

Improved cardiovascular risk stratification with PET: [¹⁸F]*meta*-fluorobenzylguanidine as a potential cardiac radiotracer

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Background and Hypothesis:

Cardiovascular disease is the leading cause of death in the United States each year, exceeding 600,000 deaths and costing over \$200B. Sympathetic dysfunction in cardiac tissue has been shown to occur in patients with recent cardiac injury or longstanding disease. The SPECT radiotracer, *meta*-[¹²³I]iodobenzylguanidine (MIBG), has been used to image neuroendocrine tumors as well as global cardiac sympathetic tone through the human norepinephrine transporter-1. We will determine the utility and improved imaging the PET radiotracer *meta*-[¹⁸F]fluorobenzylguanidine (MFBG) can afford in cardiac care. MFBG has shown several improvements over MIBG in neuroendocrine tumors but has proven difficult to reliably synthesize.

Project Methods:

A novel synthetic pathway of MFBG utilizing copper accelerated Sandmeyer fluorination conditions is being developed to streamline its radiosynthesis from seven manipulations and an unstable precursor to four with more stable intermediates.

We also explored where MFBG may be useful in cardiology by performing a literature review through the PubMed MeSH database published after 2010.

Results:

We have developed a new MFBG precursor in one step from commercially available compounds and a one-pot automated radiosynthesis is currently in development. This improves upon current methods and may provide increased clinical availability of MFBG for future studies.

MIBG has shown prognostic value for the incidence of severe cardiac events but cannot provide any local innervation data. The PET radiotracer, [¹¹C]hydroxyephedrine, can display local denervation within the myocardium. However, its 20.3 minute half-life prevents its widespread use beyond hospitals with direct access to a radiochemistry laboratory. To our knowledge, no cardiac imaging has been investigated using MFBG.

Conclusion and Potential Impact:

We believe MFBG could provide similar improvements to cardiac imaging as in neuroendocrine tumors. With a novel synthetic method being developed, we hope to begin pre-clinical imaging studies and provide future cardiologists with a new prognostic imaging modality which can direct personalized care to patients with cardiovascular disease.