The next generation in ultrasound imaging.

Key features

- Hands-free - automated transducer positioning and movement
- Requires minimal training
- Fast high-throughput imaging of 3 mice in just a few minutes
- 3D widefield acquisitions enabling whole subject imaging
- Shear Wave Elastography (SWE) mode for quantifying tissue stiffness
- CEUS acoustic angiography mode for visualization of microvasculature

The **Vega® ultrasound system** is Revvity latest addition of leading preclinical *in vivo* imaging technology. With an innovative design, Vega is a hands-free automated ultrasound platform that delivers high-resolution 2D and 3D imaging in just a few minutes.

Designed with the researcher in mind, the Vega removes the challenges associated with traditional hand-held ultrasound, and uses a bottom-up imaging approach through the use of automated hands-free transducers located under the imaging stage. This unique design requires minimal training with no dedicated sonographer needed, enables high-throughput imaging, and produces more consistent results than conventional hand-held ultrasound systems.

The imaging stage accommodates 3 mice for fast sequential scanning in just a few minutes, greatly increasing throughput with the added benefit of enabling widefield imaging. Widefield ultrasound is a unique feature that affords researchers to see beyond a localized area, enabling whole subject imaging which is ideal for visualizing effects of disease or therapies on target organs, surrounding tissues, or throughout the entire subject.

The Vega ultrasound system comes standard with two types of integrated transducers for B-Mode, M-Mode, 2D, 3D, and 4D imaging as well as Acoustic Angiography (AA) and Shear Wave Elastography (SWE) modes providing the flexibility you need for your research and drug discovery and development studies.

Vega® Pre-clinical
Ultrasound System

Vega hands-free ultrasound

Figure 1. Vega ultrasound system with RAS-4 rodent anesthesia system and computer.
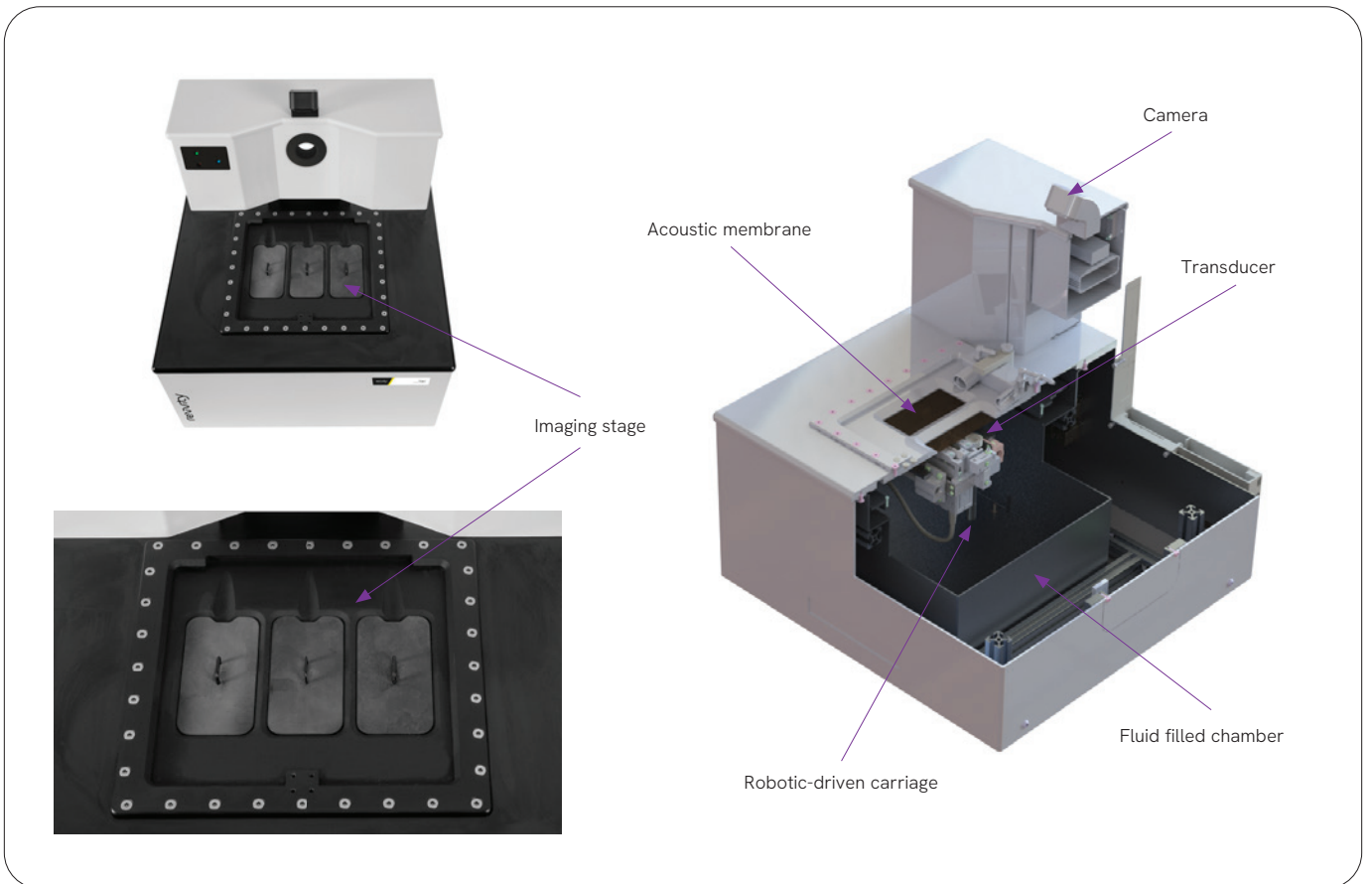

Figure 2. (Top left) Arial view of Vega showing imaging stage. (Lower left) Close up of imaging stage showing automated hands-free transducers under the stage. (Right) Cross section of the Vega ultrasound imaging system.

Innovative, hands-free, automated ultrasound

Get more consistent results with a hands-free system that removes the use of a handheld transducer. Unlike traditional ultrasound systems, the Vega uses a bottom-up approach with the transducers located under the imaging stage.

The automated positioning of the transducers can scan coronal, sagittal, and axial orthogonal planes across the whole body producing high-resolution 3D data that looks more like MRI images than traditional ultrasound.
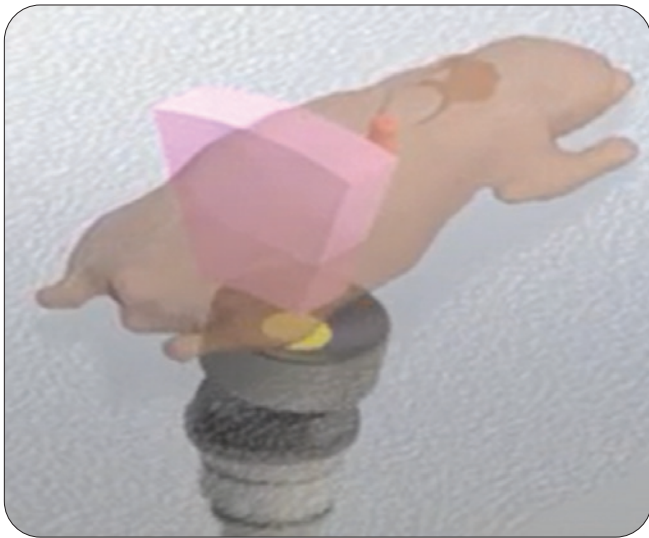

Figure 3. Automated bottom-up imaging with camera guidance for widefield imaging.

Figure 4. Top-down view of imaging stage showing transducers in middle bay.

