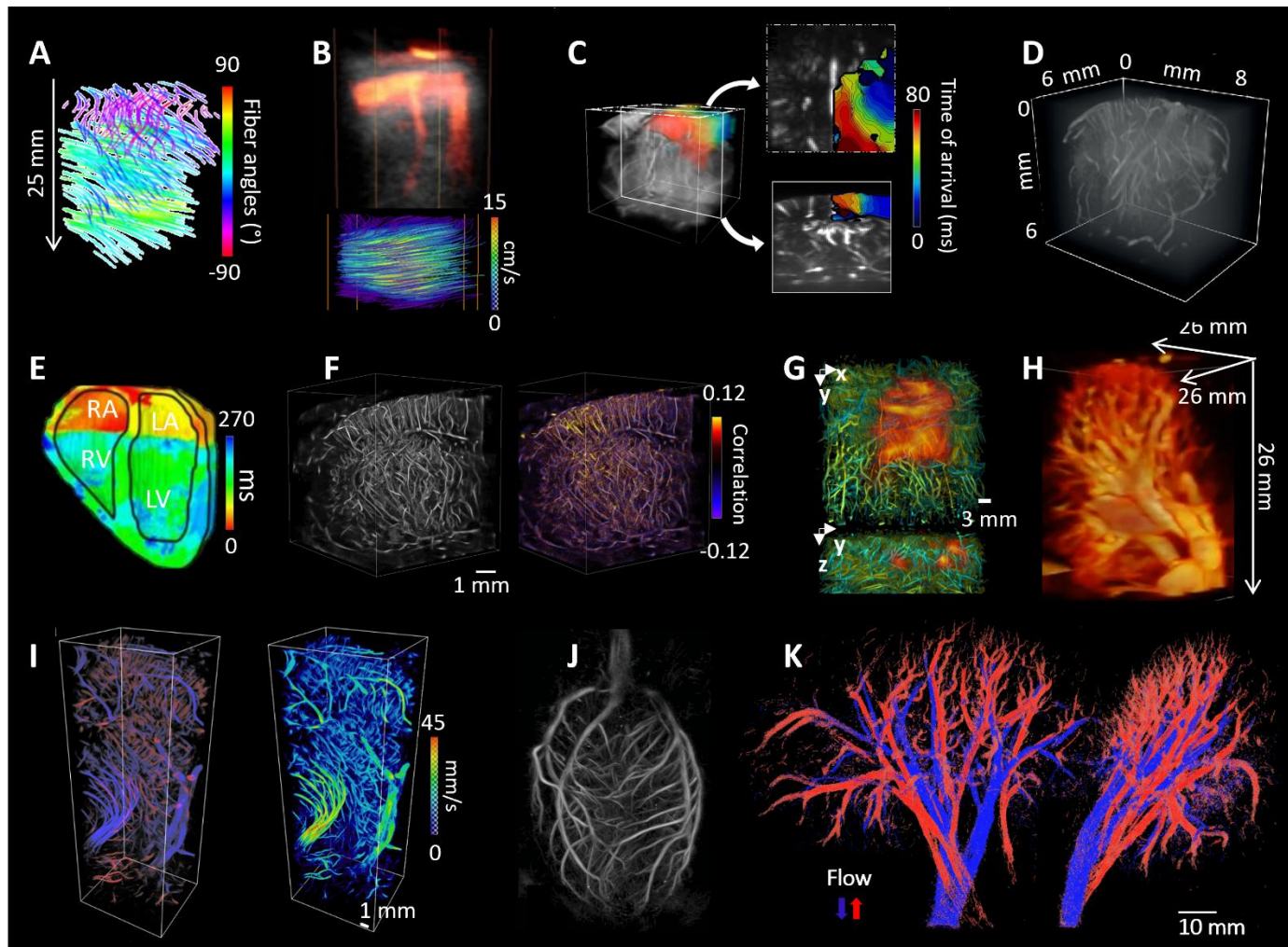


Figure 4 Preclinical applications of 4D ultrafast ultrasound. Backscatter tensor imaging maps cardiac fiber orientation over the cardiac cycle (A) (Papadacci et al., 2017). Vector Doppler quantifies coronary flow (B) (Correia et al., 2020). In rodents, 4D UF captures neurovascular coupling (epileptic wave) (C) (Rabut et al., 2019) and enables volumetric brain vascular imaging with matrix arrays (D) (Brown, 2024). 4D UF can image cardiac electromechanical waves (E) (Grondin et al., 2018). Functional ULM maps brain activity at micrometer scale (F) (Shin et al., 2025). Multimodal 3D ULM–photoacoustic imaging is demonstrated in liver (G) (Kasatkina et al., 2025), while 3D UF power Doppler images large kidney with sparse arrays (H) (Wei et al., 2023). 3D ULM further resolves vascular networks in primate brain (I) (Xing et al., 2025), rodent coronary system (J) (Demeulenaere et al., 2022), and whole kidney in large animals using multi-lens arrays (K) (Haidour et al., 2025).

multiple virtual sources was shown to improve image quality in a single volume with the same square-root scaling law observed in 2D ultrafast imaging [26], [182], [183].

In vitro studies remain particularly valuable for innovative probe development, since they allow systematic assessment of imaging performance without the complexity of in vivo conditions. A key aspect of this research is the design of custom phantoms tailored to specific applications, which has become an important subfield. Traditional phantoms containing cysts and wire targets have