Moving forward—back to the future

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Nuclear cardiology has seen impressive developments since its first steps in the 1970ies[1,2] including introduction of different generations of radionuclides accompanied by tremendous advancements of technical equipment. With regard to nuclear myocardial perfusion imaging (MPI) a large body of literature is available to document how much knowledge has been developed to understand and eventually overcome initial drawbacks. Many technical refinements over the past decades have contributed to the success of nuclear cardiology such as advanced equipment with the advent of SPECT technology, new CZT detectors and introduction of attenuation correction, alternative myocardial perfusion tracers, and advent of PET. Standardized image analysis and development of well-established software solutions allowing assessment of quantitative parameters and recent deep learning algorithms for improved outcome prediction have added to a solid ground for a clinical role of nuclear cardiology in daily routine. Introduction of PET/MR was just another small footstep[3] on the long path and multimodality cardiac hybrid[4] imaging just another link in the chain of development, which allows to precisely attributing a lesion to the subtended ischemic region for selectively targeting treatment options. Comparing Figure 1 with Figure 2 reflects exactly 45 years of this journey at our institution, the University Hospital Zurich, Switzerland. Figure 1a illustrates a planar acquisition of a Tl-201-Chloride myocardial perfusion study acquired in 1977 before (left panel) and after (right panel) coronary intervention on a proximal LAD lesion. The improved myocardial perfusion in the anterior wall (right panel) documents the success of the intervention. Figure 2 illustrates the benefit of hybrid imaging in multi-vessel coronary artery disease with complex anatomy after multiple intervention including bypass grafts. The three-dimensional hybrid image allows to easily attributing the ischemic territory (white arrows) to the subtending coronary artery with proximal lesions.

This could be the brief summary of a long but smooth journey of nuclear cardiology from an experimental idea with apparently limited value towards precision imaging as a key component of modern personalized medicine. However, this is not the entire truth. Not even half of it.

The journey was not smooth and linear, and not homogeneous neither geographically in different countries nor with respect to time course. Periods of cardiac imaging underuse where followed by massive growth, which has raised criticism about inappropriate use of cardiac imaging. About a decade ago some of our most prominent colleagues in our field saw cardiac imaging at a the crossroads.[5] They realized, that more evidence needs to be created for appropriate use of imaging because it is the downstream treatment, which cures the patient, not the imaging.[6] Their wise foresight initiated a new era with large trials evaluating the impact of imaging on outcome in large populations. Our prominent colleagues at the Ottawa Heart Center evaluated more than a decade ago the role of viability assessment by 18F-FDG for assisting decision making in ischemic cardiomyopathy. Despite the high quality of their trial the primary endpoint was not met. However, it turned out that the lack of significant impact in the original study was simply due to a high non-adherence rate to the PET results by clinical cardiologists not yet experienced with the method while in the adherence group the benefit was significant.[7] The lesson learned was that dissemination of knowledge plays a key role even before starting a trial and certainly, when it comes to integration of study results into daily routine as our clinical colleagues may not all be early adopters of novel technologies. Clinical outcome imaging trials published with broad visibility such as for example COURAGE,[8] ISCHEMIA,[9] PROMISE,[10] or DISCHARGE[11]

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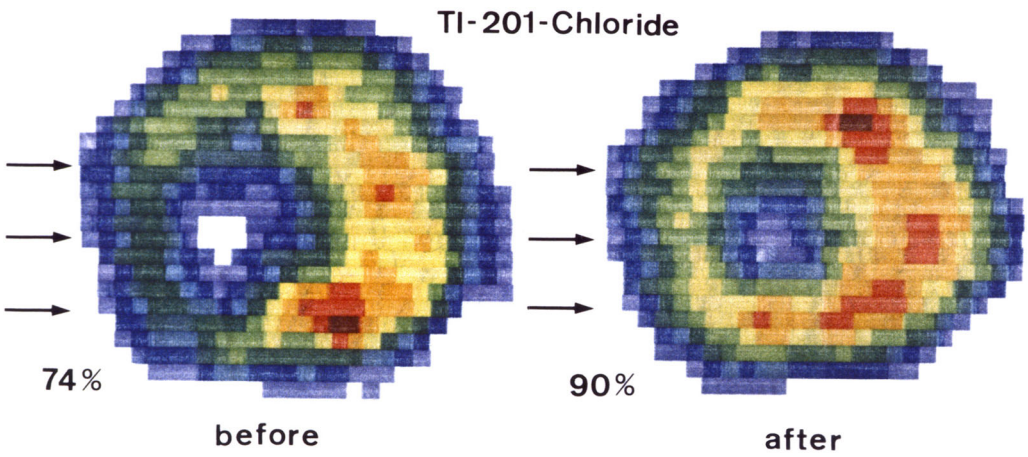

Figure 1. Planar acquisition of a stress Tl-201-Chloride myocardial perfusion study acquired in 1977 before (left panel) and after (right panel) coronary intervention on a proximal LAD lesion. The left panel displays a large stress-induced anterior defect (arrows) with recovery after intervention (right panel). Courtesy of Urs M. Lütolf.