Advantages of this unique design include:

- **Ease of use**. Requires minimal amount of training, no dedicated sonographer required

- **More consistent results**. Removes operator variability resulting in more consistent data over longitudinal studies

- **More accurate data**. By removing physical contact between the transducer and the animal, tissues are not 'distorted' or 'warped' during 3D image acquisition

- **Enables widefield imaging** relative to handheld approach. Allows whole subject imaging for visualizing effects of disease or therapies on specific organs or surrounding tissues

- **High speed scanning**. Automated hands-free transducers enable fast and consistent scanning

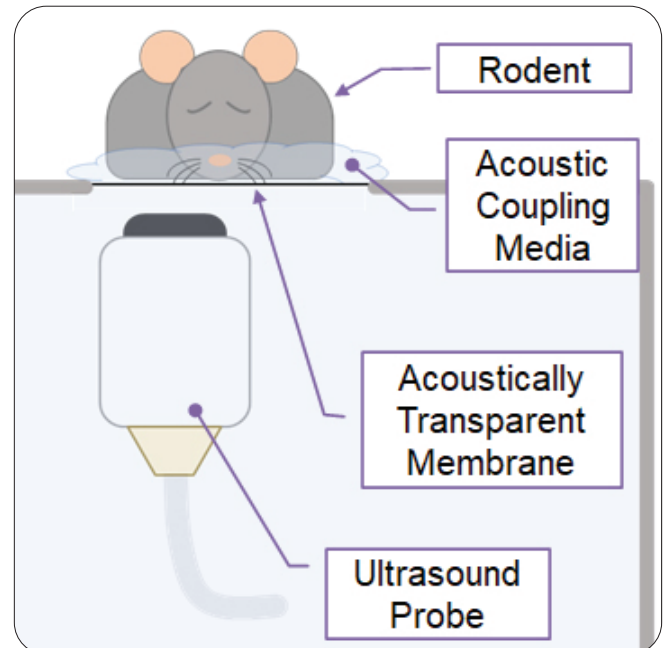- **Streamlined imaging workflow**. User can prep subjects while scanner is operating

Figure 5. Diagram showing details of bottom-up imaging design.

High-throughput capability and streamlined imaging workflow

With the transducers integrated under the imaging stage and widefield capability, the Vega enables high-throughput imaging with scan times ranging from 20 – 90 seconds with most scan times taking less than one minute.

Not only does the Vega offer fast scan times, the systems imaging stage incorporates 3 bays for sequential scanning of 3 mice at a time further increasing imaging throughput.

In addition to increased throughput, the 3-bay design streamlines imaging workflow. While a set of subjects are being scanned, the user can be prepping the next set of animals on the benchtop.

Get the full picture with widefield 3D ultrasound

The widefield imaging capability with Vega enables fast 3D whole subject imaging for visualizing effects of disease or therapies on specific organs and surrounding tissues in less than one minute.

Advantages of widefield imaging:

- Reduces the risk of missing obscured pathologies as compared to the narrow scope images obtained from conventional handheld transducers

- Analysis is much easier when visualizing target anatomy within the broader surrounding anatomical context
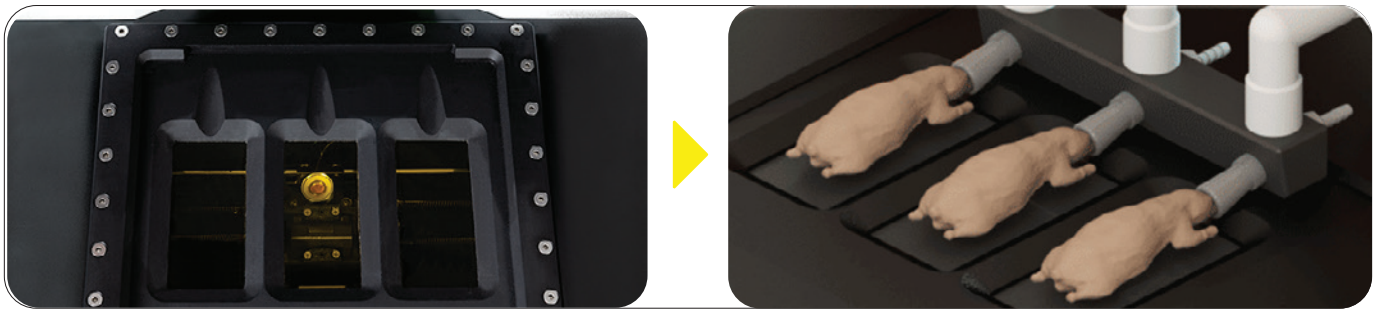

Figure 6. (Top) Imaging stage showing 3 mouse imaging bay. (Bottom) Imaging stage displaying mice in each bay.
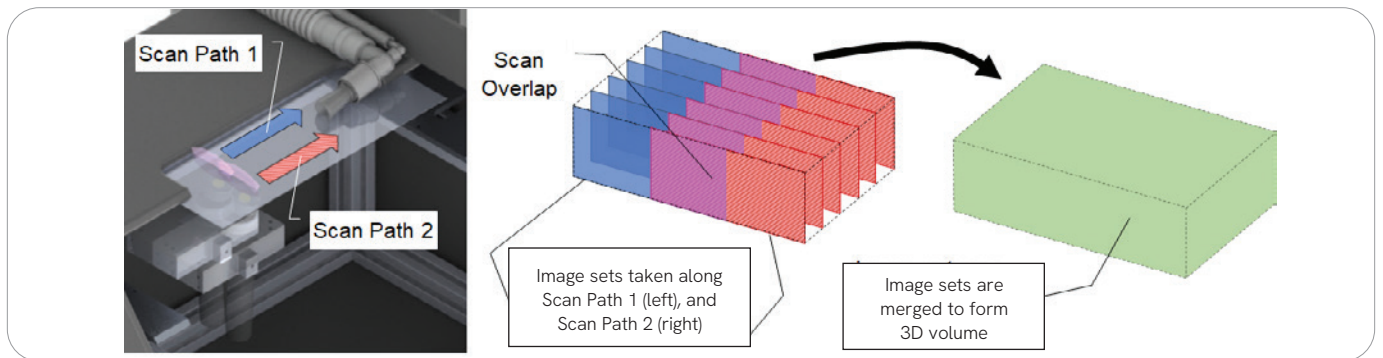

Figure 7. (Left) Path of the robotic transducers for collecting image slices in real-time. (Middle/Right) SonoEQ™ software takes image slices and reconstructs into a 3D image.
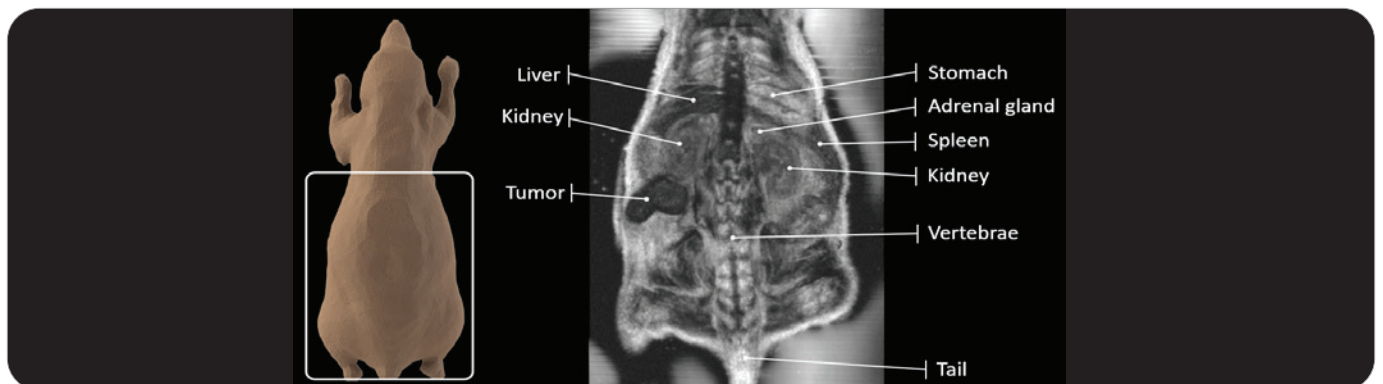

Figure 8. Example of Vega's widefield imaging capability showing detailed anatomy. Coronal plane image reconstructed from widefield 3D ultrasound data.