been used to evaluate 4D B-mode image quality. The tip of a needle or small beads embedded in a transparent phantom were imaged to assess Point Spread Function [26], [50] (Figure 3 A). Flow phantoms, ranging from straight tubes [56], [90] to complex vascular patterns [51], [167], [184], [185], [186], have been developed to test 4D Doppler methods (Figure 3 B, C, D). For volumetric elastography and strain, inclusions of different stiffness were embedded in gels [50], [140], [187] (Figure 3 E, F) and fibers were generated with a complex recipe of freezing and

elongating PVA gels [188], [60] (Figure 3 G). For ultrasound localization microscopy (ULM), phantoms with microtubes of varying diameters and branching geometries are widely employed to evaluate spatial resolution, localization accuracy, and the ability to reconstruct complex microvascular networks [61], [189], [190] (Figure 3 H). To move beyond these simplified models, researchers have also turned to ex vivo animal hearts for elastography [191], backscatter tensor imaging [192], [69], [193] or perfused and maintained at low temperature, which preserve the intricate vascular architecture and cardiac geometry while slowing physiological motion [126], [194] (Figure 3 I). A cool beating heart model can also be used for echo-particle velocimetry in the cardiac cavities [195] (Figure 3 D). This provides a realistic yet controllable environment to validate elastography and 4D ULM methods under conditions that closely approximate living tissues, bridging the gap between idealized phantoms and in vivo imaging.

