JACC: CARDIOVASCULAR IMAGING
VOL. 7, NO. 11, 2014

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcmg.2014.08.003

Quantification of Myocardial Blood Flow in Absolute Terms Using ^{82}Rb PET Imaging

The RUBY-10 Study

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ABSTRACT

OBJECTIVES The purpose of this study was to compare myocardial blood flow (MBF) and myocardial flow reserve (MFR) estimates from rubidium-82 positron emission tomography (^{82}Rb PET) data using 10 software packages (SPs) based on 8 tracer kinetic models.

BACKGROUND It is unknown how MBF and MFR values from existing SPs agree for ^{82}Rb PET.

METHODS Rest and stress ^{82}Rb PET scans of 48 patients with suspected or known coronary artery disease were analyzed in 10 centers. Each center used 1 of 10 SPs to analyze global and regional MBF using the different kinetic models implemented. Values were considered to agree if they simultaneously had an intraclass correlation coefficient >0.75 and a difference <20% of the median across all programs.

RESULTS The most common model evaluated was the Ottawa Heart Institute 1-tissue compartment model (OHI-1-TCM). MBF values from 7 of 8 SPs implementing this model agreed best. Values from 2 other models (alternative 1-TCM and Axially distributed) also agreed well, with occasional differences. The MBF results from other models (e.g., 2-TCM and retention) were less in agreement with values from OHI-1-TCM.

CONCLUSIONS SPs using the most common kinetic model—OHI-1-TCM—provided consistent results in measuring global and regional MBF values, suggesting that they may be used interchangeably to process data acquired with a common imaging protocol. (J Am Coll Cardiol Img 2014;7:1119–27) © 2014 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

ICC = intraclass correlation coefficient

LV = left ventricle

MBF = myocardial blood flow

MFR = myocardial flow reserve

RCA = right coronary artery

SP = software package

TCM = tissue compartment model

Measuring myocardial blood flow (MBF) in absolute terms with positron emission tomography (PET) is now possible in clinical routine practice (1). These measurements at rest and under stress can be completed quickly (2,3), and the reconstructed dynamic images can be analyzed in a few minutes by the majority of the available software packages (SPs) (4). The analysis produces left ventricle (LV) absolute MBF values measured in ml/min/g at rest and under stress as well as the myocardial flow reserve (MFR)—the ratio of stress to rest MBF expressed as a unitless number. These values provide unique information regarding diagnosis and monitoring of coronary artery disease (CAD), microvascular health (5), multivessel CAD (6), and risk stratification (7). Although recent studies have shown the diagnostic and prognostic value of MBF quantification over the standard relative image analysis (6,8,9), and use of the generator-produced rubidium-82 (^{82}Rb) (10,11) has brought MBF quantification closer to the clinic, its integration into clinical routine practice remains underutilized (5).

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To convert imaging data to quantitative MBF parameters, measured radioactivity concentration values need to be transformed into milliliters of blood per minute per gram of myocardial tissue (ml/min/g) by applying tracer kinetic modeling to dynamic PET images. Thus, any numerical value that any professional receives from ^{82}Rb PET is a result of this transformation. At least 8 different models have been proposed (12-19) for ^{82}Rb. Although deKemp et al. (20) and Tahari et al. (21) had addressed the reproducibility of ^{82}Rb PET analysis methods for MBF quantification, they had focused on a limited number of methods; therefore, a comprehensive comparison study was needed to analyze the current situation in ^{82}Rb PET quantification to help establish common and robust methods to support collaborative multicenter clinical trials.

The objective of the RUBY project was to compare *all* currently available SPs that can analyze ^{82}Rb PET MBF studies. The criteria for inclusion were the presence of the software in the peer-reviewed literature (16,18,19,22-26) and the willingness of the development team to collaborate according to same ground rules, including blind analysis of the same selected patient datasets. For further details on the 10 compared SPs, please see **Table 1** and "The Evaluated Software Packages" section in the Online Appendix; for the side-by-side comparison of the packages, see **Table 1** in Saraste et al. (4).

METHODS

IMAGE ACQUISITION. All ^{82}Rb PET studies were performed at the Department of Nuclear Medicine of the University Hospital of Lausanne (Switzerland), according to the routine clinical practice. The study protocol was approved by the local ethics committee. Written informed consent was obtained from each patient prior to the study. Forty-eight patients with suspected or known CAD underwent rest and adenosine-induced stress ^{82}Rb PET. Patients were studied after an overnight fast and were instructed to refrain from caffeine- or theophylline-containing products or medications for 24 h before the ^{82}Rb PET study. During the study, patients were instructed to breathe normally. For further details about the PET image acquisition, please see the Online Appendix.

IMAGE ANALYSIS. The reconstructed rest and stress images were delivered to 10 facilities located in 10 centers across 7 countries. Each investigator used 1 SP and, by the rules of this project, had been blinded to results of the image analysis of the other readers before sharing his or her results (see the Online Appendix for details of the study design).

In general, all of the 10 packages implemented variations of a 1-tissue compartment model (TCM) (27). A total of 7 packages implemented by the Ottawa Heart Institute 1-TCM model (OHI-1-TCM) (14). An eighth package also used this model; however, it used a shorter 2.5-min dynamic sequence (8×12s, 2×27s) interpolated from the original image data. Additionally, 1 SP implemented an axially-distributed blood flow model (18)—AD_Ref18, and another used a 2-TCM

served as consultants to and received revenue shares from Jubilant-DraxImage. Dr. deKemp has received royalties from technologies licensed to Jubilant DraxImage and INVIA Medical Imaging Solutions. Drs. Case and Bateman are owners of Cardiovascular Imaging Technologies, which licenses and sells ImagenQ. Dr. Bateman has served on the advisory board of Lantheus Medical Imaging, GE, and FluoroPharma. Dr. Knuuti has served as a consultant to Lantheus Medical Imaging. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. Nesterov and Deshayes contributed equally to this work as first authors. Drs. Prior and Knuuti contributed equally to this work as senior authors.

Manuscript received April 10, 2014; revised manuscript received July 9, 2014, accepted August 6, 2014.