Transducer Type	Imaging Mode	Application(s)
Wobbler Single element, high-frequency wobbler	▪ B-Mode	▪ Tumors ▪ Individual organ system studies, e.g. Kidney, Liver
Dual-element annular array, high and low frequency wobbler	▪ B-Mode ▪ Acoustic Angiography (AA)	▪ Tumors ▪ Individual organ system studies, e.g. Kidney, Liver ▪ Vascular
Linear Array	▪ B-Mode ▪ M-Mode ▪ 4D-Mode ▪ Shear Wave Elastography (SWE)	▪ Tumors ▪ Cardiovascular/cardiac function ▪ Assessments of tissue stiffness (e.g. due to fibrosis)

Multiple imaging modes to fit your specific application

With flexibility in mind, the Vega system comes standard with two integrated transducers designed to meet your imaging requirements. A dual-mode wobbler for both high-resolution scanning and Acoustic Angiography (AA) vascularity imaging, as well as a linear array transducer for fast deep tissue imaging, elastography, and cardiac imaging.

B-mode and M-mode

B-Mode, or Brightness Mode is the most common type of ultrasound mode. It uses gray scale imaging to render images in which the organs and tissues of interest are depicted as points of variable brightness resulting from ultrasound echos. The brightness of the points are dependent upon the amplitude or intensity of the echo which enables visualization and quantification of anatomical structure.

The Vega system comes equipped with 2 types of integrated transducers for B-Mode scanning. The first is a dual-mode wobbler with high frequency output to produce high-resolution images with an additional lower frequency required for Acoustic Angiography (AA). The second transducer is a linear array enabling fast, deep tissue imaging.

M-Mode, or Motion Mode is defined as time motion display of the ultrasound wave along a single ultrasound line (spatial line through tissue, over time). It provides a one-dimensional view of moving organs and with high sampling rates, which translates to high time resolution, very rapid motions can be displayed and measured over time. M-Mode is often used as a convenient and rapid technique to measure cardiac function. As seen in Figure 10, panel B, cardiac tissue is repeatedly contracting and expanding over time.
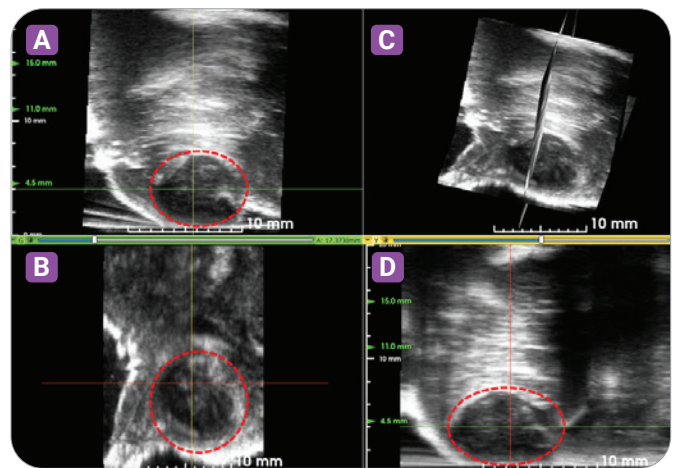

Figure 9. B-mode 3D ultrasound imaging of a subcutaneous injection of IVISbrite™ HCT-116 Red F-luc tumor cells into the right flank of a mouse and imaged after 10 days. The tumor location is indicated by the dashed circles. (A, B, & D) Axial, coronal and sagittal views. (C) 3D view of all three planes.
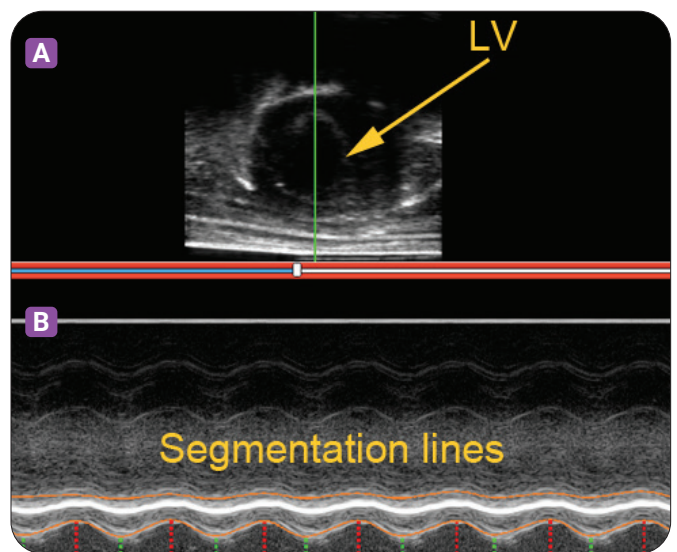

Figure 10. Mouse cardiac functional assessment using M-Mode. (A) B-Mode imaging of the left ventricle (LV). Green line indicates measuring position. (B) Cardiac motion using M-Mode with automatic segmentation used to calculate heart function metrics. Red dashed lines indicate the largest chamber diameter at the diastolic phase, green dashed lines represent the smallest at the systolic phase.

3D imaging in motion

The power of 4D imaging

The last several decades has seen significant progress in ultrasound, from 2D imaging to the emerging role of 3D imaging. 4D imaging takes ultrasound to the next level by combining motion with static 3D images. In short, 4D ultrasound imaging is 3D ultrasound in live motion.

This mode is a valuable tool for preclinical researchers studying cardiac abnormalities and function as it's highly accurate and fast compared to other modalities such as MRI. The Vega makes 4D imaging even faster than other ultrasound systems on the market with its innovative automated image scanning.

Visualize the heart in 4D

- Evaluate volumetric left ventricle (LV) measurements, the gold standard for assessing asymmetrical cardiac pathologies (i.e. myocardial infarction)

- Reconstruct 4D echocardiograms allowing retrospective cardiac measurements in any slice plane

- Set up your mice, and press go

- Collect 4D videos in < 2 min

- No ECG or respiration gating required

M-Mode 360 – Functional measurements from 4D data

- Retrospectively acquire M-Modes directly from the 4D scan.

