Title: Quantitative Hybrid PET/CT for Cancer Imaging: Diagnosis and Monitoring Treatment Response

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Structured Abstract:
Cancer is the leading cause of death in Canada. Nearly 1 in 2 Canadians is expected to be diagnosed with cancer in their lifetime. (Canadian Cancer Statistics, 2018). Hybrid PET and CT imaging is a newer imaging modality which allows contemporaneous PET metabolic/molecular imaging using tracers that target specific aberrant metabolic or molecular processes in the tumour and CT anatomical imaging with or without contrast during a single diagnostic session on a single device. However, current hybrid PET/CT cancer imaging has relied heavily on measuring the tracer accumulation in the tumour as a surrogate of the pathologic activity targeted by the tracer or tumour size measurement, both of which lack sensitivity and specificity in detecting cancer and assessing treatment response. Therefore, it is critical to develop quantitative techniques for assessing the physiologic/molecular characteristics of tumours with clinical PET/CT scanners to improve clinical decision made based on such imaging results.

We hypothesized that quantitative hybrid PET/CT imaging could sensitively diagnose cancer and monitor its treatment response. Based on the availability of patient cohorts from existing clinical trials, my PhD research focused on prostate and lung cancer. Patients with histologically confirmed cancer were evaluated using dynamic PET imaging with appropriate tracers and CT Perfusion (CTP) with iodinated contrast agent to evaluate the metabolic and pathologic molecular activity and perfusion in tumours.

In the prostate cancer (IGPC-2) study, 23 and 19 patients were evaluated with dynamic 18F-FCH/CTP or 18F-DCFPyL/CTP, respectively. The most sensitive parameter set to localize and detect prostate cancer is Ki (plasma net uptake rate) and k4 (dissociation rate constant) of 18F-DCFPyL with sensitivity, specificity, PPV, NPV, and AUC of 0.84, 0.95, 0.94, 0.86 and 0.93 respectively. BF (blood flow) and MTT (mean transit time) from CTP also showed promising results with sensitivity, specificity, PPV, NPV and AUC of 0.84, 0.84, 0.84, 0.84 and 0.93 respectively.

In the lung cancer (MISSILE) study 26 patients with early stage non-small cell lung cancer were evaluated with dynamic 18F-FDG and CTP before and after neoadjuvant stereotactic ablative radiotherapy (SABR) to assess imaging response and the results correlated with pathological evaluation. BVpre-SABR (baseline blood volume) and relative change in SUVmax was shown to be the most sensitive model to predict complete pathological response with sensitivity, specificity, PPV, NPV and AUC of 0.85, 0.92, 0.92, 0.86, and 0.92 respectively.

In conclusion, our studies show that quantitative functional parameters from dynamic PET and CTP can detect cancer and predict treatment response with acceptable performance metrics.