# WEBINAR: How High Frequency Ultrasound Imaging is Supporting Preclinical Research Applications

**Questions and answers from the March 20, 2019 webinar titled "How High Frequency Ultrasound Imaging is Supporting Preclinical Research Applications"**

This document includes questions we received and answered during the webinar, as well as those that we did not have time to address. Questions have been grouped into relevant categories.

*Prospect T1 System Hardware and Software Capabilities*

1. **Can a keyboard and mouse be attached to the tablet to make data input and measurements on the system easier?**

   Yes, the tablet is a 15-inch touch screen display, which works with gloves on. However, if you prefer to work with a traditional mouse and keyboard, which may be easier for image labelling and measurements on the system, then these can be connected to the tablet. Additionally, there is an offline software analysis package which would allow you to do all the image labelling and measurements on your own computer after the images are already acquired.

2. **What data formats can be exported?**

   Data may be saved and also exported in a variety of formats:
   - Raw data may be saved for more advanced analysis purposes
   - Cine loop images can also be saved at the time of acquisition. Measurements and other data export can be completed on this type of data, as is also the case on Raw data.
   - You can choose BMP, JPG, TIF or PNG file formats for still image export
   - Videos may be exported as AVI files
   - DICOM data may also be exported from the system

3. **What is the max range, and minimum step size of the 3D motor?**

   The maximum range of the 3D motor is 30mm, with a minimum step size of 0.05mm. These settings are both adjustable based on your requirements.

4. **What is the maximum frame rate in B-mode?**

   In traditional B-mode imaging, the maximum frame rate is 30 frames/second. However, for cardiac applications there is a post processing reconstruction mode in which images can be reconstructed up to 190 frames/second, and an entire cardiac cycle will be displayed.

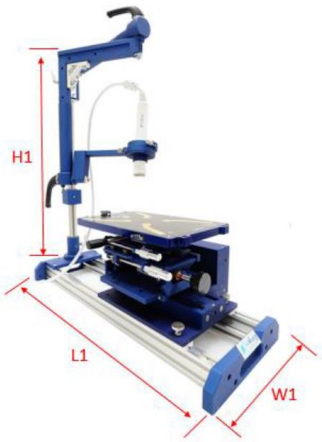
5. **At what sample rate are M-mode images acquired?**

   For M-mode, the 1D data is acquired at 35000 scan-lines/sec.

6. **What are the dimensions of the system?**

   The Tablet (which is mounted on a stand) has the following dimensions and weight: 36x28x65 cm (LxWxH); 5kg

   The scanning platform which holds the animal table and probe has the following dimensions and weight: 60x23x60 cm (LxWxH); 12kg



7. **Will the body weight of mice or rats being imaged affect the images such as for echocardiography, for example in extremely obese mice?**

   The weight can affect the images being collected. Using cardiac imaging as an example, the heart may be further from the transducer than in a smaller animal. The option would be to either move the probe closer to the skin, or switch to the lower frequency probe if required to get better depth of penetration of the signal. There is also the capability of adjusting the sound frequency with both probes slightly lower to provide better penetration; therefore, it may be sufficient to use the same probe to image an obese mouse heart as well as smaller animal.

8. **Can a nose cone be attached to the stage for inhaled anesthesia, such as isoflurane?**

   Yes, a nose cone can be attached to the stage for inhaled anesthesia. There is currently a small clip on the stage to clamp the gas delivery tubing onto the stage with any nose cone of your choosing. The team at S-Sharp can also provide a clip which would allow for tubing used for active/passive scavenging to be incorporated with the system.

*Prospect T1 System Features*

9. **Is ECG and Respiratory gating possible?**

   The mouse and rat tables provide physiological parameters which can be used for ECG and respiratory gating.

10. **Does the animal still need to be anesthetized to perform the imaging?**

    Traditionally, the animal is anesthetized to perform the imaging as this helps to acquire nice still images. However, you can handhold the probe and scruff the animal to acquire the images if you like.

11. **What Doppler modes are available on the Prospect T1?**

    The Prospect T1 comes standard with Pulsed Wave Doppler, Color Doppler, and Power Doppler to measure blood flow; the system also comes standard with Tissue Doppler to look at the movement of tissue for example at the mitral annulus.

*Cardiovascular Research*

**12. Is a fusion of E and A waves related to resolution of probe or heart rate of rat?**

The fusion of the E and A peaks in the PW Doppler spectrogram is a function of timing rather than resolution of the probe.
As the heart rate increases the relaxation of the ventricle, which causes the inflow of blood from the atrium (E peak), and the contraction of the atria to push the rest of the blood through the valve (A peak) begin to happen almost simultaneously.
The spatial resolution of the probe will not affect the ability to resolve these two events in time.

*Cancer Biology*

**13. How sensitive is the system for detecting micro/macro metastases throughout the body of the mouse?**

The 40MHz probe can be used to image most anatomical targets within the mouse; the exception being the brain and the lungs as ultrasound cannot see through bone or air. This probe has a resolution of 30µm; to be confident that you are visualizing a lesion in a specific organ of interest it would need to be 300-500µm in diameter to have confidence in differentiating it from the normal surrounding tissue.

**14. Is there any way to detect the temperature of a treated tumor by using Prospect T1 system?**

With ultrasound imaging there is currently no way that we are aware of to be able to detect a temperature change. It may be possible to use the RAW data to do this, but it requires further investigation.