- Assess infarct, cardiomyopathy, and more, using the complete 4D dataset provided by the Vega system

Artificial Intelligenence (AI) enabled software to automatically analyze M-Mode data

- AI automatically segments cardiac boundaries and computes LV functional parameters

- Global LV function is measured and calculated including ejection fraction (EF), fractional shortening (FS), cardiac output (CO), and LV mass

Find the heart quickly and repeatably using Vega's rapid heart-localization scan

- Using widefield acquisition, a scout-scan of the abdomen/chest region is captured and location of the heart is automatically identified
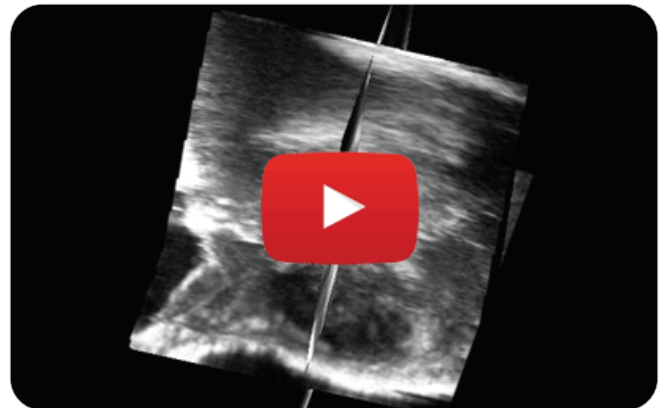

Figure 11. 3D ultrasound in live motion.

Visualize microvasculature like never before with acoustic angiography

A standard feature with the Vega system, Acoustic Angiography (AA) is a minimally invasive contrast enhanced ultrasound (CEUS) imaging mode that uses VesselVue® injectable microbubbles as a contrast agent. Microbubbles have a lipid-encapsulated gas core and are non-toxic to the animal.

AA enables high-sensitivity imaging of microvasculature of tumors or organs and can be used to evaluate tumor angiogenesis or explore therapy response or injury changes in tissue over time.

Benefits of AA include:

- Quantitative assessment of tumor vessel network architecture and density
- Reveal response to therapy before tissue changes
- Collect images of 3D microvessel trees with 100 µm resolution in minutes
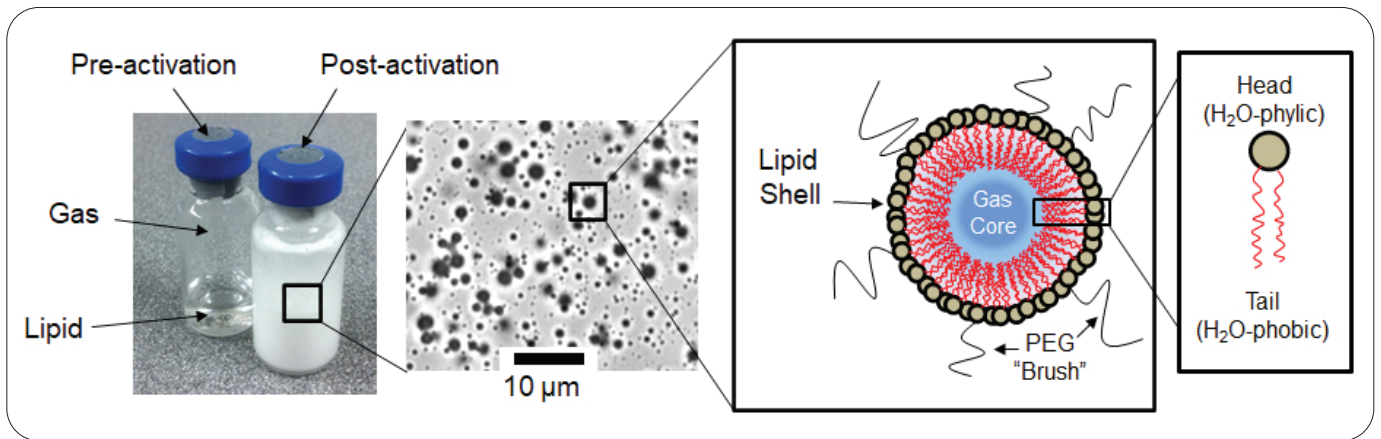- 2D image capture in less than one seconda

Figure 12. (Left) Microbubble contrast agents (1.5 mL vials) pre and post mechanical agitation. (Middle) Scale bar in bright field microscope image = 10 µm. (Right) Structure of microbubble.
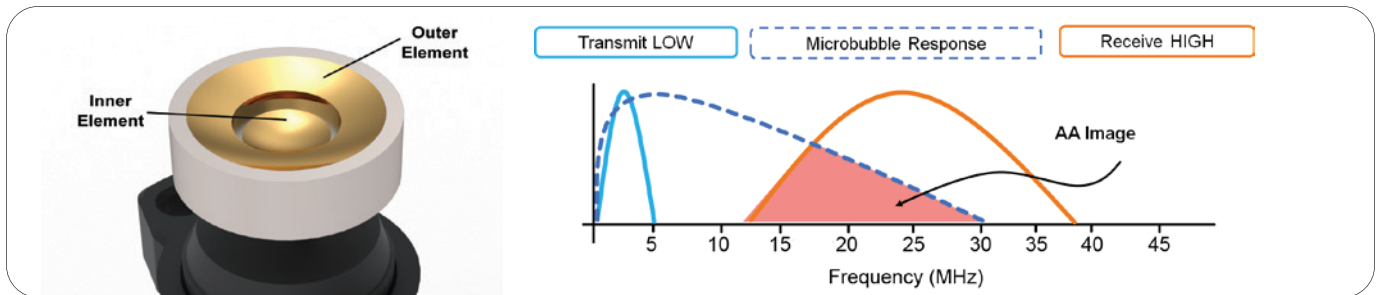

Figure 13. High sensitivity is achieved with a dual-element transmit-low/receive-high pulsing wobbler. Lower frequency outer element is necessary for Acoustic Angiography.
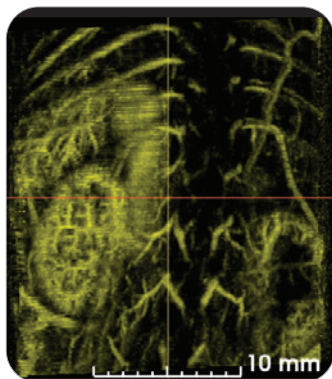
Figure 14. Acoustic Angiography of mouse kidney vasculature.
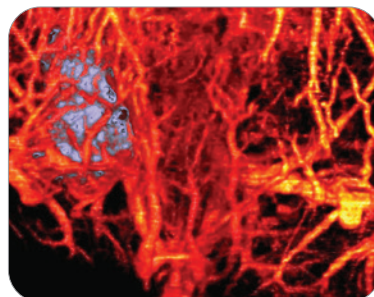
Figure 15. Acoustic Angiography showing vasculature surrounding tumor .

Figure 16. ((Left)) A traditional B-Mode image showing 2D and 3D representations of a tumor. This mode would allow tumor volume to be quantified. (Right) The same tissue as above imaged with Acoustic Angiography mode. Note that the only features seen are microvessels in and around the tumor, while all other tissue appears invisible. This allows tissue vascularity to be quantified.

Measure tissue stiffness with shear wave elastography (SWE)

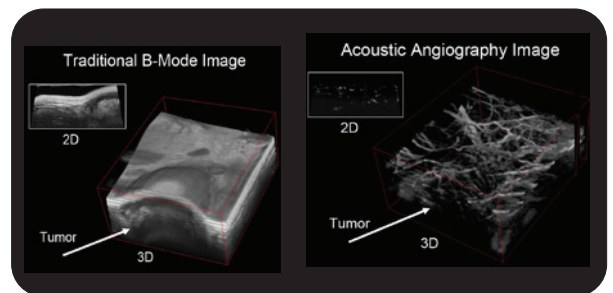Tissue stiffness assessed via manual palpation has been used historically by physicians to access disease state noninvasively. Although an indicator of disease, it is qualitative and does not provide the clinician with any measurement behind the disease state.

