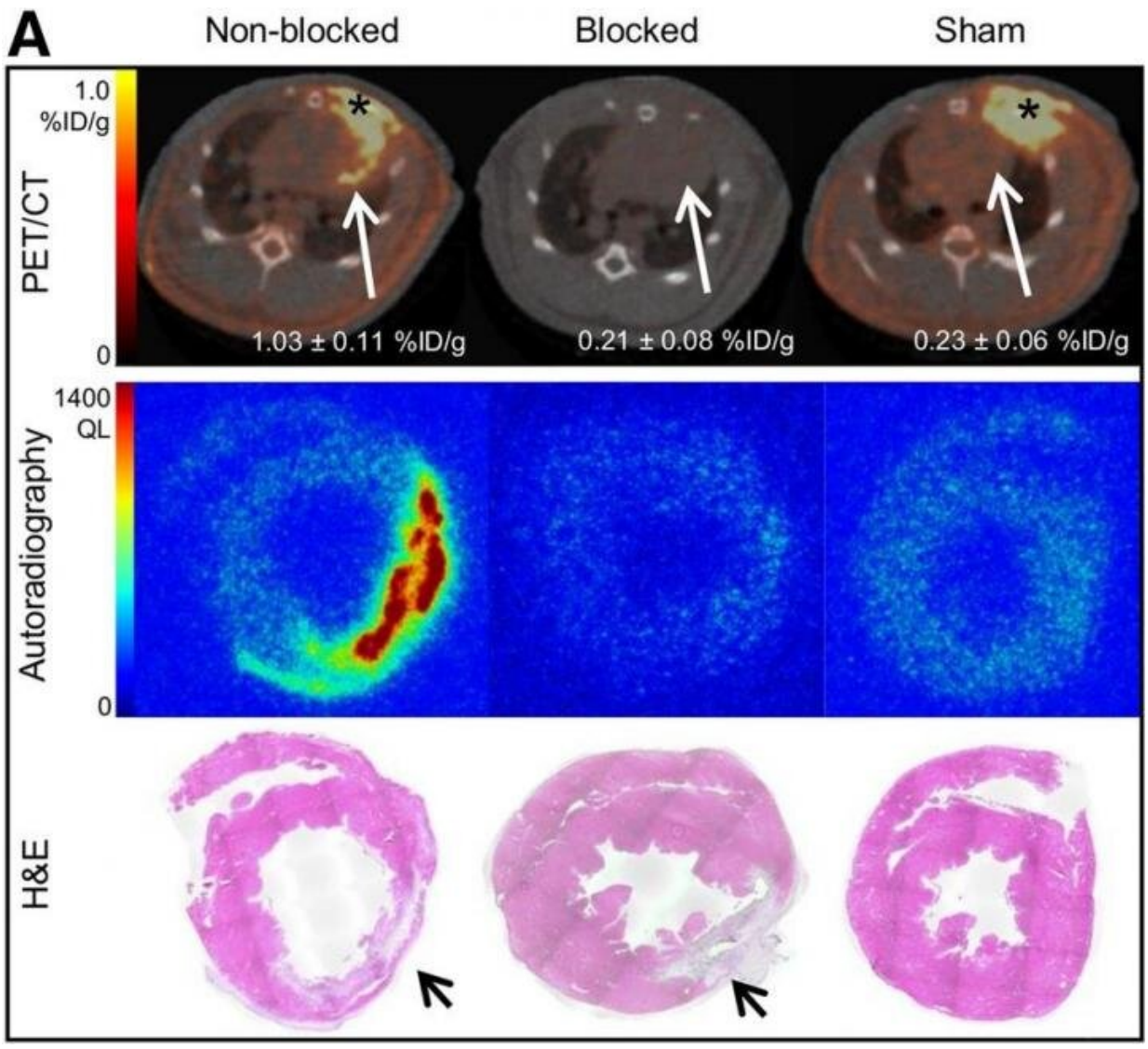
New radiotracer offers opportunities for earlier intervention after heart attack