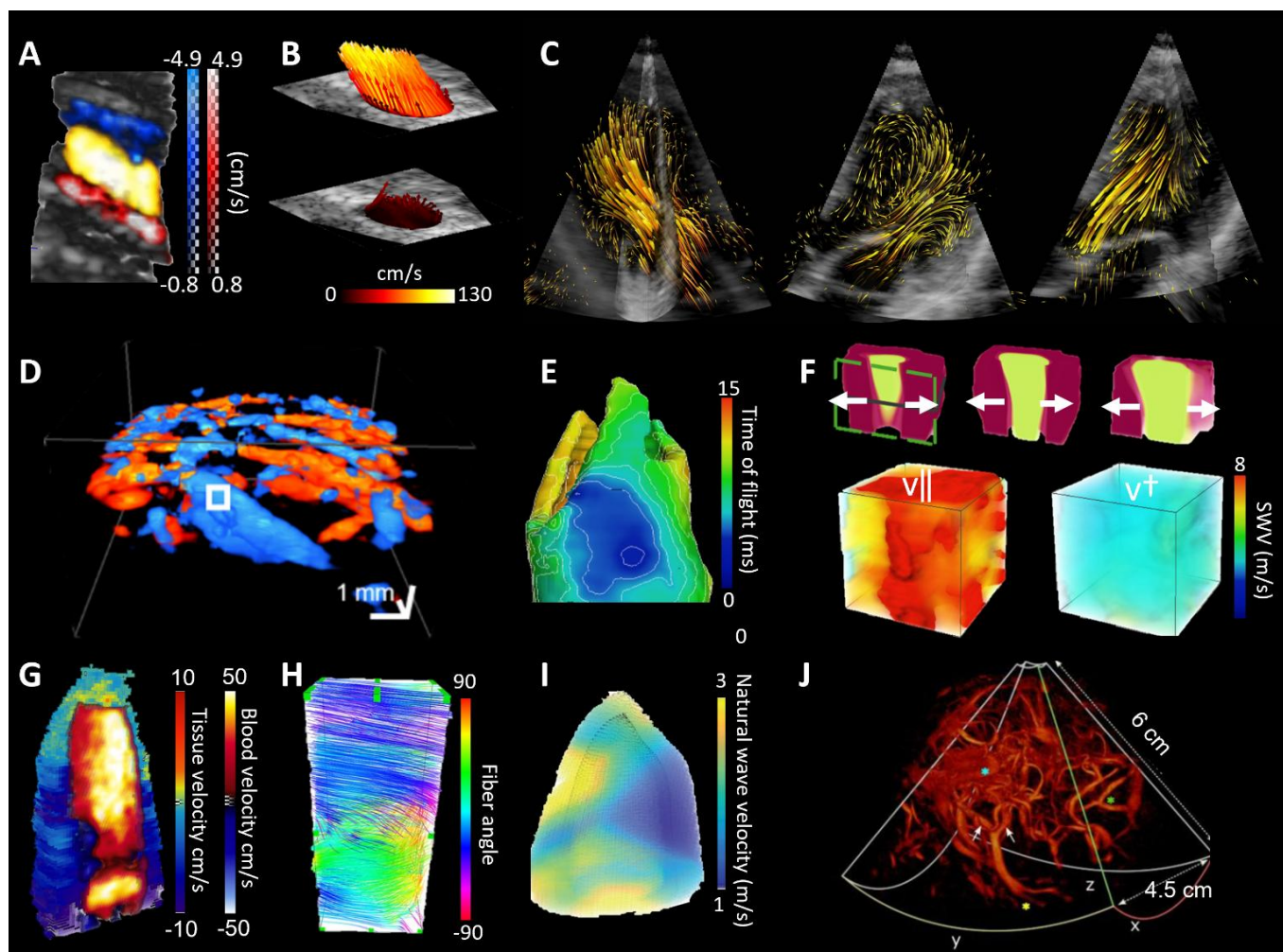


Figure 5: Human and clinical applications of 4D ultrafast ultrasound. Early studies demonstrated simultaneous power Doppler and pulsed-wave imaging in small volumes (A) (Provost et al., 2014). Vector Doppler quantifies carotid flow across cardiac phases (B) (Holbek et al., 2017) and reveals intracardiac flow patterns (C) (Wigen et al., 2018). High-sensitivity 4D UF Doppler visualizes microvascular networks (e.g., finger) (D) (Blancquart et al., 2025). In the heart, 4D UF captures electromechanical waves (E) (Papadacci et al., 2020) and their velocity (I) (Salles et al., 2021), while enabling simultaneous blood and tissue velocity mapping for functional assessment (G) (Papadacci et al., 2020). Backscatter tensor imaging reveals dynamic myocardial fiber architecture (H) (Papadacci et al., 2017). Beyond the heart, 3D shear wave elastography maps muscle anisotropy (F) (Meki et al., 2025), and intraoperative 3D ULM images dense cerebral microvasculature (J) (Wei et al., 2026).

