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INSTRUMENTATION

Questions & Answers

WEBINAR:

Seeing Double: Preclinical Multiplexed PET for Dual Isotope Imaging

Questions and answers from the September 13, 2023, webinar titled "Seeing Double: Preclinical Multiplexed PET for Dual Isotope Imaging"

This document includes questions we received and answered during the webinar, as well as those that we did not have time to address.

1. **Would it help to have energy resolution that could discriminate the "extra" gamma and just use the two actual annihilation photons for the image but still know which radionuclide is which?**

   In a in a perfect world, if we had a triple emitter that was perfect, a triple coincidence. Then yes, that would totally work. We have the energy discrimination where we could see this is a triple event and it is let's say 700 K EV and then there's just the five elevens. We have a lot of radionuclides that only emit triple in a certain percentage. And so that's where we really need this sensitivity correction to account for the doubles that will show up in our list mode that are actually from the triple Emitter. For us to leverage that is we acquire a mixture of these two radioisotopes on the scanner prior and then we actually can get that. Basically, sensitivity maps out to understand what is that bias that we have from that.

2. **What's the limit on activity in MBq that mPET can cope with? How do you deal with randoms compared to double randoms?**

   The point of those phantoms that we we used were really to contain, 0 amounts or low becquerel counts, although obviously for preclinical scanner they're high for a clinical scanner. So, in terms of how low we can go, it really comes down to what type of isotope we're using in that case. So, I really can't say definitively, it's like x-mega becquerels. But I think the other thing to keep in mind is that the geometry of your scanner is also very important too, because every radionuclide combination that's going to have a different number of randoms and double randoms just based

upon the type of emissions that are present in from those radionuclides. So, it's hard to say definitively just which one to use, but the key is that we can experimentally acquire that data with a prior scatter phantom and just kind of know what our limitation is.

3. **Can mPET also do more than 2 isotopes if you compare it to flow cytometry?**

   mPET as we published is a dual isotope. So, I mean maybe not a very, you know, informative flow cytometry plot, but the hope and the vision is that you can really add in with the energy discrimination as I mentioned from a list mode scan, then you can really get into, five, six, eight color kind of images. Now that may sound ridiculous and in some ways it also means you have to make five, six, eight different radio tracers at the same time or apply them in the same or correct window for your imaging, so that does get very complicated, but I think that's kind of where I want to move people a little bit is understand that there is heterogeneity in our systems and adding in at least the second color is going to be very important enough for our own research needs.

4. **Since this tech is based on refining the reconstruction file of the PET scan, does this tech stick to a specific scanner or brand of scanner, for instance, Siemens?**

   So no, the beauty of it is that list mode is just list mode. So as long as you as an individual has access to a scanner that collects list mode that you're able to copy and send - let's say to Joaquin or you could process locally in the future, that's the only thing you need. So, if you don't have list mode access, I think that's where you know it would be nice to have a conversation with a vendor to see if that is somehow possible. So, I think that's the key here is that it's not machine specific. It really can be used for any machine that has a list mode and, some of the things that we've done, like for example, with the Inveon, it may work in older scanners too. We just haven't tested it. So that's The thing, if you have list mode data, it could very well work and Joaquin's very happy to help you find that as well.

5. **Are we already in a resolution we could see tissues hypoxic regions nuances among cells or Tumor microenvironment?**

Part of the resolution also comes into things like time of flight of the actual positron. So, for using things like a copper 64 based hypoxia imaging agent versus an 18 F based hypoxia imaging agent, we could probably get different nuances of resolution. But in terms of our needs for multiplex PET, there shouldn't be any difference. But at the same time, though, I think the real good question is will that second marker be the one you want to image hypoxia and then some other agent with that too? What are the two that give you some interesting biological, you know answer you know to your study.

6. **Is mPET transferrable to other systems apart from Siemens Inveon? The service for the Siemens µPET systems will end soon.**

We kind of hit on this before it's not machine specific. This is more of a reconstruction method. So as long as you have a system with a list mode that can add in the coincidences and especially - I should also mention too that if coincidences of triples are recorded differently, we can also reconstruct that. We just have to figure out how to parse the data set. The key is just having the list mode available, the reconstruction can be done the same. So, it's really just finding that original list mode data set and making sure that you when you acquire the data, it has the sufficient ability to capture the most triples without getting too much of the randoms and secondary randoms as we mentioned before.

7. **If for instance, we collect - and this I guess would be counterintuitive to the whole idea of mPET. But if we collect data with a double coincidence emitter first and then on that same animal, maybe a day after we collect with a triple coincidence emitter. Could we somehow overlap that list mode data in a pre-reconstruction and like time stamp it across those two scans.**

In practice, that's what we've been doing with PET traditionally. We've been using one isotope that is quickly decayed to get our image A and then we wait to get image B. In general, I've never seen a spliced together list mode, and I can see there's also consequences of doing that later for clinical use. But, for right now for as an individual, I mean, I think the key is that you almost don't have to, you could just take the two data sets alone and use

multiplexed PET on them and you can just then collect the double from that one image and then for the 2nd acquisition with the triple emitter, you just collect the triple and then go from there. So, I think there's no reason why you couldn't just process those twice. Instead of time to splice them in, especially now since we've got GPU processing systems, time is not exactly as critical as it could be. I know with the clinical setting we'd like to keep it short so there could be a few reiterations to get a quick image and then more of an analytical reconstruction later, for the proper diagnosis maybe. That's a good question about moving data sets back and forth, but there's a lot in those list mode data sets that we don't even get to tackle, so it's a wealth of knowledge really.