Webinar Q&A Report

A New Frontier of Precision Medicine: Using PET for Image-Guided Neurointerventions

Questions in this Q&A Report were submitted during the live webinar, A New Frontier of Precision Medicine: Using PET for Image-Guided Neurointerventions.

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1. How do MRI and two-photon microscopy compare to and complement PET for this research?

P. Walczak, M. Janowski, W. Lesniak: MRI provides anatomical background as well as it allows to predict which territory therapeutic agent will be injected. However, it uses surrogate gadolinium-based contrast agents, whose distribution in the brain might be different compared to actual drug due to different physicochemical properties such as size and lipophilicity. As discussed during our seminar, it is very difficult to label therapeutic agents for MRI and it is not quantitative.

Two-photon microscopy facilitates visualization of injected agents with microscopic resolution.

Limitations of two-photon microscopy are very small field of view and restricted depth of imaging. Also, it is not clinically applicable.

PET is a highly sensitive and quantitative but low resolution modality, so all three methods are complementary and help us to understand mechanisms of drug delivery to the brain and its retention, providing crucial information on therapeutic response.

2. Is it possible to do real-time PET?

P. Walczak, M. Janowski, W. Lesniak: Obviously, it is possible to acquire data in real-time and post-process, but so far algorithms for reconstruction and quantification of data in real-time are not available. Our PET scanner can collect data in dynamic mode (as we have shown during the seminar) and in list mode, which collects data continuously, and you can see the distribution of radioactivity in real-time.

T. Coulthard: Yes, it is possible to do real-time PET. The SuperArgus offers a minimum temporal resolution of 2.5 millisecons; with list mode acquisition the user may choose how to reconstruct the images with whatever temporal resolution is desired. In addition to real-time imaging, the SuperArgus state-of-the-art electronics allows for conscious/awake imaging using fiducial markers. Again a list mode acquisition is performed and the software can use the fiducial markers during image reconstruction to create either a single 3D image, or a dynamic set of 3D images over time.

3. Can you measure two radioisotopes at the same time?

P. Walczak, M. Janowski, W. Lesniak: You can measure two gamma-emitting radioisotopes by SPECT, or one gamma-emitting radioisotope by SPECT and positron-emitting radioisitope by PET. For PET imaging, it must be that one radioisotope produces additional gamma radiation such as 89Zr, and the second does not such as 18F or 11C. As for now, you cannot visualize 18F and 11C together.

T. Coulthard: Yes, multiplex PET imaging is possible on the SuperArgus system. When doing multiplex PET the user must choose a standard radioisotope which traditionally gives off double coincidence events, such as fluorine, carbon, and oxygen, as well as a non-standard radioisotope which traditionally gives off a triple coincidence, such as copper, technetium or iodine. The software is then able to deconvolve the images on reconstruction.

4. How does focused ultrasound (fUS) of the blood-brain barrier opening compare to mannitol/artery cannulation?

P. Walczak, M. Janowski, W. Lesniak: In general, fUS opens BBB for a longer period of time (which is good or bad, depending on your application) and it is probably more difficult to avoid

brain damage, especially in small animals. Also, thickness of the skull plays role in fUS and it is difficult to optimize delivered energy to avoid brain damage.

However, if intra-arterial route is found to be more effective for the delivery of specific molecules and a catheter is introduced in cerebral vessels for drug injection, then it is natural to pre-inject it with mannitol for BBB opening. Adding fUS in this setting would add complexity. On the contrary, when a drug is injected systemically, fUS may be advantageous, as it offers superior special selectivity.

5. How does transferrin receptor-mediated delivery compare to arterial delivery?

P. Walczak, M. Janowski, W. Lesniak: It is difficult to say. In general, the use of transferrin receptor is associated with considerable toxicity as it is also expressed by immune cells. The reported increase is up to 10-fold, which is rather modest considering extremely poor brain accumulation after systemic delivery. Delivery of the drugs to the brain via transferrin is very inefficient; at best it can reach 1–2% of the injected dose.

6. How do you measure immunoreactivity of nanobodies, antibodies and dendrimers after surface modification?

P. Walczak, M. Janowski, W. Lesniak: At this stage we are primarily focused on optimizing labeling efficiency and ensuring that labeling does not affect drug activity. For that we use ELISA, but you can also use *in vitro* cell binding.

7. What is the uptake of your isotype control?

P. Walczak, M. Janowski, W. Lesniak: In our studies, the injected macromolecules had no targets in a mouse brain, so the experiments themselves should be considered as isotype controls.

8. What is the success rate of the intra-arterial delivery method itself with regards to surgical training in mice?

P. Walczak, M. Janowski, W. Lesniak: It strongly depends on the experience and skill of a surgeon. Some master it within a month, and others will never manage it as vascular microsurgery is complex. With good training and skills the success rate is nearly 100%. The surgical and imaging procedure should last no more than 30-40 minutes, and if longer the complications are precipitating. In general, it is much easier to do it in humans than in mice… :)

Contact Information

If you have additional questions Scintica Instrumentation regarding content from this webinar, or if you would like to receive additional information about their products and laboratory services, please contact them by phone or email:

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