Elastography refers to a class of medical imaging techniques that map and/or quantify mechanical properties of biologic tissues. In general, these techniques work by introducing a mechanical force into the tissue (compression, vibration, etc.) and observing how the tissue behaves to infer its stiffness. With Shear Wave Elastography (SWE), radiation force is created by the transducer which induces mechanical waves ("shear" waves) that propagate in the tissue. Under simplifying assumptions, the speed of the shear waves can be directly correlated to Young's modulus, the engineering unit of stiffness. The higher the speed, the higher the modulus and the stiffer the tissue.

Since the force is precisely generated by the probe and not the operator, SWE is less operator-dependent, more reproducible, and quantitative compared to compressive elastography techniques. SWE has been used in thousands of clinical publications across a variety of diseases and organs including liver disease, cancer, and more.

The Vega system is designed with a linear array transducer that can measure tissue stiffness in seconds. As demonstrated in the figure below, false color SWE images are displayed on top of anatomical grayscale B-Mode images providing a window into the tissue's mechanical properties at that location. Below are four example images within a set of Computerized Imaging Reference Systems, Inc. (CIRS) calibration phantoms.
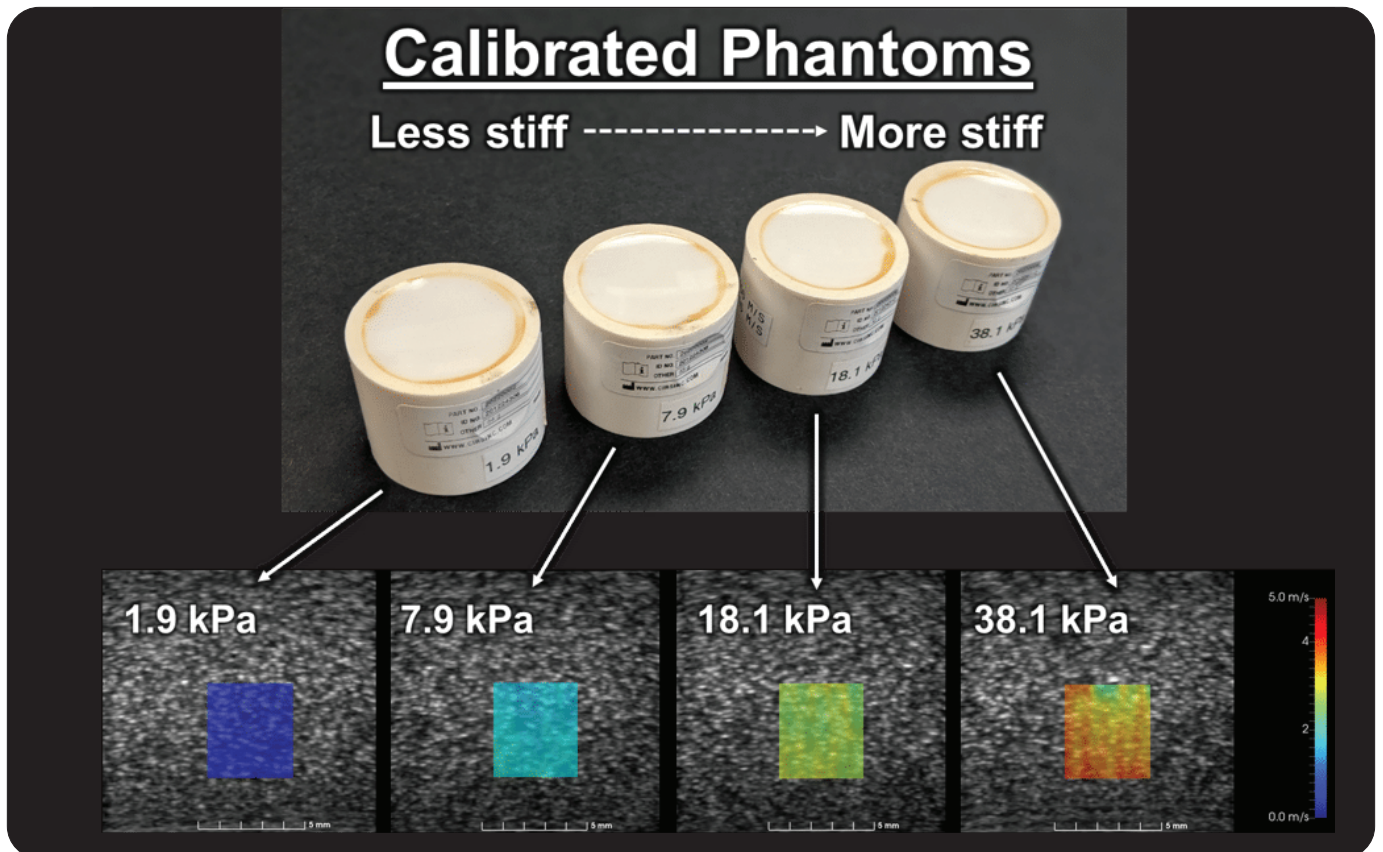
Figure 17. Shear wave velocity maps of calibrated elasticity phantoms. Through the use of calibrated elasticity phantoms which are color matched to specific levels of stiffness, researchers can obtain an elasticity modulus value, a unit to measure and quantify tissue stiffness. Grayscale is background tissue anatomical imaging, while color corresponds to underlying tissue stiffness. Units of m/s correspond to shear wave velocity (faster = stiffer).

Rapid and easy data analysis with SonoEQ™ software

Software with the goal of getting data from your images to advance your preclinical research as quickly and efficiently as possible.

Acquire, explore, quantify

- Built on 3D Slicer an open-source software platform for image processing and 3D visualization

- User-friendly, highly intuitive user interface with a fast learning curve

- Site-wide license allows user to analyze data from any location with their personal laptop

- Quantification tools include simple linear caliper measurements and complex geometrical contouring tools for abnormally shaped structures

- Data can be exported in multiple formats including 2D PNG screenshots for illustrative examples in publications or presentations, and open source MHD/MHA format for 3D datasets

Diverse ultrasound for diverse applications

There are many advantages to incorporating ultrasound into your preclinical research studies, and Vega makes it even easier to get the results you need to better understand disease states or evaluate drug candidates or therapies.

Here are some of the areas where the Vega ultrasound system can help advance your research:

- Oncology
- Developmental biology
- Liver disease
- Cardiotoxicity
- Kidney disease
- Regenerative medicine
- Cardiology
- Drug discovery and development
- Vascular disease
- Focused therapy

Figure 18. (Left) Software control panel. (Middle) Video of imaging stage. (Right) B-Mode Imaging.

