

# Integrating Nuclear Imaging and Cardiology in Clinical Practice

A Conversation Between Jeroen J. Bax and Frank M. Bengel

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**F**rank M. Bengel, director of the Department of Nuclear Medicine and Dean of Research at Hannover Medical School (Germany), talked with Jeroen J. Bax, a professor of medicine and cardiology, director of noninvasive imaging, and director of the Echo Lab at the Leiden University Medical Center (The Netherlands), about contributions at the intersection of advanced cardiology and nuclear medicine/molecular imaging. Dr. Bax studied medicine from 1984 to 1990 before launching his research career at the University of Miami (FL), where his primary foci were in the fields of immunology and associated basic science. In 1996, he received his doctorate from the Vrije Universiteit Amsterdam (The Netherlands) with a focus on SPECT metabolic imaging. He completed his training as a cardiologist in 2002 at the Leiden University Medical Center. His main interests include clinical cardiology, heart failure, cardiac resynchronization therapy, and the application of a wide range of imaging modalities to these clinical fields. He has served on the editorial boards of various journals, including as associate editor for the *Journal of the American College of Cardiology (JACC)* and *Heart*. From 2016 to 2020, he served as president of the European Society of Cardiology (ESC). Dr. Bax has authored more than 700 papers in international peer-reviewed journals. He received the ESC Silver Medal in 2008, the American Society of Nuclear Cardiology Distinguished Service Award for contributions to cardiovascular imaging and cardiology in 2019, and the American College of Cardiology Distinguished Scientist Award (Clinical Domain) in 2020.

**Dr. Bengel:** *Jeroen, not many people started their careers in nuclear cardiology and moved on to become worldwide leaders in general cardiology. Your perspective on nuclear medicine today and your view on the role of diagnostic imaging in clinical medicine should be of interest to readers of The Journal of Nuclear Medicine (JNM). Let's start from the beginning: Early in your career, you chose a PhD thesis in nuclear cardiology in Amsterdam and worked on myocardial viability imaging with <sup>18</sup>F-FDG. What attracted you to this technique and to nuclear imaging in general?*

**Dr. Bax:** After 3.5 years of learning the fundamentals of medicine in Leiden in The Netherlands, I wanted to do something else. I went to the University of Miami, where I did my first research in immunology, leading to my first scientific publication. During the rest of my medical school training, I did research in neurology, and this confirmed my interest in doing scientific projects. When I finished medical school, cardiology excited me most, and I completed my PhD thesis in Amsterdam at the Free (or Vrije)

University Medical Center. I spent 4 years on developing <sup>18</sup>F-FDG imaging with SPECT, using special collimators. There was high hope that <sup>18</sup>F-FDG SPECT would support a broader availability of the technology. We performed perfusion and <sup>18</sup>F-FDG studies to determine viability and echocardiography before and after revascularization to determine functional outcome. Also, we compared <sup>18</sup>F-FDG imaging to stress echocardiography, thallium imaging, and MRI. During my PhD studies, then, I learned about many cardiac imaging techniques before I even started training in cardiology.



Jeroen J. Bax, MD, PhD

**Dr. Bengel:** *So you always appreciated the range of different imaging techniques and the ways in which they complement one another. Were you able to continue along that path during your cardiology training?*

**Dr. Bax:** I used my specialty training to learn more about cardiac imaging modalities, but I also started to approach problems from a clinical perspective. Imaging has to have clinical and therapeutic relevance, just like viability imaging is used to predict whether impaired cardiac function will improve after revascularization. I trained in cardiology in Leiden and for 1 year in Brussels (Belgium). I learned everything about echocardiography there. But I also learned how to build up a laboratory, because they had a fantastic organization, with perfect scheduling and standardized reporting. This helped me to build a well-structured echocardiography laboratory after my return to Leiden. From structured imaging and reporting, we created a large database. That turned out to be critically important for my future research, which has built significantly on database analyses. Today, we have very big databases of all imaging procedures and for different diseases, therapies, etc., and we use these to identify ways in which imaging can improve clinical outcomes for cardiac patients.

