

Researchers investigating how to make PET imaging even sweeter

13 January 2014

An international research team led by Mount Sinai Heart at Icahn School of Medicine at Mount Sinai, is testing its novel sugar-based tracer contrast agent to be used with positron emission tomography (PET) imaging to help in the hunt for dangerous inflammation and high-risk vulnerable atherosclerotic plaque inside vessel walls that causes acute heart attacks and strokes.

Their findings, reported Jan. 12 in *Nature Medicine*, investigate the possible advantage of the proposed imaging agent, fluorodeoxymannose (FDM) sugar-based tracer in comparison to fluorodeoxyglucose (FDG), the current glucose-based tracer widely-used in patients undergoing PET imaging.

"Our pre-clinical testing shows that PET imaging with the radiotracer FDM may potentially offer a more targeted strategy to detect dangerous, high-risk plaques and inflammation that may be associated with serious cardiovascular events," says Jagat Narula, MD, PhD, the principal investigator for the study who serves as Director of the Cardiovascular Imaging Program at The Mount Sinai Hospital, and Associate Dean of Global Health at Icahn School of Medicine at Mount Sinai.

Glucose forms the source of main energy supply in the human body and in the radiolabeled form FDG it has been traditionally used for the identification of atherosclerosis. Valentin Fuster, MD, PhD, the Director of the Mount Sinai Heart and Physician-in-Chief of The Mount Sinai Hospital, was one of the earliest investigators to use FDG for the detection of atherosclerosis.

A known biomarker for high inflammation in arterial plaque is the presence of an abundant level of macrophage cells. Macrophage-rich inflammation lining the artery walls filled with plaque is known to be associated with increased risk of heart attack and stroke. "Macrophage cells have a very high metabolic demand for sugars and are dependent

on the exogenous source of sugars, and that's why the sugar-based tracers are able to identify the inflamed or dangerous plaques," according to Dr. Fuster.

"Although the research team's investigations of the FDM tracer shows that it performs comparably to the traditional FDG tracer, it is expected that the new sugar tracer may have an advantage to more specifically target inflammation because the plaque infiltrating macrophages develop mannose receptors (MRs)," according to Dr. Narula.

Co-author Jogeshwar Mukherjee, PhD, and his team of radiochemists at the University of California, Irvine had labeled the FDM with Fluorine-18, which like glucose enters the cells through glucose transporters. The current study results show mannose is taken up by a specific subset of macrophage cells that dwell in high-risk plaques, which have developed the mannose receptors. This may represent the theoretical advantage of FDM over the FDG tracer. These macrophages called "M2" within atherosclerotic plaques, tend to overly express MRs, and are especially common in inflamed and hemorrhagic arterial lesions.

In the study FDG and FDM were compared using PET imaging in atherosclerosis animal models. While uptake of each tracer within atherosclerotic plaques and [macrophage cells](#) were similar, according to the researchers the experimental FDM tracer showed at least a 25 percent higher FDM uptake advantage due to MR-bearing macrophages.

"The FDM binds to MR-bearing macrophages while FDG does not bind to the MR receptors. This specific binding provides clinically relevant avenue why FDM uptake in high-risk plaques should be further investigated," says study co-author Zahi Fayad, PhD, the Director of the Translational and Molecular Imaging Institute at Icahn School of

Medicine at Mount Sinai. Researchers also observed FDM uptake occurred in the presence of atherosclerosis and almost none in non-atherosclerosis control models.

"We are excited about our possibly sweeter imaging breakthrough, but further research and clinical trial testing will need to confirm its potential advantage," stresses Dr. Narula.

"The labeling of FDM is cumbersome and the yield of radiolabeled material is extremely low; the labeling methodology would need to be perfected," Dr. Mukherjee cautions.

Provided by The Mount Sinai Hospital

APA citation: Researchers investigating how to make PET imaging even sweeter (2014, January 13) retrieved 12 November 2019 from <https://medicalxpress.com/news/2014-01-pet-imaging-sweeter.html>

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