Investigation of [F-18]Fluoro-L-Thymidine with PET to Assess Radiotherapy Response

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With the rapid growth of positron emission tomography (PET) in the field of oncology, there is a great need for cancer-specific radiopharmaceuticals. The standard oncology radiopharmaceutical, ^{18}F-fluorodeoxyglucose (^{18}F-FDG), is based glucose metabolism and used for the detection and staging of many types of cancer. However, ^{18}F-FDG is far from specific to tumor sites and its uptake in macrophages as well as in granulation and inflamed tissues hinder effective assessment of radiotherapy response. ^{11}C-thymidine has been used to image cellular proliferation *in vivo* for twenty years, but degradation of the tracer in the body means that arterial blood sampling is needed to do metabolite analysis for image correction. Also, the short half-life ($t_{1/2}$ = 20 minutes) of carbon-11 limits ^{11}C-thymidine scanning to sites that have a cyclotron and radiochemistry lab nearby. A thymidine analog labeled with fluorine-18 would resolve the problems associated with ^{11}C-thymidine PET. To that end, ^{18}F-fluoro-L-thymidine (^{18}F-FLT) has been developed to provide a measure of cellular proliferation *in vivo* using PET.

Existing synthetic methods of ^{18}F-FLT production were implemented using three different precursors: 2,3'-anhydrothymidine, 5'-O-(4,4'-dimethoxytrityl)-2,3'-anhydrothymidine and 3-N-*t*-butoxycarbonyl-[5'-O-(4,4'-dimethoxytrityl)-2'-deoxy-3'-O-(4-nitrobenzenesulfonyl)-β-D-*threo*pentofuranosyl]thymine. Once implemented,

various parameters were adjusted in an attempt to increase the radiochemical yield. A microwave "steeplechase" was performed in order to test the abilities of three different single mode microwave cavities. The winning microwave cavity was then used in ^{18}F-FLT syntheses to increase the decay-corrected radiochemical yield in comparison to conventional heating. Once the chemistry was reliable enough to provide single study quantities of ^{18}F-FLT, the ability to assess radiotherapy response using ^{18}F-FLT was explored in a canine model. The animals were imaged before and during radiotherapy treatment to see if ^{18}F-FLT could measure early response to the anti-cancer treatment using SUV and Patlak analysis techniques.