
DECLARATION OF VENKATESH L. MURTHY, M.D., Ph.D.

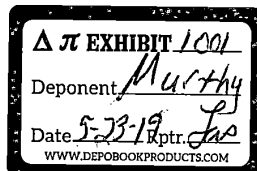
I, Venkatesh L. Murthy, declare as follows:

1. I have been retained by Jubilant DraxImage, Inc. ("Jubilant") to offer the instant declaration. I understand that Jubilant is petitioning the United States Patent and Trademark Office for *inter partes* review of patents related to rubidium-82 elution systems. I have been retained by Jubilant to explain, in this declaration, medical uses of rubidium-82 and standard medical procedures therefor. I have not been asked to analyze or provide legal opinions regarding any patent.

I. INTRODUCTION AND QUALIFICATIONS

2. I am a board-certified physician in internal medicine and cardiovascular disease and an associate professor at the University of Michigan in its Department of Radiology, Divisions of Nuclear Medicine and Cardiothoracic Radiology, and Department of Internal Medicine, Division of Cardiovascular Medicine.

3. I received a B.S. in Biology and a M.S. in Chemistry from the Massachusetts Institute of Technology in 1996. I received a Ph.D. in Biophysics and Biophysical Chemistry from Johns Hopkins School of Medicine in 2001 and a M.D. from Johns Hopkins School of Medicine in 2004. I completed my Internal Medicine Internship at Johns Hopkins Bayview Medical Center in 2005. In 2006, I completed one year of Radiology Residency at the Mallinckrodt Institute of



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Radiology at Barnes-Jewish Hospital. In 2008, I completed my Internal Medicine Residency at Johns Hopkins Bayview Medical Center. Between 2008 and 2012, I completed a Cardiovascular Medicine Fellowship and a Cardiovascular Imaging Fellowship at Brigham & Woman's Hospital. I hold a Level 3 certification from the Certification Board in Nuclear Cardiology, a Level 2 Comprehensive certification from the National Board of Echocardiography, and have completed Level 3 training in Cardiovascular MRI. I am a Fellow of the American College of Cardiology, the American Heart Association, and the American Society of Nuclear Cardiology.

4. At the University of Michigan, between 2012 and 2017, I served as a Clinical Assistant Professor in the Department of Radiology's Division of Nuclear Medicine and Cardiothoracic Radiology, and the Department of Internal Medicine's Division of Cardiovascular Medicine. Since 2017, I have served as a Clinical Associate Professor in Department of Radiology's Division of Nuclear Medicine and Cardiothoracic Radiology, and the Department of Internal Medicine's Division of Cardiovascular Medicine. Since 2016, I also have served as the Director of Cardiac PET Research at the Frankel Cardiovascular Center. I am a member of the American College of Cardiology (2008), the Society of Cardiovascular Magnetic Resonance (2006), the American Society of Nuclear Cardiology (2010), the American Heart Association (2010), and the Society of Nuclear Medicine and Molecular Imaging (2010). I serve as a reviewer, editor, or board member of more

than four dozen peer-reviewed journals in the areas of cardiology, nuclear medicine, and related topics. I am an author of 96 peer-reviewed articles, many of which I was the lead author. I am an author of several articles related to rubidium-82 elution systems, including:

- Boyden, et al., "Risk stratification with myocardial perfusion Rb-82 positron emission tomography," *Curr. Cardiovasc. Imaging Rep.* v. 7, pp. 9266 (2014);
- Moody, et al., "Limitations of 82Rb weight-adjusted dosing accuracy at low doses," *J. Nuclear Cardiology*, v. 24, pp. 1395-1401 (2017); and
- Lee, et al., "Optimization of temporal sampling for 82Rb myocardial blood flow quantification," *J. Nuclear Cardiology*, v. 24, pp. 1517-29 (2017).

5. I have personal experience working with rubidium-82 elution systems.

I first started working with rubidium-82 elution systems during my ^{time} at Brigham & Woman's Hospital, which began in July 2008. There, I trained in the use of such systems, particularly the Cardiogen-82® Infusion System, discussed below. As part of my training, I reviewed journal articles describing medical applications of rubidium-82, and product documentation, describing operating procedures of the Cardiogen-82® Infusion System, as it existed in 2008. Also, I received training from faculty at Brigham & Woman's Hospital regarding such procedures. Thus, I am familiar with prevailing medical practices in 2008 generally and as they apply to rubidium-82 elution systems.

6. I have participated in approximately 3,000 to 4,000 rubidium-82 patient elutions over my career. Since 2012, I have been responsible for training new physicians in rubidium-82 elutions and supervising the rubidium-82 elution procedures at the University of Michigan. The University of Michigan, where I am employed, purchased rubidium-82 generators for the Bracco CardioGen-82 rubidium-82 elution system for over ten years, from 2007 to 2017. As such, I have first-hand knowledge about the day-to-day operation of rubidium-82 elution systems, including the accepted practices for infusion of various radiopharmaceutical agents for use in Positron Emission Tomography and the use of rubidium-82 as one such radiopharmaceutical.

7. My curriculum vitae, which is attached hereto as Exhibit A, contains a more detailed description of my background.

8. I am being compensated at my usual consulting rate of \$500 per hour for my technical analysis in this matter. My compensation is not contingent upon the results of my work.

II. OVERVIEW

9. I was asked to provide an overview of the clinical and institutional use of rubidium-82, and specifically, to explain the medical procedures used with rubidium-82 chloride infusion systems as they existed prior to June 2008.

10. At a high level, rubidium-82 elution systems are employed in Positron Emission Tomography (commonly, "PET") systems, a type of nuclear molecular imaging system. A rubidium-82 eluate is infused into a patient's body, where it is absorbed by cardiac tissue. The rubidium-82 eluate generates positrons as it decays, which annihilate with electrons and emit a pair of photons in opposite directions. The photons are captured by imaging equipment, a PET scanner, and an estimate of the location of the rubidium-82 can be generated therefrom. Two-dimensional and/or three-dimensional images of the absorption of rubidium-82 into cardiac tissue may be generated from the PET scans.

11. Below, I provide an overview of nuclear imaging generally, an introduction to rubidium-82 elution protocols and attendant risks, and an explanation of medical procedures performed in 2008 to manage some of those risks. In this discussion, I refer to several publications that describe these issues, as follows:

- Klein, "Precise ⁸²Rb infusion system for cardiac perfusion measurement using 3D positron emission tomography", Ottawa-Carleton Institute for Electrical and Computer Engineering (Feb. 2005) ("Klein");
- Chatal, et al., "Story of rubidium-82 and advantages for myocardial perfusion PET Imaging," *Frontiers in Medicine*, v. 2, art. 65, pp. 1-7 (Sept. 11, 2015) ("Chatal");
- Alvarez-Diez, et al., "Manufacture of Strontium-82/Rubidium-82 Generators and Quality Control of Rubidium-82 Chloride for Myocardial Perfusion Imaging in Patients using Positron Emission Tomography," *Applied Radiation and Isotopes*, v. 50, pp. 1015-23 (1999) ("Alvarez-Diez");

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