Scintica: INSTRUMENTATION

WEBINAR: Bedside to Bench: How Clinical Imaging of Patients with COVID-19 is Informing Preclinical Investigations

Questions and answers from the August 26, 2020 webinar titled "Bedside to Bench: How Clinical Imaging of Patients with COVID-19 is Informing Preclinical Investigations"

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.

General Imaging Questions

1. **How are motion artefacts handled in MRI and CT imaging, specifically when multi-modal imaging includes PET (i.e. PET/MRI and/or PET/CT)?**

   This is a good question, and different systems handle motion artefacts in different ways. Generally, motion artifacts are minimized both during the scan, and can be further reduced in post processing.

   Initially, measures are taken to prevent motion artifacts. Motion is inherent to *in vivo* lung imaging; cardiac motion is always present and breathing motion can be handled by acquiring images within breath-holds, a technique known as respiratory gating (or triggering). On both the Aspect Compact MRI system and the Sedecal PET/CT system, respiratory gating is available to reduce the effect of artifacts due to breathing. For neuroimaging

applications, both systems have integrated bite bars in their animal handling systems to reduce head motion during the scan.

Many post-processing techniques are available to reduce any residual motion artifacts. On the Aspect system, VivoQuant is available to co-register images within modalities (i.e. registering multiple MRI acquisitions over time), or between modalities (registering PET images acquired with the Brightonix SimPET insert to MRI acquisitions). This software has been optimized for use between the two systems and thus co-registration is available directly within the console. Similarly, the Sedecal PET/CT system also uses VivoQuant to co-register images within and between modalities to reduce motion artifacts.

Additionally, these systems use standard data formats and thus multiple third-party software packages are available to further process these images.

2. **What possible radioligands can be used to image COVID-19?**

There are many possible radioligands which may be used in lung imaging of COVID-19. In the examples shown throughout the presentation, the most commonly used radio ligand was ^{18}F - FDG (Fluorodeoxyglucose), This glucose analogue can be used to highlight the areas of increased metabolic activity in the lungs. This increase in metabolic activity is most often associated with an inflammatory response. ^{13}NN can be used to measure lung ventilation, perfusion, and ventilation/perfusion mismatch, either using a bolus injection or inhalation. To date, ^{13}NN PET has been applied small clinical asthma and COPD studies. Lesser known radioligands such as ^{68}Ga-Citrate ^{11}C-PK11195 can also be used to image infection in the lungs. In all cases, selection of the

ligand is specific to the underlying process, time course, and anatomical location being imaged in the study.

3. **Have other imaging modalities been used clinically to investigate COVID-19 patients?**

During the webinar examples of CT and MRI were shown, CT to examine the lungs, and MRI to show changes in the brain. Additionally, PET images were shown, where a routine oncology follow-up scan incidentally found changes in the lung which were later confirmed to be from COVID-19. A verbal note was also made during the webinar that planar chest x-ray is the most common modality used for clinical COVID-19 assessment of the lungs. This is because it is rapid, uses low radiation dose compared with CT, and it is portable. CT was covered more in depth during the webinar because its high-resolution structural information can provide a deeper understanding of COVID-19 infection in the lungs.

Ultrasound is an area of debate at the moment, as it's utility in imaging pleural effusion or other changes in the lungs, which may be associated with COVID-19 is not clear. Utilizing ultrasound to image other organ systems and vasculature is possible, including the heart to look at cardiac function, and the veins for deep vein thrombosis. There has yet to be a lot of published data on the use of ultrasound in COVID-19 patients, however its utility would be appropriate in these situations. Its utility can also be challenging in clinical settings of active COVID-19 because it requires direct patient contact.

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Scintica Instrumentation Product Questions

4. **Can any of the imaging products offered by Scintica Instrumentation be used in a BSL-3 environment?**

Yes, all of the imaging systems we offer are well suited to be placed within a BSL-3 containment facility.
Compact MRI – specifically the M-Series systems from Aspect imaging are permanent magnets, which are self shielded. What this means in a BSL-3 environment is that no additional infrastructure is required to site the system, and other laboratory equipment and tools can be placed right next to the system with no safety concerns. Being a permanent magnet means that no cooling is required, that is no liquid helium or water is used to dissipate the heat which is created in superconducting magnets that use electricity to generate the magnetic field. This means that there is minimal yearly maintenance, and no need to decontaminate a tremendous amount of water that would be generated in some other systems on the market.
This system can also be combined with a PET insert to increase the imaging capabilities and applications of the device.
A containment imaging cassette is being developed to allow animals to be sealed off from the outside environment throughout the imaging session, if inhaled anesthesia is being used then a HEPA filter is inserted inline with the gas delivery and exhaust.

PET/CT – specifically the Super Argus systems from Sedecal are self-shielded so again, no additional infrastructure is required to cite these instruments safely. This system can be configured with a containment vessel for the animals to be sealed off from the outside environment throughout the imaging session, if inhaled

anesthesia is being used, then a HEPA filter is inserted inline with the gas delivery and exhaust.

High Frequency Ultrasound – specifically the Prospect T1 system from S-Sharp is a very compact system which can fit within the busiest of labs. The imaging platform can be disinfected between imaging subjects, along with the probe.

Optical Imaging – specifically the Newton 7.0 system from Vilber is a well-equipped optical imaging system capable of bioluminescence, 3D tomography, and fluorescence. An optional isolation chamber is available to seal the infectious animals off from the outside environment through the imaging session. If inhaled anesthesia is being used, then a HEPA filter is inserted inline with the gas delivery and exhaust.

5. **What sequences are available on the M-Series compact MRI system that Scintica offers?**

The following pulse sequences, procedures and protocols are available on all the preclinical M-Series systems with updated electronics and the "One Product" software.

Available Pulse Sequences:

- **Spin Echo (SE)**
- **Fast Spin Echo (FSE), 2D and 3D**
- **Gradient Echo (GRE), 2D and 3D**
- **Inversion Recovery modules for Gradient Echo, Spin Echo and FSE**
- **FSE with Dixon water/fat separation**
- **FSE with cardiac/respiratory trigger**
- **Gradient echo with cardiac/respiratory trigger**
- **Gradient echo cardiac Cine**
- **FSE Single-shot and segmented diffusion imaging**
- **Diffusion weighted imaging (DWI)**

Procedures:

Procedures are pulse sequences that are combined with dedicated post-processing routines.

- **Water/fat separated images (based on Dixon FSE)**
- **T1-mapping (based on 2D Inversion-recovery gradient echo 'snapshot')**
- **ADC (apparent diffusion coefficient) mapping (based on FSE diffusion imaging)**
- **FA (fractional anisotropy) mapping, based on FSE DTI (diffusion tensor imaging)**
- **SWI (susceptibility weighted imaging)**

Protocols:

In general, sequences and procedures can be executed with a wide range and combination of acquisition and processing parameters. These parameters can be varied to adjust for contrast, SNR (signal to noise ratio) and spatial resolution.

Some generic protocols for T1-weighted and T2-weighted imaging on mice and rats are pre-installed on the systems as they leave the factory. The detailed list of these pre-installed protocols is of limited significance. That is because protocols which are tailored to the specific needs and applications of each customer can easily be created during the applications training.