**Dr. Bengel:** *You are emphasizing the importance of a clinical perspective for the best use of imaging techniques.*

**Dr. Bax:** Yes, I used my training to also learn more about specific therapeutic aspects of cardiovascular medicine. I worked closely with cardiac surgeons, helping them with their procedures by providing standardized echocardiography. I also spent time in invasive angiography and in fundamental electrophysiology, implanting devices such as pacemakers, cardiac defibrillators, and others. And I tried to learn how multimodality imaging can be used to optimize these powerful therapeutic procedures.

**Dr. Bengel:** *At the end of your cardiology specialty training, the question came: What's next?*

**Dr. Bax:** Leiden offered me a position to build a noninvasive imaging department with a very strong focus on echocardiography. I built the echo lab using my experience from Belgium. Then we started to collaborate with the other imaging modalities, including nuclear medicine. We also did CT coronary angiography, then with 320 slices. Eventually we began to work more and more with MRI, specifically for assessing myocardial viability and later in nonischemic cardiomyopathies. We gradually built this imaging hub in cardiology where we had all the modalities, and noninvasive imaging had a fixed role in standard care algorithms of patients admitted to our hospital. This approach of having standardized imaging in almost all patients of a given disease entity was fundamental for big database generation. From those databases, we generated all of our observational research and publications.

**Dr. Bengel:** *Your approach toward noninvasive cardiac imaging is that you want to use the modality or the combination of modalities that is best for answering specific clinical questions. Are multimodality skills generally recommended to cardiac imagers?*

**Dr. Bax:** Every disease is characterized by an anatomic, a functional, and a molecular or inflammatory component. Take a heart valve as an example: the anatomic point is that you have, let's say, an aortic valve with 3 cusps and other features, and you can measure size and geometry. The functional component is the extent of the gradient over that valve; that is, what are the functional consequences of the anatomic substrate? Then comes the component of

and patient-oriented approach: Which test to start with? What information is needed so that the clinician can treat the patient? Nuclear physicians have an important role in such an environment. You can never be an expert in all modalities. Your goal, instead, is to have a multimodal platform. Knowing what the other modalities can provide is already a big step toward a multimodal approach.

**Dr. Bengel:** *You mention inflammation as a key component of cardiovascular disease. This also plays a role in other organ diseases, where it can often be identified using the same nuclear medicine approaches. What do you think of systems-based medicine, which looks less at specific organs and more at biologic mechanisms and their effects on the body as a whole?*

**Dr. Bax:** I like the concept of systems-based expertise. Nuclear medicine typically is a cross-sectional specialty that reaches into many other, often organ-centered, specialties. There, nuclear medicine can bring in its functional- and molecular-focused information, and this may be increasingly relevant as therapies start to target molecular mechanisms. A good example in cardiology is the increasing attention toward what we call "myocardial diseases" (although many of them are systemic diseases that affect the heart but have effects on the rest of the body). This includes amyloidosis, sarcoidosis, infectious diseases, and others. Those diseases are very good targets and areas in which nuclear medicine is increasingly relevant for decision making.

**Dr. Bengel:** *Let's get away from the specifics of nuclear imaging, toward more general aspects of academic medicine and research. You built an extremely prolific program, producing a*

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inflammation. We are learning now more and more that the earlier phases of valve stenosis formation involve inflammation. You cannot address all these different aspects with a single technique. You need very high anatomic resolution, provided by CT or MRI. You need good measures of functional consequences of anatomic abnormalities, provided by MRI or echocardiography. And you also want to know about inflammation, where nuclear imaging can help. Integration of different modalities is important to understand, diagnose, and risk-stratify and ultimately to decide on the best treatment for each specific disease.

