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Development of DNP-MRI visualizing alterations of kidney cancer-associated genes

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Abstract

Kidney cancer is a complex disease, originated from a variety of nephron cells under alterations of various kidney cancer-associated genes, most of which are associated with metabolic pathways, and an incomplete development of imaging modalities frequently leads to under- or over-treatment for each patient in both surgical and drug therapies. Here, we present our recent strategy for the development of metabolic imaging modalities, which may classify kidney cancers based on metabolic alterations. DNP-MRI using C13-labelled metabolites successfully displayed metabolic alterations in our PDX library established from various kidney cancer specimens. Of note, the renal tumor with deficiency of fumarate hydratase *(FH)*, an enzymatic gene in TCA cycle, displayed an increased flux from C13-labelled pyruvate into C13-labelled lactate, whereas the renal tumor with deficiency of folliculin *(FLCN)*, a critical regulator for mitochondrial biogenesis, displayed a decreased flux. Our aim is to integrate those imaging data with multi-omics data from WGS, WES, RNA-seq, single cell RNA-seq and spatial RNA-seq analyses and develop imaging modalities, which may non-invasively identify altered kidney cancer-associated genes in each tumor as well as delineate intra-tumor heterogeneity developed in each patient.