Despite these advances, standardized phantoms and benchmarking protocols specifically designed for 4D ultrafast ultrasound remain largely lacking. While flow phantoms are increasingly used to evaluate volumetric Doppler and flow estimation, there is currently no broadly accepted framework to quantitatively compare 4D imaging performance across probes, acquisition strategies, beamforming algorithms, and processing pipelines. This represents an important limitation for reproducibility and comparison between systems, particularly given the diversity of emerging 2D array architectures. The development of standardized volumetric phantoms and protocols assessing spatial and temporal resolution, contrast, sensitivity, and quantitative accuracy will therefore be important for benchmarking future 4D ultrafast ultrasound systems and facilitating their translation.

C. Preclinical Applications

Preclinical studies have been central to demonstrating the potential of 4D ultrafast ultrasound in living systems, bridging

the gap between controlled in vitro experiments and clinical translation. Animal models provide both the complexity of physiological environments and the flexibility for invasive validation, making them ideal for validating 4D methods as well as studying fundamental physiological phenomena. In the following, applications are:

1) Cardiovascular imaging

The heart is one of the most challenging organs to image due to its rapid motion and complex volumetric geometry. 4D ultrafast Doppler was used to map a coronary artery in pigs and on the porcine heart [196] (Figure 4 B). 4D ULM has been successfully demonstrated in the Langendorff ex vivo heart preparation [194] (Figure 4 J) and on in vivo rodent models [194], providing high-resolution maps of the coronary microvasculature and dynamic flow patterns. Beyond vascular imaging, 4D ultrafast ultrasound has also been applied to fiber orientation assessment over an entire cardiac cycle in a porcine model [69] (Figure 4 A). Volumetric strain imaging in the canine left ventricle was used to detect radiofrequency ablation



lesions with high sensitivity, opening perspectives for guiding and monitoring cardiac interventions [197]. In addition, 4D imaging of electromechanical wave propagation in a canine model revealed the spatiotemporal dynamics of electrical activation and mechanical contraction [198] (Figure 4 E). Together, these studies underscore the ability of 4D ultrafast imaging to resolve not only coronary microcirculation but also myocardial strain and electromechanical waves, providing a comprehensive volumetric view of cardiac function.

2) Cerebral imaging

Preclinical animal models have advanced 4D ultrafast ultrasound for cerebral imaging, with distinct modalities and species-specific adaptations.

4D fUSi which relies on ultrasensitive power Doppler has enabled high spatiotemporal resolution monitoring of brain activity primarily in rodents [28], [132], [148], [199], [200], [201] (Figure 4 C). Due to the need for highly sensitive power Doppler imaging, most of these works rely on a craniotomy while transcranial fUSi in mice remains challenging due to skull attenuation and can be performed with hybrid multiarray setups with sensitivity and volume rates optimized to transcranial mice functional and connectivity assessment [202] (Figure 4 D). ULM, however, has achieved transcranial 4D cerebrovascular mapping in rodents, rats [100], [152], [199], [203], [204], mice [151], [153], [205], [206], and cats [104], as well as in larger brains like primates [207] (Figure 4 I) and sheep [208], where aberration correction [209] mitigates skull-induced distortions. Recent dynamic and functional ULM approaches [104], [151], [206], [210] further combine localization microscopy with dynamic hemodynamic monitoring in rodents (Figure 4 F). Recently, whole-brain non-linear imaging of gas vesicles with row-column arrays were demonstrated in rats, marking a significant step toward volumetric molecular imaging [211].

Together, these advances demonstrate the versatility of 4D ultrafast ultrasound for noninvasive brain mapping across species and scales, with 4D ULM showing broader transcranial applicability than fUSi.