**Dr. Bengel:** *What would be your advice for a nuclear physician who is trained in using radioisotopes for diagnosis but not necessarily trained in echocardiography or clinical cardiovascular disease? How can nuclear physicians acquire the depth of knowledge needed to provide clinically relevant services in a multimodality environment?*

**Dr. Bax:** We need to strive for clinical collaboration and integration. Some modalities may be run by radiology, some by cardiology, and some by nuclear medicine, but the final common pathway is the patient with a specific disease. And that specific disease needs a specific treatment. For that treatment, you need to have diagnostic information, which may include anatomic, functional, or inflammatory abnormalities. What is unique for nuclear medicine is the ability to reliably assess inflammation and other molecular components of a disease. And, of course, nuclear imaging can also assess functional components of a disease. So, what is needed is an integrated

*large number of publications and educating many young trainees. How did you build your research program in Leiden?*

**Dr. Bax:** It started with just 1 fellow in the early 2000s, and the program grew from there. The key is to have the right projects and to attract motivated young people. Having imaging databases and expanding them in a structured way was another very important point, because this provided the data for our projects. Today, we have on average about 15 to 20 researchers in the lab. As the program grew, we collaborated with other labs, so that many other centers wanted to send individuals to train in multimodality imaging and to do research.

**Dr. Bengel:** *You also mentioned that clinical databases were an important component for your research program.*

**Dr. Bax:** In the early 2000s, cardiology moved toward following clear guidelines, provided by the American College of Cardiology, the American Heart Association, and later the ESC. We decided in Leiden to set up clinical care tracks for different diseases. All patients undergo the same diagnostic tests and therapeutic procedures for specific diseases, based on our care track algorithms. Results are protocolized and put into databases. We adjusted these time after time as the field changed and when new medications, diagnostics, or therapies were introduced. Through these care track-driven clinical databases, large and well-structured cohorts of patients were generated. These clinical care pathways directly feed into our research. Our data resource is not prospective trials or experimental science but analysis and reporting of true practical clinical care.

**Dr. Bengel:** *This feedback algorithm, where the research can directly lead to adjusting clinical care, would be a very useful approach in nuclear medicine, where theranostics are rapidly growing and where we have both diagnostic as well as therapeutic options in our own hands.*

**Dr. Bax:** Randomized controlled trials are, of course, fundamental for introduction of new therapies, but they do not fully answer the question of how a new therapy is best implemented in daily practice. There is often a significant difference between a randomized controlled trial in a completely optimized and well-defined environment and its implementation in daily clinical practice. That is what makes the creation and analysis of our own clinical databases interesting and a way in which care can be further refined.

It is very important for clinicians to think academically and ask questions. We do this every day, but why do we do this? Does a technique or innovation really work, or can it be improved? If so, then how? Those sorts of questions help to advance the field. It is our current experience using research from our big clinical databases that this sort of resource can be used to design evidence-creating randomized trials.

**Dr. Bengel:** *Very good point. Let's get to your "second career" as a leader in the ESC and international cardiology. How did this happen?*

**Dr. Bax:** Through our research, I visited many cardiology clinics, which resulted in a broad international network, building bridges and relationships. This also included interactions and involvement in scientific committees of various societies, including the ESC, the American Society of Nuclear Cardiology, and our international meeting, the International Conference of Nuclear Cardiology. I was asked by the ESC president to become the program chair of the large ESC congress. This showed me the importance of coming together and being engaged and learning from each other. Later on, I became chair of the ESC Guideline Committee. Finally, I was asked whether I wanted to run for vice president of the ESC and then president. During that presidency, I realized the importance of relationships with industry. On the one hand, frequent criticism suggests that medical societies should not be working too closely with industry and that boundaries should be clearly defined. But when it comes to education, congresses, guidelines, etc., all these activities constantly bring the two together. Modern drug development, for example, is so advanced today that industry and medical doctors really need to work together.

**Dr. Bengel:** *That is quite relevant to nuclear medicine, where major pharmaceutical companies are now increasingly involved as a result of the success of theranostics in oncology. How do you make sure that you can still shape the future of the field with sufficient independence from—but at the same time sufficient integration with—industry?*

**Dr. Bax:** For many organizational activities in the ESC, we worked closely together. In education, for example, a committee was asked to build programs based on clinical needs and created by physicians. These were then communicated to industry for support. Industry needs clinical advice and vice versa. When it comes to daily practice, however, you want to be independent and not biased by specific industry relations. Hence, we need to be transparent and self-reflective.

