



Application Brief: Abdominal Aortic Aneurysm

Executive Summary

"The Vevo, as a dedicated small animal echo system, is no longer a nice to have; it is a necessity..."

- Dr. Tom Kimball

Cincinnati Children's Hospital

Abdominal Aortic Aneurysm (AAA) is a serious and potentially fatal disease that is prevalent in the older population. Scientists are making use of animal models to study the progression of this disease and the effects of therapeutic interventions over longitudinal studies.

However, AAA research in animal models has long been hindered by the lack of a fast, high-resolution, research and animal focused imaging system that can visualize vessel structure and evaluate cardiac function and blood flow *in vivo*, in real-time and most importantly, non-invasively. Luckily, VisualSonics' revolutionary Vevo® micro-ultrasound systems satisfy all the above criteria, allowing researchers to collect a plethora of important data over the lifespan of animals, thereby significantly reducing the number of animals needed. Flow velocities, vessel thickness and diameter, ejection fractions and cardiac output can be quantified within seconds, while tools such as VevoStrain™ software, provide sophisticated analysis of myocardial velocity and strain rate that are on the cutting edge of research.

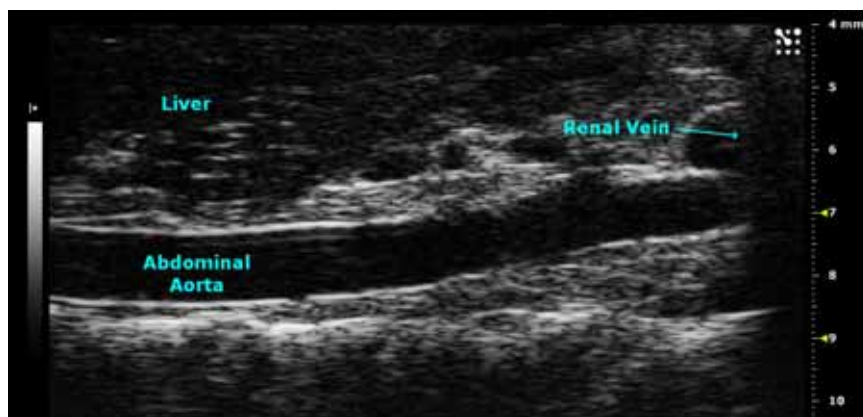
Numerous satisfied Vevo customers from institutions such as Harvard, Johns Hopkins and Oxford are publishing articles in leading journals such as Cell, Science, PNAS and Nature Medicine. This stands as a strong testament of the power and versatility of high-resolution ultrasound.

Background on Abdominal Aortic Aneurysm

Abdominal Aortic Aneurysm is a serious condition that is not only potentially lethal to patients, but also poses a serious burden on society. AAA is present in 6-10% of the population above the age of 65,¹ and when coupled with today's rapidly ageing population, is cause for extreme concern. Depending on the severity of the disease, aortic rupture may occur, causing a startling mortality rate of 90% or more.² These factors contribute to an annual death of 15,000 due to AAA in the U.S. alone.³ Clearly, the current situation demands significant research efforts to treat the disease and decrease the number of aortic ruptures cases. It is no wonder that AAA is currently one of the hottest fields in biomedical research.

Research in AAA has remained challenging despite decades of work. Much of the knowledge we have today comes from pathological specimens after surgical intervention,⁴ which is obviously not enough, since physicians remain largely incapable of altering the natural disease progression.⁵ Small animal research offers the possibility of longitudinal studies to fully understand this intractable disease. However, traditional clinical ultrasound systems are ill-suited for such purpose, offering unsatisfactory resolution and data unoptimized for researchers. Other *in vivo* imaging systems such as micro-CT or micro-MRI lack the real-time effectiveness of echocardiography to monitor and quantify blood flow, measure vessel size and thickness and track fast physiological events.

In today's research, time is of the essence. To test novel hypotheses and discover new drugs, scientists need access to an imaging modality that will grant them the ability to quickly, accurately and reproducibly measure real-time events such as blood flow and cardiac function. All of this must be accomplished with no invasiveness to the test subject, to ensure fidelity of longitudinal studies. This is where high-frequency ultrasound comes in.



Longitudinal view of abdominal aorta in normal mouse



Micro-Ultrasound in Abdominal Aortic Aneurysm

Many highly regarded researchers have published their work on AAA with help from Vevo micro-ultrasound systems. Here are two such examples to demonstrate how our systems can aid in research and publication efforts.

