Biomere

COMMUNITY BLOG

IMAGING TUMORS IN PRECLINICAL ANIMAL MODELS

Imaging methodologies are critical in the diagnosis and prognostic monitoring of solid tumors in humans. Methods such as CT (computed tomography), MRI and PET are widely used in humans and these methods have continued to improve in terms of resolution, sensitivity and data analysis. More recently, the use of AI enablement was reported to improve detection of different solid tumors including skin, breast and head and neck[1]. Additionally, the combination of different imaging modalities such as MRI and PET have been shown to increase accuracy of tumor detection[1]. The use of imaging methods to noninvasively detect and monitor tumors in preclinical oncology animal models is becoming more widespread especially due to the translational value of the protocols, tracers and data analysis methods[2]. Similar to humans, multi-modal preclinical imaging can be used to obtain data on various tumor characteristics including size, morphology, metabolic activity, vasculature and inflammation[2].

Preclinical imaging methods can be segmented into the following types: MRI, CT, ultrasound, photoacoustic (PAT) imaging, PET, SPECT and optical imaging (fluorescent and bioluminescent imaging)[2,3]. MRI is considered the gold standard of imaging modalities and has been shown to have the best tissue resolution that can be enhanced with specific tracers[2]. Additionally, there are various subtypes of MRI that are tailored to measuring specific characteristics – for example, tissue oxygen levels can be measured via functional tissue oxygen-level dependent MRI that could be used to monitor response to radiotherapies[2]. The use of contrast agents such as gadolinium chelate allow the visualization of changes in blood vessel architecture in tumors and there are ongoing studies to use gadolinium-based agents to identify cell surface receptors in tumor cells[2]. Certain imaging methods are more suited for specific tissues types – for example, CT imaging is the optimal method to identify lung lesions due to excellent contrast between air and tissues[2]. Clinically, ultrasound imaging is the method of choice to detect pancreatic cancers in both human and animal models. Preclinically, ultrasound is also sued used to guide orthotopic model development by helping researchers inject cells in the correct tissue space[2] and can be combined with PAT imaging to provide physiological data on the tumor. The basic principle of PAT imaging uses short laser pulses to irradiate tumor tissues leading to heat induced tissue expansion that creates acoustic waves[4]. The acoustic waves can be measured using ultrasound[4].

PET imaging is used to monitor physiological changes in metabolic activity, vasculature etc. and uses radiolabeled tracers such as ^{18}F-fludeoxy-glucose (FDG) to monitor glucose uptake in tumors. Since tumors are more metabolically active than surrounding tissues, ^{18}F-FDG PET imaging is a useful method to monitor tumor size and evaluate changes in tumor metabolism after therapeutic intervention[5]. While ^{18}F-FDG is the most well-known tracer, PET imaging can be performed using multiple radiopharmaceutical tracers and some of the tracers can also be used for SPECT imaging which uses a gamma camera instead of a positron emission scanner. One of the key advantages of using PET and SPECT imaging is that radiolabeled tracers can be used to monitor specific reception expression levels or physiological markers[2]. For example, ^{18}F-fluorothymidine can be used to monitor DNA synthesis and cell proliferation in tumors. Given the huge focus in immune-oncology, "immuno-PET" has emerged as a specific imaging method where antibodies to select receptor targets or T-cell targeting molecules can be labeled with radiopharmaceutical tracers to monitor the response to specific checkpoint inhibitor therapies[2,5]. One such reported tracer is a ^{64}Cu-labeled Axl antibody that was used to monitor the efficacy of an hsp90 inhibitor (17-AAG) to downregulate Axl regulation in triple negative breast cancer[6].

In vivo optical imaging methods such as fluorescent and bioluminescent require the insertion of a fluorescent tag or a luciferase enzyme into tumor cells or the therapeutic modality[2]. The tags can be inserted into microbes, viruses, antibodies, peptides etc. so noninvasive luminescent imaging is an easy way to track tumor cells or therapeutic modalities in an animal model. While several fluorescent proteins are used in preclinical studies, one challenge is autofluorescence in specific tissues that can obscure or interfere with the fluorescent signal[2]. Bioluminescent imaging using luciferase reporters has gained significant traction in preclinical *in vivo* studies and there is active research to engineer more sensitive luciferase enzymes that have more catalytic activity and improved emission signals[7].

In summary, there are several imaging modalities that are available to noninvasively monitor tumor development and therapeutic responses can be translate well to the clinic.

References:

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8945965/
[2] https://aacrjournals.org/cancerres/article/81/5/1189/649702/Preclinical-Applications-of-Multi-Platform-Imaging
[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3687654/
[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6515147/#
[5] https://www.itnonline.com/article/role-pet-imaging-preclinical-oncology
[6] https://pubmed.ncbi.nlm.nih.gov/29097911/
[7] https://pubs.acs.org/doi/10.1021/acschembio.1c00549