The same is true for the creation of guidelines, a key process within the ESC. Randomized controlled trials are the best evidence, and nonrandomized trials form only a middle layer of evidence. Guidelines are being constructed purely based on evidence and expert opinions, and this is done by medical specialists.

Industry is not taking part here. They do not even see anything of the process until it is finalized and published. Achieving a bias-free perception of our work is ultimately beneficial to everybody.

**Dr. Bengel:** *The successful creation of clinical guidelines that define the specialty is a key achievement of the ESC. Publication of guidelines also makes up a large part of the success of the European Heart Journal, where the guidelines contribute greatly to the numbers of citations. Has this been an active political development in the ESC?*

**Dr. Bax:** At the time when I led the congress program, the then president of ESC taught me that 3 things are important within the society: the congress, guidelines, and journals. There was always a strong focus on these issues. ESC now holds several other meetings in addition to their main annual congress. All of these create revenue and educate specialists. Scientific societies should make use of their broad membership resources to create valuable content such as meetings, which move the field forward.

You also asked about journals. In the 1990s to early 2000, there were 2 top journals in the field, *Circulation* and *JACC*, where I served as an associate editor for a few years. Then came the *European Heart Journal*, benefiting indeed from the success of ESC guidelines and emerging as the third major cardiology journal. I also served as an associate editor there. This experience helped me recognize that, in the end, it is important how a journal is run. If you work diligently on interpreting the submitted science and keep in touch with what is clinically relevant, this will lead to success.

**Dr. Bengel:** *JACC, Circulation, and the European Heart Journal all have their cardiovascular imaging spin-off journals today, where good science that cannot be accommodated in the main journal can be published in the spin-offs. JNM also wants high-quality cardiovascular contributions so that cardiovascular imaging remains well represented within the nuclear medicine community. What is your advice for JNM to sustain a leading position in cardiovascular imaging publications and continue to receive good submissions?*

**Dr. Bax:** As a leading journal in nuclear medicine, *JNM* should have outstanding review articles contributed by leading physicians in cardiovascular disease. Such reviews may highlight the clinical needs of cardiologists that can be addressed by nuclear medicine. Then for the research itself, you can also actively recruit submissions by leaders in the field. Abstracts from congresses may be screened for this purpose. You could think about topics that are of more specific relevance for the nuclear medicine community so that these may be preferentially submitted to *JNM*.

**Dr. Bengel:** *In your leadership role at the ESC congress in Rome in 2016, you were able to meet Pope Francis. How much does the pope know about medical science and maybe even nuclear medicine?*

**Dr. Bax:** It was a huge honor for the ESC that Pope Francis really came. He was very interested in treatment of patients, patient care, and was really engaged, discussing openly about medicine, the congress, and our specialty. We felt that he really cared. Caring for people remains important in today's medicine, where technology tends to dominate and where there is so much time pressure and need for documentation. Let's not forget to look each other in the eyes and just listen and find out what is important for patients, so that they are comfortable. That's something that the meeting with Pope Francis helped to reinforce.

**Dr. Bengel:** *Final question: Your son is studying medicine—what is your advice for young people? How can they find their way in the field of medicine, and what will be important for their careers?*

**Dr. Bax:** It is difficult, because just as we were different from the generation before us, the younger generation is different from our generation. The world is changing very rapidly. When it comes to medicine, patient care is central, and the next generation of doctors will understand that. I think that the work/life balance needs to be discussed more with this younger generation. Members of the next generation definitely think more about these things than we did, and

we should accept this. My specific advice to the next generation of medical doctors is that becoming a good clinician is very important. If possible, combine this with research. The way we are practicing medicine is becoming more difficult, with expanding rules, regulations, protocols, and administrative and computer tasks that keep us away from the patient. To become a good physician, you can also become a good researcher and must always be a good human being.