

# IMAGES IN PULMONARY, CRITICAL CARE, SLEEP MEDICINE AND THE SCIENCES

## *In Vivo* Thrombosis Imaging in Patients Recovering from COVID-19 and Pulmonary Embolism

Rong Bing<sup>1</sup>, Jack P. M. Andrews<sup>1</sup>, Michelle C. Williams<sup>1,2</sup>, Edwin J. R. van Beek<sup>2</sup>, Christophe Lucatelli<sup>2</sup>, Gillian MacNaught<sup>2</sup>, Tim Clark<sup>2</sup>, Norman Koglin<sup>3</sup>, Andrew W. Stephens<sup>3</sup>, Mark G. MacAskill<sup>1</sup>, Adriana A. S. Tavares<sup>1</sup>, Kevin Dhaliwal<sup>4</sup>, David A. Dorward<sup>4</sup>, Christopher D. Lucas<sup>4</sup>, Marc R. Dweck<sup>1</sup>, and David E. Newby<sup>1,2</sup>

<sup>1</sup>British Heart Foundation Centre for Cardiovascular Science, <sup>2</sup>Edinburgh Imaging, and <sup>4</sup>Centre for Inflammation Research, University of Edinburgh, Edinburgh, United Kingdom; and <sup>3</sup>Life Molecular Imaging GmbH, Berlin, Germany

ORCID IDs: 0000-0002-8305-4906 (R.B.); 0000-0002-7523-0295 (C.D.L.).

<sup>18</sup>F-GP1 is a novel radiotracer that binds to the platelet glycoprotein IIb/IIIa receptor and can image *in vivo* venous and arterial thrombi, including deep vein thrombosis and pulmonary thromboemboli (1–3). We performed <sup>18</sup>F-GP1 positron emission tomography–computed tomography in six patients recovering from coronavirus disease (COVID-19) with concomitant pulmonary embolism (median age 56 [interquartile range, 53–60] years, one female, five requiring supplemental oxygen, no intensive care admissions) and undertook <sup>18</sup>F-GP1 autoradiography of postmortem lung tissue in three patients who had died from COVID-19 (4).

All patients demonstrated increased pulmonary <sup>18</sup>F-GP1 uptake at a median of 69 (interquartile range, 56–98) days after index presentation despite ongoing therapeutic oral anticoagulation. Focal intravascular uptake in persistent pulmonary embolism (Figure 1A) was seen, as described previously (1). However, we also noted parenchymal uptake in regions of consolidation (Figure 1B) as well as systemic uptake in an occluded saphenous vein coronary artery bypass graft and left ventricular thrombus, which was subsequently confirmed on echocardiography (Figure 1C). <sup>18</sup>F-GP1 autoradiography also demonstrated focal and specific uptake colocalizing to intravascular thrombus in patients with confirmed diffuse alveolar damage (Figure 1D).

Protracted systemic and pulmonary thrombosis may be a feature of COVID-19 that can persist despite systemic therapeutic anticoagulation. <sup>18</sup>F-GP1 is able to detect pulmonary and systemic arterial thrombosis and has potential applications across a broad range of pathologies. ■

**Author disclosures** are available with the text of this article at [www.atsjournals.org](http://www.atsjournals.org).

### References

- Kim C, Lee JS, Han Y, Chae SY, Jin S, Sung C, *et al*. Glycoprotein IIb/IIIa receptor imaging with (18)F-GP1 positron emission tomography for acute venous thromboembolism: an open-label, non-randomized, first-in-human phase 1 study. *J Nucl Med* 2018;60:244–249.
- Chae SY, Kwon TW, Jin S, Kwon SU, Sung C, Oh SJ, *et al*. A phase 1, first-in-human study of <sup>18</sup>F-GP1 positron emission tomography for imaging acute arterial thrombosis. *EJNMMI Res* 2019;9:3.
- Lohrke J, Siebeneicher H, Berger M, Reinhardt M, Berndt M, Mueller A, *et al*. (18)F-GP1, a novel PET tracer designed for high-sensitivity, low-background detection of thrombi. *J Nucl Med* 2017;58:1094–1099.
- Dorward DA, Russell CD, Um IH, Elshani M, Armstrong SD, Penrice-Randal R, *et al*. Tissue-Specific Immunopathology in Fatal COVID-19. *Am J Respir Crit Care Med* 2021;203:192–201.

Ⓢ This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License 4.0. For commercial usage and reprints, please e-mail Diane Gern.

Supported by the British Heart Foundation (RG/16/10/32375, RE/18/5/34216, and PG/19/40/34422).