Example applications using the vega ultrasound system

Oncology

- Measure tumors throughout the body, including deep orthotopic tumors
- Quantitative measurements of tumor volume in 3D even when tumors are abnormally shaped
- Easily evaluate labeled or unlabeled patient-derived xenograft (PDX) tumors

- Visualize vascularity of tumors using Acoustic Angiography Mode
  - Obtain functional information about tumor vascular supply
  - Quantitatively assess tumor microvessel architecture and density
  - Explore angiogenesis over time in response to therapy
- Complimentary to optical imaging
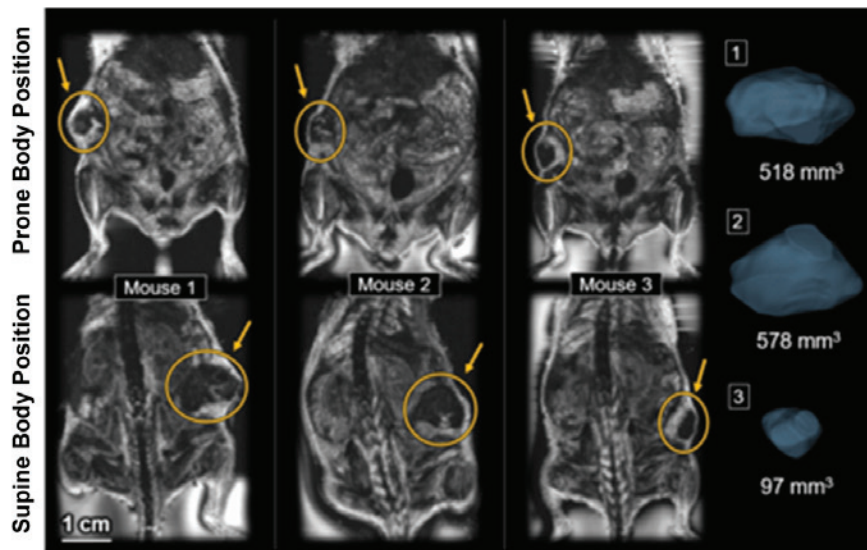
Figure 19. Coronal planes reconstructed from 3D volumetric data in three mice with subcutaneous tumors (orange arrows).
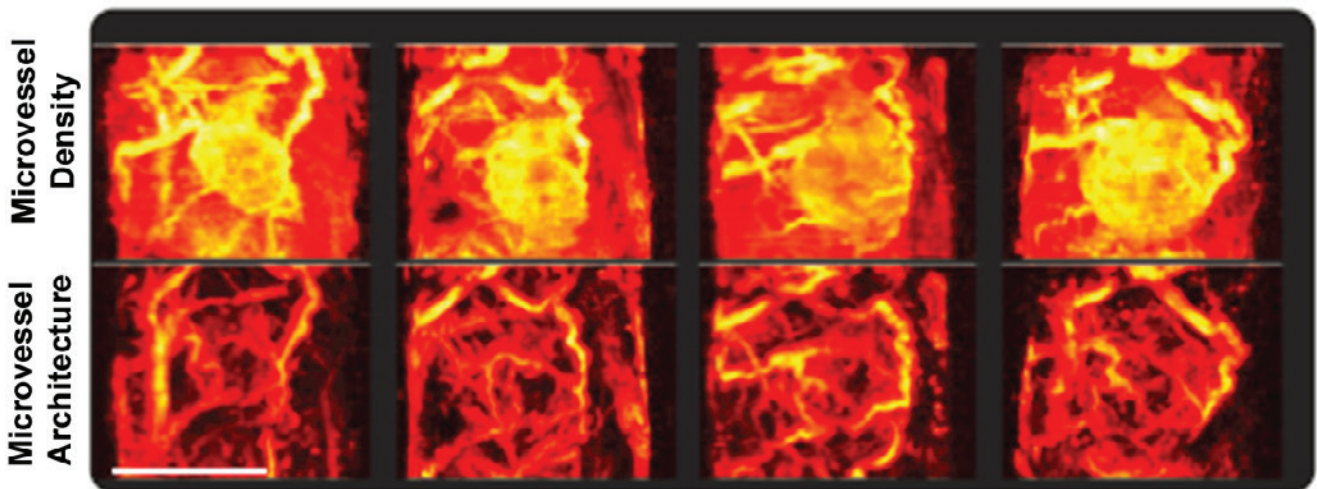

Figure 20. Acoustic Angiography used to visualize tumor microvascular supply over time. (Top) Microvessel density. (Bottom) Microvessel architecture. Scale bar is 1 cm. From: Czernuszewicz et al. (2018). A new preclinical ultrasound platform for widefield 3D imaging of rodents. Review of Scientific Instruments. 89, 075107.

Study liver disease

Liver stiffness is used as a marker for disease progression as a result of repetitive or long-lasting liver injury or inflammation to the organ causing scarring (fibrosis). Shear wave elastography (SWE) is a technique to evaluate stiffness non-invasively and can be used to monitor the onset and progression of nearly every type of chronic liver disease including hepatitis B and C, alcoholic diseases, dysmetabolic steatopathies (NASH), and biliary conditions.

Below is an example of a non-invasive longitudinal study evaluating liver stiffness using SWE ultrasound in a murine choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) model to induce NASH.
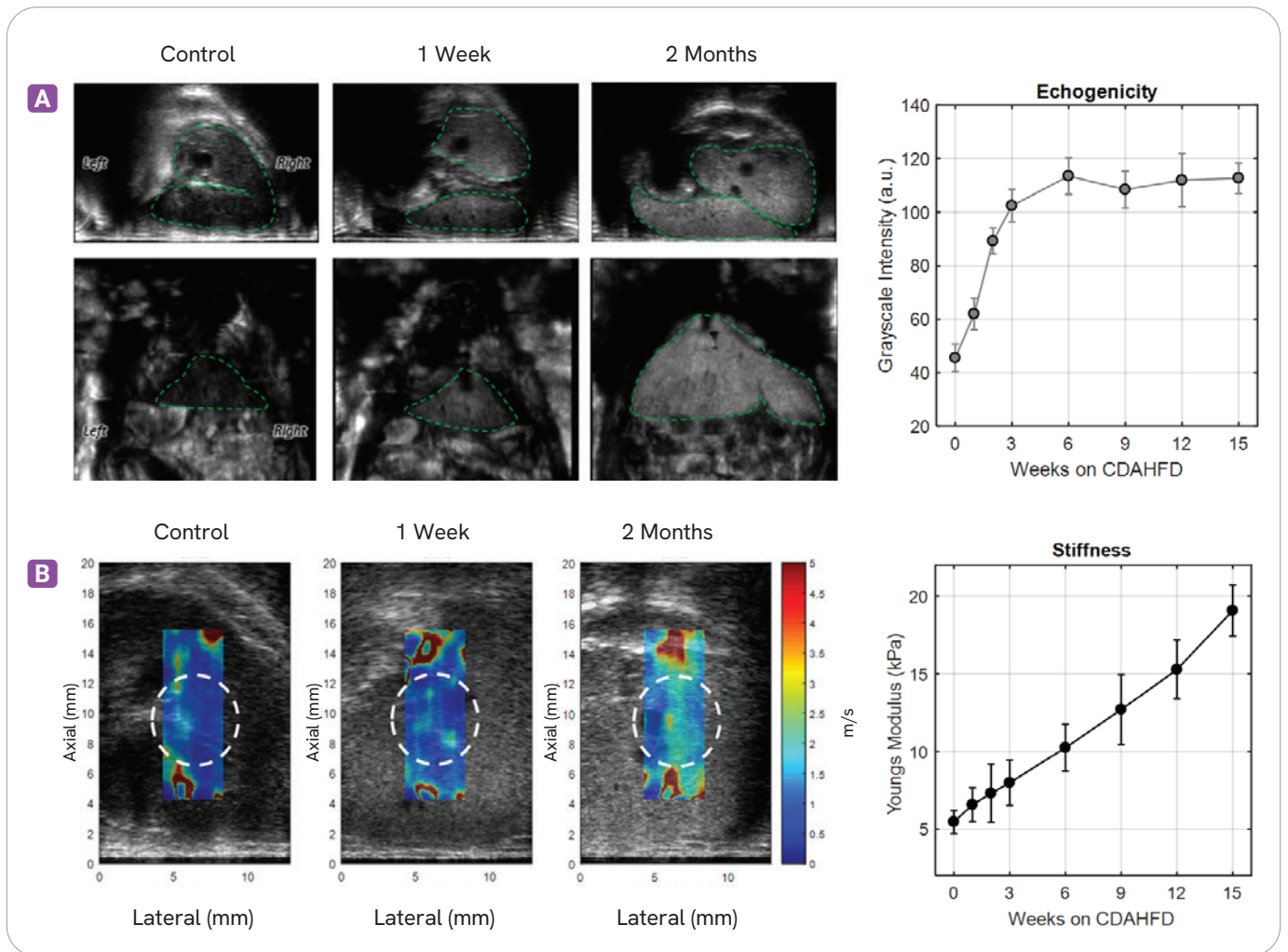
Figure 21. Longitudinal ultrasound imaging of CDAHFD mouse model used to induce NASH. (A) Axial (upper) and coronal (lower) imaging in B-Mode showing liver brightness and enlargement over time (green dash). (B) SWE colormap overlay showing an increase in liver stiffness at 2 months. (C) Graphs demonstrating echogenicity and liver stiffness over time. Note how both fat deposition (top graph), associated with steatosis and tissue stiffness (bottom graph), associated with fibrosis, can be monitored dynamically, and exhibit different onset and progression characteristics.

