WEBINAR:

Imaging Hypoxia

1. **for imaging richly vascularized organs (heart, lung) in non-cancer models of hypoxia, which approach would you recommend?**

   I would suggest using either ultrasound or photoacoustic imaging. With ultrasound you could use either doppler or microbubbles to image the vasculature. With PAI, you can also image vasculature and measure oxygen saturation. Additionally, both modalities have reporter genes that could be used to acquire a more indirect measurement of hypoxia based on gene expression/transcription.

2. **What do you think of EPR oximetry?**

   EPR imaging is another great option that we didn't have time to get into during today's webinar. Recent developments in EPR imaging have really improved image acquisition time, sensitivity and the overall accuracy of oxygen measurements. However, there are still some challenges that have limited its widespread use. These include poor SNR, limited depth penetration especially at high frequencies and the requirement of an exogenous probe.

3. **Do you think these hypoxia imaging can be used for kidney cancer? Especially using PET for orthotopic implantation, I'm worried about high background signaling. If you could comment on other imaging modalities for kidney cancer too, that'd be awesome.**

   I do think PET would be feasible. See the paper below where they used FMISO in a mouse model of kidney cancer. However, the washout time and background levels will definitely need to be considered for your specific model.

   https://jnm.snmjournals.org/content/jnumed/52/7/1048.full.pdf

   Many groups prefer MRI for studying hypoxia in various models of kidney cancer. See an example below that uses OE-MRI

   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6122194/

Alternatively, something like optical imaging may be worth considering if you are worried about background. You could engineer your cancer cell line to express a luciferase under hypoxic conditions and perform bioluminescence imaging. In this case, you would only get signal from hypoxic cancer cells and should not have any background signal.

4. **Thanks for your nice presentation. My question is a bit off-target from your presentation on imaging hypoxia, but I'm curious what your thoughts might be on the future prospects for hypoxia selective prodrugs that target highly potent anticancer agents to regions of profound hypoxia, as found in many tumors?**

   Yes, I think this is a really exciting area of research that shows a lot of promise in the clinic. It provides a way to target hypoxic, less-responsive cell populations, without potentially compromising surrounding healthy tissue. Some recent concerns that have come to light in recent studies are the window of opportunity for these therapies as some evidence shows that hypoxic cells may only live 2-3 days in vivo prior to becoming necrotic. This would suggest imaging could play a very important role in determining the optimal treatment schedule. Micro-metastases and tumor cells in ascites may be another suitable target for HAPs.