3) Kidney and Liver imaging

Beyond the brain and heart, 4D flow and particularly 4D ULM have been applied to abdominal organs. In small animals, it has enabled volumetric vascular imaging and flow characterization in the kidney [102], [155], [156], [212], [213], [214], where microcirculation is of key physiological and pathological interest. Recently, 3D ULM was combined with photoacoustic imaging to deliver complementary structural, functional, and molecular information (Figure 4 G). Using a hemispherical 2D transducer, 4D ultrafast ultrasound at 215 Hz enabled high-resolution mapping of hepatic microvasculature alongside optical contrast [215], [216]. Extending to larger models, [43], [126], [163] reported 4D ULM imaging of an entire kidney and/or large liver volume in the pig, using a sparse array (Figure 4 H), a multi-lens array (Figure 4 K) and a curved RCA, respectively to achieve sufficient volume area. These results demonstrate that 4D ultrafast ultrasound can address not only small-scale preclinical physiology but also large-organ imaging in anatomies approaching clinical relevance.

D. Human and Clinical Applications

Human studies of 4D ultrafast ultrasound are still largely in the proof-of-concept stage [217], but they already illustrate the broad potential of this technology across vascular and cardiac applications and application to breast cancer [140], [159].

1) Vascular imaging

The carotid artery has served as an ideal first model, since it can be approximated as a large pulsatile tube and is easily accessible. Several studies have demonstrated 4D Doppler imaging of the carotid (Figure 5 A), using a variety of probe technologies including dense matrix arrays [56], [68], row-column arrays [157], [158], [159], and multi-lens systems [128]. These approaches consistently revealed pulsatility in the Doppler spectrum, validating the feasibility of volumetric flow imaging. In addition, vector flow Doppler methods have been developed in 4D, enabling simultaneous quantification of both axial and transverse flow components [68], [159] (Figure 5 B). RCA for deep vessel [218], microvascular monitoring in the thyroid [46] and finger [160] (Figure 5 D) were also recently proposed. Recently, a multi-lens system combined with 3D ULM was applied to the human kidney, enabling whole-organ vascular imaging and paving the way for clinical translation [219]. In another study, pulse wave was observed in the human carotid [220].

2) Cardiac imaging

Cardiac applications represent one of the most ambitious targets for 4D ultrafast imaging, and several important proof-of-concept studies have already shown their potential. Intraventricular flow has been visualized using 4D color Doppler imaging [26], while simultaneous volumetric acquisitions of flow and tissue Doppler have enabled the estimation of all major cardiac indices within a single heartbeat, opening the way toward automated functional assessment [221] (Figure 5 G). 4D intracardiac vector flow was also demonstrated with a clinical system [27] (Figure 5 C). Beyond hemodynamics, the technique has been used to track the propagation of natural waves generated by mitral and aortic valve closure or the atrial kick [49], [93], [222], [223], whose velocity can be used to assess myocardial (Figure 5 E, I). Other methods further demonstrated 4D shear wave elastography of both the right and left ventricles during diastole with a simplified matrix probe, confirming the feasibility of myocardial stiffness quantification in humans [224]. Structural assessment has also been obtained through volumetric backscatter tensor imaging, which allows in vivo reconstruction of myocardial fiber orientation at different moments of the cardiac cycle [69] (Figure 5 H). Finally, the mapping of electromechanical waves in human volunteers has provided volumetric information on the spatiotemporal sequence of electrical activation and mechanical contraction [198]. Collectively, these proof-of-concept studies demonstrate that 4D ultrafast ultrasound can simultaneously assess vascular hemodynamics, myocardial stiffness, fiber architecture, and electromechanical coupling in humans.

3) Musculo-skeletal applications

Musculo-skeletal applications have also been reported sporadically to characterize complex anisotropic structures. 4D shear wave elastography and 4D backscatter Tensor Imaging were proposed to assess mechanical properties and anisotropy

on the biceps of human volunteers under different stages of contraction [225] (Figure 5 F). 4D strain quantification based on ultrafast acquisition was proposed on the calf muscle [50].