Evaluate cardiotoxic effects of candidate therapies

Possible side effects of various therapies are the effects they may have on cardiac function and being able to assess toxicity of drugs early in drug development is critical. The study below shows how powerful pairing optical and ultrasound imaging can be to quickly and non-invasively characterize early efficacy/biomarker changes and long-term changes in heart physiology using the chemotherapy agent 5-fluorouracil (5-FU) known to be cardiotoxic at higher doses.
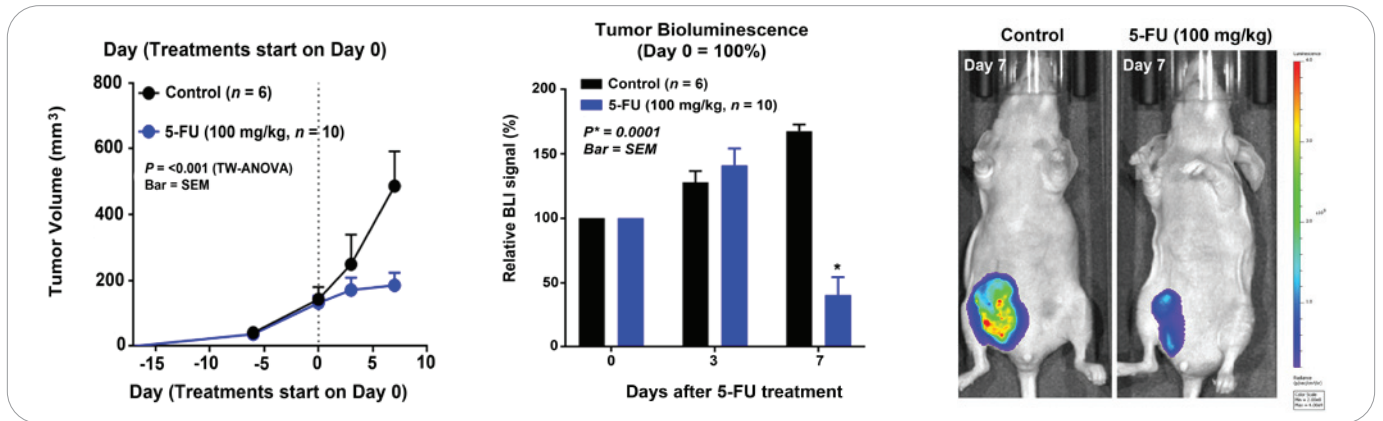
Figure 22. Mice injected subcutaneously (s.c.) with IVISbrite™ HT29 Red F-luc bioluminescent tumor cell line. (Left) Effects of 5-FU on tumor volume. (Middle) Relative tumor bioluminescence on day 0, 3 and 7 after daily 5-FU treatment start (day 0 = 100%). (Right) Representative bioluminescence images of tumor-bearing mice on day 7.
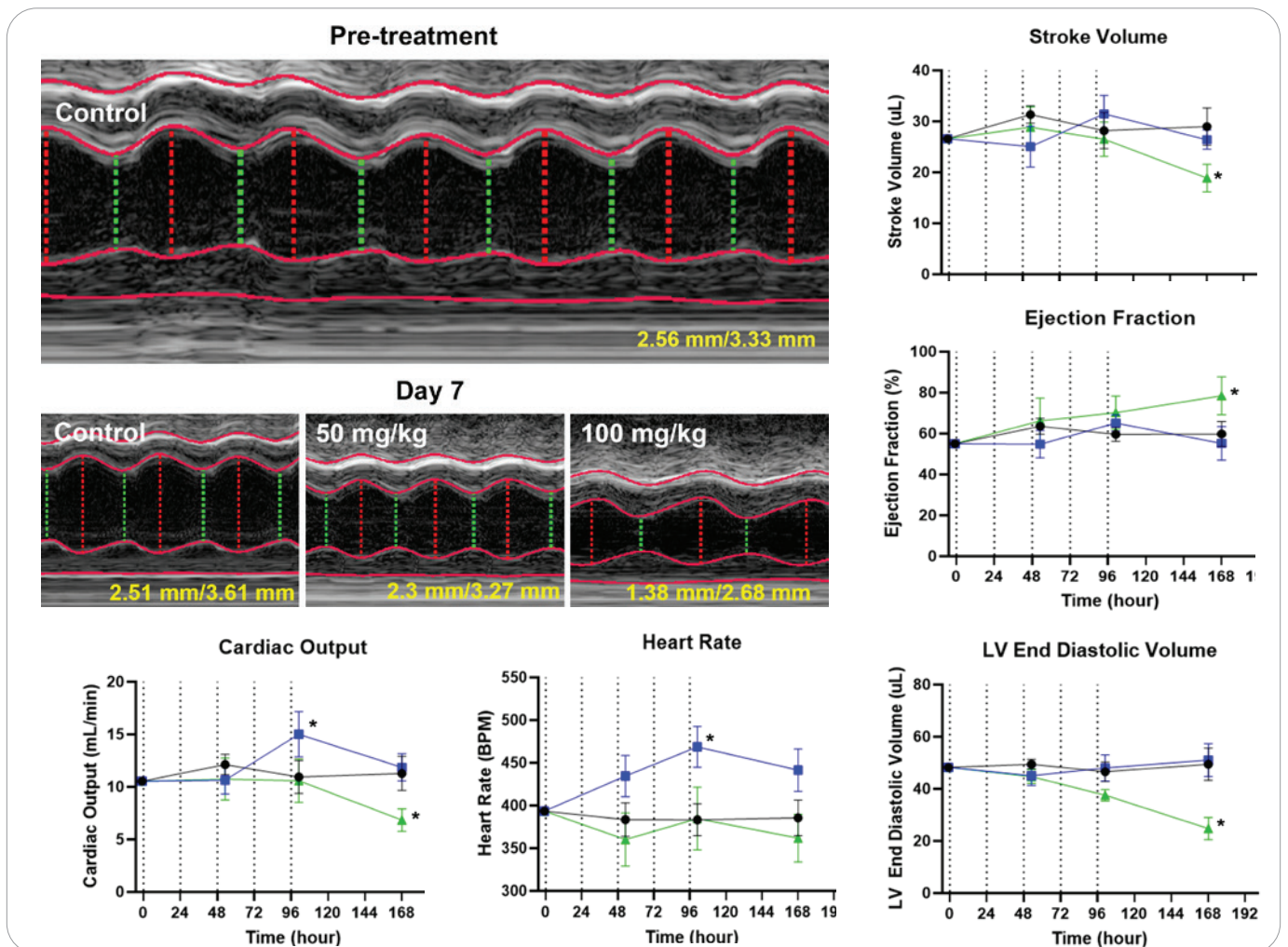
Figure 23. Mice were repeatedly treated with 5-FU. Noticeable effects of treatment in the 100 mg/kg group was observed on day 7 with the decreased internal diameter in both systole and diastole (yellow text).