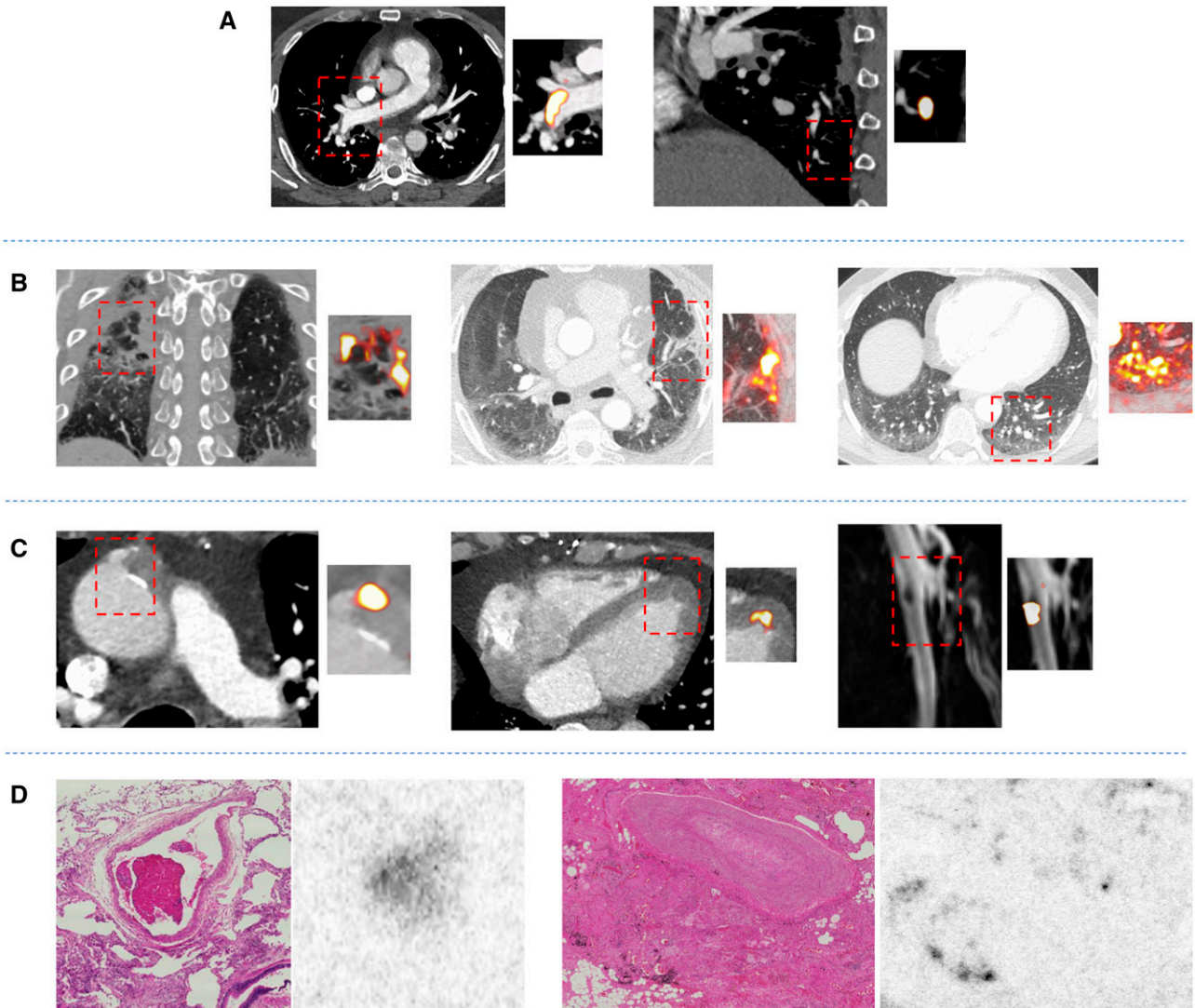
Author Contributions: R.B., J.P.M.A., M.C.W., E.J.R.v.B, M.R.D., and D.E.N. designed the study. R.B., J.P.M.A., M.C.W., E.J.R.v.B, C.L., G.M., T.C., N.K., A.W.S., M.G.M., A.A.S.T., K.D., D.A.D., C.D.L., M.R.D., and D.E.N. contributed to data acquisition and analysis or interpretation. R.B. drafted the work. All authors revised the final version and approved it for publication. R.B. is responsible for data integrity.

Am J Respir Crit Care Med Vol 204, Iss 7, pp 855–856, Oct 1, 2021

Copyright © 2021 by the American Thoracic Society

Originally Published in Press as DOI: 10.1164/rccm.202011-4182IM on August 10, 2021

Internet address: [www.atsjournals.org](http://www.atsjournals.org)



**Figure 1.** (A) The left shows segmental pulmonary embolus with associated <sup>18</sup>F-GP1 uptake, and the right shows focal <sup>18</sup>F-GP1 uptake without computed tomography pulmonary angiogram evidence of subsegmental thrombus. (B) Three examples of parenchymal <sup>18</sup>F-GP1 uptake associated with consolidation (left), healing peripheral infarction (middle), and nodular uptake in ground-glass changes with an associated dilated pulmonary artery but no evidence of pulmonary embolism at this site on computed tomography pulmonary angiogram (right). (C) Incidental systemic intravascular thrombosis and associated <sup>18</sup>F-GP1 uptake at the site of an occluded saphenous vein coronary artery bypass graft (left), apical left ventricular thrombus (middle), and left common femoral vein deep vein thrombosis (right). (D) Hematoxylin and eosin-stained sections of postmortem pulmonary tissue with corresponding <sup>18</sup>F-GP1 autoradiography in two patients who died of coronavirus disease (COVID-19). Diffuse alveolar damage and microvascular thrombosis was seen on histopathology. <sup>18</sup>F-GP1 colocalizes to intravascular thrombus (left, center-left) but not to more organized thrombus of older duration (center-right, right). There is also <sup>18</sup>F-GP1 signal in smoking-related anthracotic pigment.