4) Cerebral applications

While real-time, high-resolution brain monitoring remains a challenge due to the skull's barrier to 4D ultrafast ultrasound, recent work introduces the use of miniaturized microbeamformer probes. The device, equipped with 3,072 transceivers coupled to 192 receive channels through on-ASIC microbeamforming, achieves 450 Hz volumetric imaging up to 8 cm depth. Validated in clinical scenarios (skull prosthesis, cranial defect, and neurosurgery), it successfully mapped somatotopic finger representations and decoded individual finger movements during piano playing [95]. Building on this miniaturized probe technology, 4D ULM was further explored in a patient with an arteriovenous malformation and identified feeding, draining, and non-tumoral vessels, with high-resolution volumetric maps, revealing complex internal vascular structures [226]. A more recent study from the same group using the same miniaturized matrix probe, highlighted the clinical usage of 4D ULM in a cohort of 10 patients identifying deep cerebral perforating arteries and thereby exceeding the capabilities of current intraoperative imaging modalities [227] (Figure 5 J).

V. PERSPECTIVES, CHALLENGES AND FUTURE DIRECTIONS

4D ultrafast ultrasound is emerging as a transformative paradigm in biomedical imaging, extending the capabilities of ultrafast ultrasound into three dimensions and enabling the observation of physiological processes with unprecedented spatiotemporal resolution. The field has rapidly evolved from early demonstrations of high-frame-rate volumetric imaging to a broad range of applications encompassing Doppler imaging, shear wave elastography, electromechanical imaging, functional ultrasound, and ultrasound localization microscopy.

The development of 4D ultrafast ultrasound has been closely linked to innovations in transducer technology and acquisition hardware. Fully populated matrix arrays provide the most direct extension of conventional arrays to volumetric imaging, while alternative architectures such as microbeamforming, sparse arrays, row-column addressed arrays, multi-lens arrays, and wearable probes offer different compromises between acoustic performance, channel count, and clinical practicality. Importantly, no single technological approach has yet emerged as a clear winner. The optimal implementation of 4D ultrafast imaging remains strongly application dependent, with tradeoffs between sensitivity, image quality, field of view, penetration depth, system complexity, and cost guiding the choice of architecture.

Parallel progress in post-processing methods, including GPU-accelerated volumetric beamforming, motion and clutter filtering, and sophisticated algorithms for 4D ULM, has transformed massive data streams into interpretable images. Yet, as history shows, acquisition alone is never sufficient; the development of advanced visualization tools is equally crucial. Just as Galileo's telescope reshaped the scientific questions of its era [228], [229], interactive volumetric renderings, streamline blood flow mapping, and graph-based

microvascular reconstructions are now indispensable epistemological tools in 4D ultrasound.

Applications have rapidly expanded from in vitro validation in phantoms to preclinical models, where 4D ultrafast ultrasound has been applied to the heart, brain, kidney, and liver, revealing phenomena inaccessible to 2D imaging. Proof-of-concept studies in humans have already demonstrated feasibility for intraventricular flow, vector Doppler, shear wave elastography, electromechanical wave imaging, and microvascular mapping. These studies showcase the transformative potential of 4D ultrafast ultrasound but also highlight the vast uncharted territory that remains.

A. Technical and Computation challenges

The technical challenges ahead remain substantial. Progress will depend on continued innovation in probe design, whether through ever higher element counts or intelligent channel-reduction architectures, as well as advances in data management and real-time visualization and feedback. The ability to process, display, and interact with volumetric ultrafast data streams in real time will be critical for clinical translation and practical usability.

At the same time, the sheer volume of data generated presents a major bottleneck: long acquisitions, such as 4D ULM studies lasting 20 minutes to an hour, can produce terabytes of data per patient, making storage, transfer, and retrieval formidable challenges for large clinical cohorts. Continued advances in computational power, compression, and on-the-fly processing will be essential to mitigate these limitations, particularly for beamforming, ULM post-processing, and SVD clutter filtering.