The Vega ultrasound system advantages at a glance

AUTOMATED ULTRASOUND

- Enables widefield imaging → Improved FOV relative to handheld → Easier to interpret images (ease of analysis); Facilitates AI analysis of several organs
- Reduced training requirements → Minimal expertise required → Doesn't require dedicated technician
- Allows for a more streamlined acquisition relative to handheld → User can be prepping next set of subjects while the scanner is operating; Has three bays for rapid sequential scanning
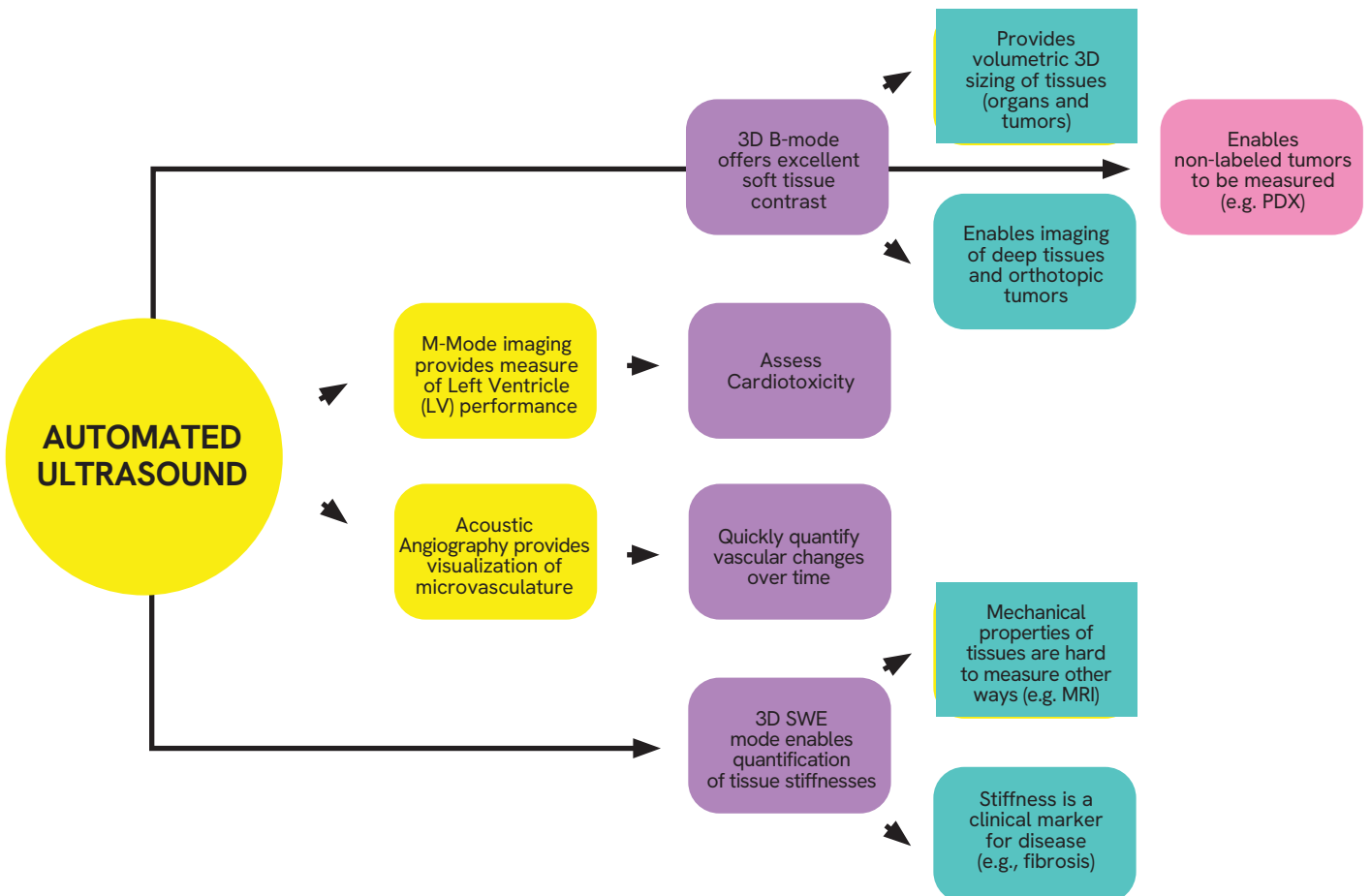
AUTOMATED ULTRASOUND

- 3D B-mode offers excellent soft tissue contrast → Provides volumetric 3D sizing of tissues (organs and tumors); Enables imaging of deep tissues and orthotopic tumors; Enables non-labeled tumors to be measured (e.g. PDX)
- M-Mode imaging provides measure of Left Ventricle (LV) performance → Assess Cardiotoxicity
- Acoustic Angiography provides visualization of microvasculature → Quickly quantify vascular changes over time
- 3D SWE mode enables quantification of tissue stiffnesses → Mechanical properties of tissues are hard to measure other ways (e.g. MRI); Stiffness is a clinical marker for disease (e.g., fibrosis)

Vega hands-free ultrasound

System Specifications	
Dimensions (D x W x H)	29 x 25 x 42 in (74 x 64 x 107 cm)
Weight	100 lbs (45 kg)
Power	100 - 120 VAC | 50/60 Hz | 15 A 220 - 240 VAC | 50/60 Hz | 10 A
Ambient Temperature	60 - 75 °F (15 - 24 °C)
Ambient Humidity	50 – 80% non-condensing
# Of Imaging Bays	3
Imaging Bay Field of View (D x W))	2.0 x 4.4 in (5.0 x 11.1 cm)

Transducers			
Ultrasound Transducers	Center Frequency (mHz)	Aperture Width (mm)	Lateral Field of View (mm)
Wobbler Single element, high-frequency wobbler	35	9	21.4
Dual-element annular array, high and low frequency wobbler	35 (high) 2 (low)	24.3	21.4
Linear Array	18	16.2	12.8

Anesthesia System Specifications	
Vaporizer and Multiplexer Dimensions (D x W x H)	6 x 15 x 13 in (15 x 38 x 33 cm)
Vaporizer and Multiplexer Weight	100 lbs (45 kg)
Number of Anesthesia Supply Ports	5
Anesthesia Supply Rates	0 cc/min (OFF) | 500 cc/min | 1000 cc/min
Oxygen Gas Supply Line Fitting	DISS Male
Active Scavenger Dimensions (D x W x H)	6 x 10 x 7 in (15 x 25 x 18 cm)
Active Scavenger Power Supply	12 VDC
Number of Active Scavenging Ports	2
Active Scavenging Range	0-10 L/min

Computer	
Power	100 - 120 VAC | 50/60 Hz | 15 A 220 - 240 VAC | 50/60 Hz | 10 A
OS	Microsoft Windows 10 (64-bit)
Processor	Minimum of 4 CPU logical cores
Graphics	Dedicated GPU with support for OpenGL 3.2 or later (1 GB is recommended)
Display	Two supported resolutions of 1920 x 1080 or 1920 x 1200
Memory	Minimum RAM of 4 GB (8 GB or more is recommended)
Mouse	Two supported resolutions of 1920 x 1080 or 1920 x 1200
Other	A PDF viewer (Adobe Acrobat Reader is recommended)

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