January 3 2020



Binding specificity test. (A) PET/CT axial views, autoradiographs, and corresponding H&E stainings of 10-micron cross-sections prepared from MI

nonblocked, blocked, and sham-operated rats. Autoradiographs and H&E stainings from nonblocked hearts show increased Ga-68-FAPI-04 uptake in infarcted area at 7 days after MI, whereas uptake is negligible after sham operation or injection of nonlabeled FAPI-04 (blocked). Infarcted areas in H&E stainings are identified with arrows. (B) PET image-derived infarct-to-noninfarct uptake ratio (derived from 6 nonblocked and 3 blocked rat hearts subjected to coronary ligation). (C) Autoradiography image-derived infarct-to-noninfarct uptake ratio (derived from 3 nonblocked and 3 blocked MI hearts). QL = quantum level. Credit: Z Varasteh and S Robu, Department of Nuclear Medicine, Klinikum rechts der Isar der TUM, Munich, Germany.

Insights into how the heart recovers after myocardial infarction (heart attack) can be obtained with a new radiotracer that targets fibroblast activity prior to it causing permanent damage. According to research published in the December issue of The *Journal of Nuclear Medicine*, 68Ga-FAPI-04 positron emission tomography (PET) can effectively image fibroblast activation after myocardial infarction, identifying a time window during which cardiac fibrosis can be prevented and the disease course altered.

After a heart attack, fibroblasts play an important role in tissue replacement, preserving the structural integrity of the heart. However, excessive fibrosis can lead to increased left ventricle stiffness and decreased cardiac contraction. As heart failure remains a major source of late morbidity and mortality after a heart attack, study authors sought to evaluate the feasibility of imaging activated fibroblasts after myocardial infarction using a novel 68Ga-labeled fibroblast activation protein (FAP) inhibitor.

"We know that the temporospatial presence of activated fibroblasts in the injured myocardium predicts the quality of cardiac remodeling after a heart attack," noted Zohreh Varasteh, Ph.D., research fellow at

Klinikum rechts der Isar der TUM in Munich, Germany. "Therefore, imaging of activated fibroblasts using 68Ga-FAPI-04 PET may have significant diagnostic and prognostic value, which could aid in the clinical management of patients after myocardial infarction."

The preclinical study included 20 rats subjected to myocardial infarction by permanent ligation of the left anterior descending coronary artery, as well as four sham-operate rats that underwent the same procedure except the ligation. *In vivo* imaging with 68Ga-FAPI-04 PET was performed at one, three, six, 14, 23 and 30 days after the myocardial infarction and with 18F-FDG three days after myocardial infarction. Dynamic 68Ga-FAPI-04 PET and blocking studies were performed on the myocardial infarction rats on day seven. *Ex vivo* imaging, autoradiography, histologic studies and immunofluorescence staining were also conducted to validate results of *in vivo* imaging.

Researchers found that uptake of 68Ga-FAPI-04 PET peaked six days after ligation and decreased rapidly to the background level by two weeks after infarction. Uptake accumulated mainly at the border zone of the infarcted myocardium, with high contrast and minimal uptake in normal myocardium. Minimal uptake was noted in rats that received a blocking dose of non-labeled FAPI-04. The exact location of the 68Ga-FAPI-04 uptake was confirmed by *ex vivo* imaging, as well as autoradiography and histologic findings.

"While preclinical development of potential anti-fibrotic approaches is far advanced, there has been little clinical validation due to the lack of sensitive and specific imaging technologies for assessing cardiac fibrosis progression or regression. In this regard, 68Ga-FAPI-04 PET has emerged as an important tool for the detection of fibrotic processes in the efforts to improve heart failure therapy," Varasteh said.

Varasteh continued, "In the future, these advances in imaging may also

be applied to other conditions associated with the activation of fibroblasts, such as hypertension, ischemic, dilated and hypertrophic cardiomyopathies, cancer therapy-related cardiotoxicity, liver cirrhosis and pulmonary fibrosis."

More information: Zohreh Varasteh et al, Molecular Imaging of Fibroblast Activity After Myocardial Infarction Using a 68Ga-Labeled Fibroblast Activation Protein Inhibitor, FAPI-04, *Journal of Nuclear Medicine* (2019). DOI: 10.2967/jnumed.119.226993