**15. Both high and low frequency ultrasound can be used as a therapeutic approach for cancer treatment. Do you have any thought on delivering focused ultrasound to a specific tumor and monitor the changes?**

This is a very active area of research in cancer research. For imaging purposes, the power of the ultrasound is controlled to specifically have minimal or no effect on the tissue, making it ideal for imaging. For a therapeutic approach, an increased power, or modulation of sound wave, would be necessary to cause changes within the tumor. Changes in the tumor could be monitored using ultrasound imaging to see changes in growth or perfusion, if contrast agents were used.

**16. Can you explain in a bit more detail the tissue/tumor perfusion work you discussed using contrast agents?**

Contrast agents are used to study perfusion through smaller blood vessels than can be detected using Power Doppler. Contrast agents from ultrasound are typically a microbubble; this is some type of biologically compatible shell (lipid, albumin, etc.) and gas. The gas helps to reflect the sound, and the bubbles are small enough to pass freely through the capillary bed. In this way we are able to detect their presence as they flow through the image.

Microbubbles may be non-targeted, that is to study perfusion; or targeted, that is to study molecular targets accessible to the blood pool on the endothelial cell surface. The contrast agents are typically injected IV and will perfuse throughout the animal. There are two ways to detect the contrast agent:

1) Reference subtracted – this is where a baseline reference image is taken on your 2D image, and this is used to subtract from the cine loop image that is acquired when the contrast agent is injected. This will create a false color overlay (green) that is displayed on the cineloop to show where the contrast agent is detected.

2) Harmonic imaging – this is a contrast agent specific mode in which the 20MHz transducer is used to detect the harmonic signal coming back from the contrast agent (would come back at 40MHz). This is a more specific way to detect the contrast agent.

Quantification can be performed by drawing various regions of interest on the image to generate a time vs. intensity graph. This can be used to study the perfusion within the region of interest.

*Abdominal Imaging*

**17. Have you used any imaging tools to assess fatty liver disease?**

We have not specifically done this work, however the RAW data format (the RF data from the image being acquired) could be analyzed further to detect differences between normal and fatty liver.

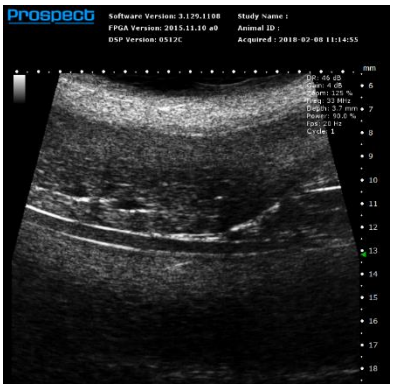
*Other Anatomical Imaging Target*

**18. Is it possible to image optic nerve?**

The optic nerve is quite small and sits deeply behind the eye. This is not an anatomical target that we have attempted to image in the past and may be challenging.

**19. Is it possible to image peripheral nerves?**

We have an example of the system imaging the sciatic nerve in the rat:




By identifying a variety of anatomical targets, including nearby blood vessels (which can be highlighted using Doppler techniques), we can develop confidence in identifying the peripheral nerve structures.

**20. Can this system be used to image flows around or near implanted medical devices such as LVADS (Left Ventricular Assist Devices)?**

The challenge with medical devices is the materials that they are made from. If they do not allow the ultrasound signal inside, or they are a very strong reflector of the ultrasound signal, then detecting flow in and immediately on the outside will prove difficult. However, in the nearby areas, Doppler can be used to visualize blood flow in larger vessels, or contrast agents could be used to detect the presence of flow in smaller blood vessels.

*Developmental Biology*

**21. Is there a probe designed, or that could be used to image neonatal aged pups (i.e. P1 to P7)?**

With this specific system, the smallest probe (40MHz) is 2.6cm in diameter and is round in its shape. We have not tried this on the specific sized pups that you mention. I can understand the challenges in trying to work with the small neonates. We have been able to image developing embryos prior to delivery using all of the imaging modes.

*Other Animal Model*

**22. A lot of the animals you spoke of are small. Can this be used in larger animals (goat, pigs, bovine, etc.)?**

This system, and its probes have been designed for use on small animals, however the main limitation is not animal specific, but more depth of penetration. The probes may be hand held to image a variety of animals, samples, and targets. When considering larger animals, the location of the anatomical target becomes important. For example, imaging the skin or superficial structures should not be a problem, whereas deeper structures like the heart will be a challenge.

*Shear Wave Elastography*

**23. Would the shear wave elastography be able to detect mechanical or elastic changes in the heart?**

At this point, the 20MHz push probe used to create the shear wave is designed for superficial targets such as the liver and musculoskeletal targets. The heart, being a deeper target with rapid movement, would require some advanced techniques to get this working.

**24. Can shear wave elastography be applied in 3D?**

At this point, the 3D motor is not linked to the shear wave elastography component. You are able to move the stage manually, in small increments, using the micro positioning knobs on the stage. In this way you could manually complete multiple 2D shear wave images throughout the organ.

25. **Can the instrument make quantitative elastography measurements?**

    Yes, the software creates a color map of the elastogram which is displayed over the B-mode image. The scale of this color map relates to the calculated shear wave velocity, and regions of interest can be drawn to generate quantifiable data.

*Pricing Information*

**26. What is the cost of the system?**

The system cost entirely depends on the configuration. Variations come into play depending on the animal model being used for imaging, additional components for multiple species (i.e. mouse and rat), add-ons like the 3D motor or image guided injection mounts, and of course the shear wave elastography or sonoporation add-ons.

The system does come standard with all the imaging modes discussed during the webinar (the measurement package, etc.) so there are no additional charges there. Please reach out to discuss more about your research so we can more accurately provide pricing.