A key technical challenge common to all ultrafast imaging setups is the substantial loss of transmit focusing, which leads to reduced signal-to-noise ratio. In 4D ultrafast imaging, this occurs in both azimuth and elevation, which can limit feasibility in difficult-to-image patients. Advanced probe designs and full transmission flexibility may partially compensate for the lack of focal gain using coherent compounding approaches, but these solutions often come at the cost of reduced frame rates.

B. Exploiting the Richness of 4D information

Despite these challenges, the spatiotemporal richness of volumetric ultrafast data opens substantial new opportunities. Conceptually, the field must move beyond simply extending 2D paradigms and instead develop new frameworks, metrics, acquisition workflows, use cases, and visualization strategies that fully exploit the spatiotemporal richness of 4D data.

For example, in shear wave elastography of skeletal muscle, methods must be designed to quantify stiffness anisotropy in three dimensions. In fUSi, the field should evolve from 2D correlation maps toward volumetric analyses such as 3D connectome mapping. Similarly, in 3D ULM, organs should be analyzed as integrated vascular networks, with quantitative metrics that capture the hierarchical relationships between large vessels and the microvascular architecture within complex 3D organizations.

Dimensionality reduction and summarization will remain essential for clinical use, providing concise quantitative parameters that capture key physiological events. However,



these simplified metrics can only be derived after an immersive exploration of the full high-dimensional 4D datasets, which enables the identification of relevant features and complex patterns. In this sense, complexity is a prerequisite for clarity: thorough analysis of the rich volumetric data allows the generation of meaningful, clinically actionable summaries, bridging the gap between discovery and practical decision-making.

C. Toward whole-organ and Continuous Volumetric Imaging

Another important direction for 4D ultrafast ultrasound is the expansion of the field of view toward panoramic volumetric imaging. Many physiological processes extend beyond the limited aperture of conventional probes, making whole-organ characterization essential to fully exploit volumetric ultrafast imaging. Wider coverage could enable integrated assessments of organ-scale physiology. Achieving this goal will require innovations in probe design, acquisitions, and compounding strategies capable of recombining large volumes while preserving ultrafast volume rate.

A complementary direction is the development of conformable wearable multi-linear and two-dimensional arrays. Unlike handheld probes designed for brief examinations, these devices could remain attached to the body for extended periods, enabling long-duration recordings of physiological dynamics. Combined with ultrafast imaging, such systems could enable continuous monitoring of hemodynamics, tissue mechanics, or electromechanical activity, transforming ultrasound from a diagnostic tool into a monitoring modality.

D. Future System Architecture and Clinical Translation

A broader question concerns the long-term trajectory of ultrasound system architecture. Should future systems continue to scale toward ever larger channel counts, or has the field reached a practical plateau near the current generation of approximately 1,024 channels? Increasing the number of independent channels offers the most direct path toward fully sampled large-aperture matrix probes, but this strategy rapidly encounters practical constraints related to system cost, power consumption, cabling, data throughput, and physical size.

If channel counts remain limited, probe design must instead rely on architectures that reduce the number of independent electronic channels while preserving volumetric imaging capability. Approaches such as microbeamforming, row-column addressed (RCA) arrays, sparse arrays, and large-element probes combined with acoustic lenses represent different strategies toward this goal. These designs trade electronic complexity for acoustic or computational solutions and may ultimately provide the most scalable route to large field-of-view volumetric imaging without requiring “million-channel” ultrasound systems.

An alternative strategy consists in integrating analog-to-digital conversion directly within the probe and relying on high-speed data-transfer protocols to stream digitized signals. While attractive in principle, this approach introduces significant practical constraints, including increased probe size, higher power consumption, and associated thermal management challenges, which are particularly critical in

clinical settings. The optimal balance between channel scaling and architectural efficiency remains an open question, and future developments will likely involve hybrid solutions combining moderate channel counts with intelligent probe designs.