Leeper *et al.* from the Division of Cardiovascular Medicine in Stanford University recently published in *Am J Physiol Heart Circ Physiol* their findings of using apelin to prevent AAA.⁵ The authors sought to test if apelin could attenuate AAA by limiting vascular wall inflammation, as the peptide has been discovered to be a potent antiatherogenic inodilator.⁵ The authors used pancreatic elastase to create infrarenal AAA in C57BL/6 mice, which were treated with either apelin or saline. At the end of the experiment, it was found that apelin significantly decreased aneurysm formation, which the researchers hypothesized to be due to decreased macrophage burden.⁵ The authors were able to assess aortic diameter *in vivo* through the use of a Vevo micro-ultrasound imaging system, at the time of pre-aneurysm and 7 days after pancreatic elastase perfusion. In addition, aortic velocity was quantified using the Pulsed-Wave Doppler Mode.⁵ These functionalities were crucial to the experiment and aided the authors in discovering a potentially beneficial therapy for AAA and other vascular diseases.

Gavish *et al.* recently published in *Cardiovascular Research* of inhibiting AAA progression in apolipoprotein E-deficient mice, by using low-level laser irradiation.⁶ The authors had originally found that this method was effective at altering cellular processes fundamental to AAA *in vitro* and wanted to test the possibility of the treatment in an *in vivo* mouse model. Indeed, low-level laser irradiation prevented mice aneurismal dilation in suprarenal segments from progressing, >50% over baseline, compared with around half of control mice progressing over this threshold.⁶ The authors were able to quantify this effect using a Vevo micro-ultrasound system (30 μ m resolution), and accurately assessed parameters such as maximal supra-renal diameter and inter-renal diameter.⁶ In addition, the authors quantified radial wall velocity with advanced software on the system and found a substantial effect on arterial wall elasticity by the treatment. The authors also concluded that this study, together with several other validation studies, showed high-resolution ultrasound as being both accurate and reproducible in measuring AAA in living mice, including effects of treatments and surgical manipulations over time.⁶

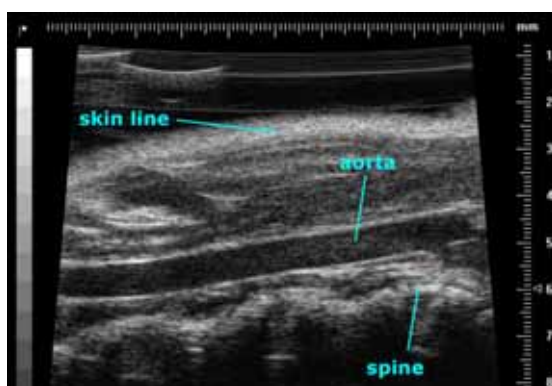
Many other cardiovascular researchers have been using Vevo micro-ultrasound systems to take their research to higher levels. To view a list of top papers, please consult the document titled **VisualSonics Bibliography 2010 – Cardiovascular Research.**



VisualSonics' Value Proposition

With the Vevo micro-ultrasound systems, researchers now have access to a system to visualize small animals in real-time and *in vivo*, with images rivaling MRI quality.⁷ Below is a summary of the unique value proposition VisualSonics delivers to researchers with these high-frequency, high-resolution ultrasound systems:

1. **Non-invasive, *in vivo* imaging.** This is especially useful for imaging physiological developments over a period of time, such as abdominal aortic aneurysms.
2. **High-resolution (30 μ m) imaging** to observe murine models in the clearest detail, such as the abdominal aorta and vessel walls.
3. **Real-time imaging (up to 1000 frames per second).** Monitoring flow rates, ejection fractions and cardiac output in anesthetized or conscious animals has never been so easy.
4. **Advanced cardiovascular software**, such as Color Doppler Mode and EKV™ software allow flow velocity, direction and regurgitation / disturbances to be accurately, reproducibly quantified.
5. **Cutting-edge strain analysis** with the VevoStrain software, which quantifies longitudinal, circumferential and radial strain and strain rate, including velocity and displacement within the myocardial wall.
6. **3D visualization of vessels** provides the researcher with powerful tools for presentation or publication.
7. **Dedicated animal platform** to monitor ECG, heart rate, body temperature and respiration rates. Our systems are specifically designed for preclinical researchers.



Longitudinal view of abdominal aorta in normal mouse



Vevo 2100 Micro-Ultrasound Imaging System

References

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