Beyond hardware architecture, advances in computational methods will also play an important role in the evolution of 4D ultrafast ultrasound systems. AI, and in particular deep learning, is rapidly becoming a valuable tool to achieve time- and data-efficient image formation and analysis. As the expansion of 4D ultrasound leads to increasingly large datasets, it will become possible to develop more specific and efficient deep learning models, which in turn could accelerate processing while improving data quality. In parallel, new deep learning strategies, such as the combination of smaller specific networks, knowledge distillation [230] or weight quantization [231], allow for more condensed and efficient models, lowering the need for extensive databases and computationally intensive model training. Small neural and tensor processing units are also emerging as a way to perform neuronal inference at the edge [232], which could potentially further enhance the overall efficiency of 4D ultrasound systems. Another emerging domain in deep learning is physics-informed neural networks, which include physics-based a-priori knowledge in the deep learning process. These could represent an optimal tool for 4D Ultrafast Ultrasound processing in an attempt to combine the best of both worlds. Today, architectures can be implemented and trained in real-time [233]. Deep learning is also increasingly used to propose diagnostic models based on clinical ultrasound data, to assist physicians in the decision-making process. With the powerful data analysis and exploration tools provided by deep learning, clinical datasets obtained with 4D Ultrafast Ultrasound will allow for the development of even more efficient and accurate diagnostic assistance and unprecedented clinical discoveries.

Additional challenges concern robustness and clinical translation. In highly dynamic organs such as the heart, robust 3D motion compensation remains necessary for quantitative 4D imaging. In parallel, the growing integration of AI raises challenges related to generalizability, validation, and regulatory approval that will need to be addressed for clinical translation.

Among imaging modalities, ultrasound occupies a unique position. Unlike 4D flow MRI, it is not constrained by long acquisition times, gating, or poor temporal resolution; unlike CT or PET, it can capture real-time dynamics at the bedside without ionizing radiation. Only 4D ultrafast ultrasound combines volumetric coverage, millisecond-scale resolution, and portability, making it uniquely suited to capture transient, dynamic physiological events in vivo.

As with previous revolutions in imaging such as PET for metabolism, fMRI for brain function, and high-speed microscopy for cellular dynamics, the true impact of 4D ultrafast ultrasound will come through discovery. New ways of seeing generate new scientific questions, and the richness of 4D ultrafast data promises to enhance our understanding of cardiovascular, neurovascular, and musculoskeletal physiology. The coming decade will require close collaboration between engineers, physicists, computer scientists, and

clinicians to translate these capabilities into robust biomarkers, diagnostic tools, and therapeutic monitoring strategies.

Crucially, clinician buy-in will play a decisive role in this transition. As the vast majority of current clinical scanners do not yet support 4D ultrafast imaging, strong clinical demand will be needed to drive its integration into commercial systems. This will depend on identifying compelling clinical use cases, particularly in high-stakes scenarios where 4D ultrafast imaging can directly impact life-saving decisions, or in contexts where it significantly improves workflow efficiency and patient throughput. In this perspective, intraoperative imaging represents a particularly promising domain: 4D ultrafast ultrasound can provide real-time, volumetric, and hemodynamic information with intuitive visualization, enabling physicians to make rapid and accurate decisions during procedures—capabilities that remain out of reach for modalities such as MRI, CT, PET, or fluoroscopy in a truly real-time setting. Demonstrating such clear clinical and economic value, while maintaining acceptable system and implementation costs, will be essential to foster widespread adoption.

Ultimately, the promise of 4D ultrafast ultrasound lies not only in sharper images or higher frame rates, but in its ability to change the questions we can ask about living systems. By capturing physiology in four dimensions, it offers a new way of seeing—and with it, the possibility of discoveries that were once unimaginable. In this sense, it echoes the shift brought about by Galileo's telescope: not merely improving vision, but transforming our understanding of the world by revealing dynamics that had always been there, yet remained unseen.

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