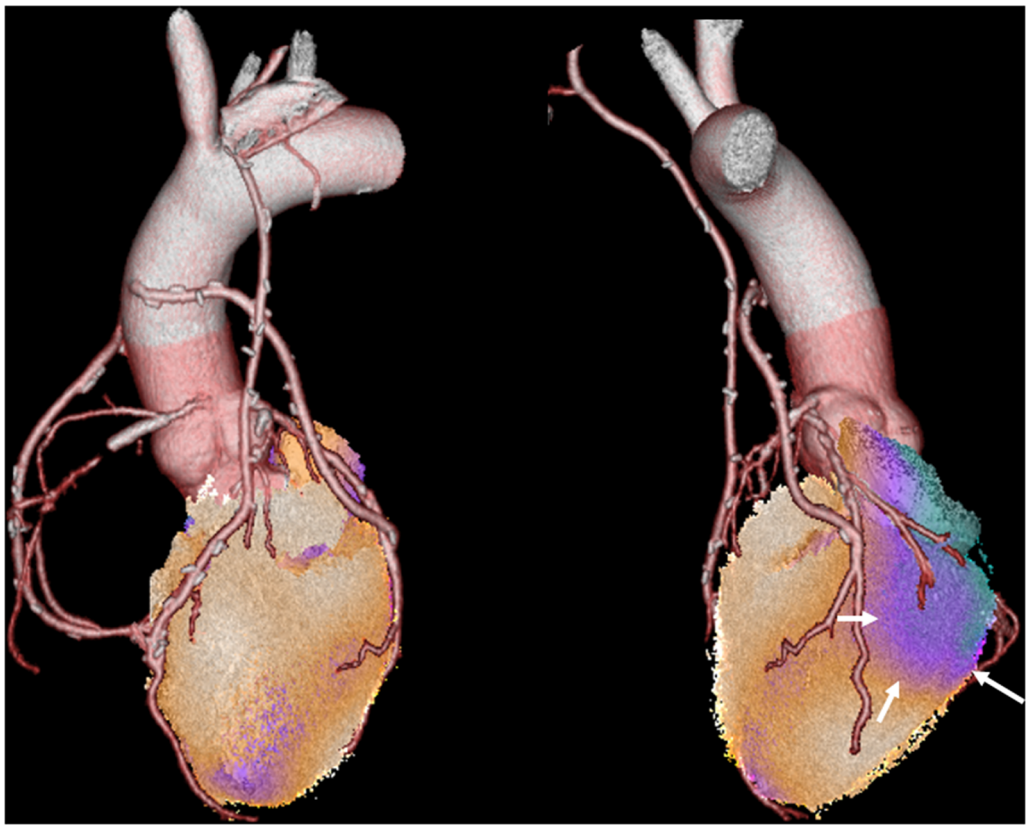

Figure 2. Illustration of the potential benefit of hybrid imaging (perfusion MPI and CT coronary angiography) in multi-vessel coronary artery disease with complex anatomy after multiple intervention including bypass grafts. Left panel: anterior view. Right panel: left lateral view. The three-dimensional hybrid image allows to easily attributing the ischemic territory (white arrows) to the subtending coronary artery with proximal lesions.

accompanied by large coverage in medical literature and vivid discussion at many clinical conferences have paved the way for implementation of their results into appropriateness criteria and guidelines adopted by many societies.[12] Nevertheless, the gap between knowledge, acceptance and clinical application remains a challenge as discordances between cardiac imaging results and subsequent management can still prevail.[13]

For a specialized Journal as ours it is important that we remain open to new developments despite the uncertainty at the very begin of a new idea. This is a fundamental challenge, which journals publishing large-scale trials do not face to the same extent. It is our task to give a fair trial to a potentially important novelty, although predictions are particularly difficult at early stages of new developments, and we always risk that retrospectively sometimes they appear very wrong. One famous example is the often cited quotation on the potential of the stethoscope: ''That it will ever come into general use, notwithstanding its value, is extremely doubtful; because its beneficial application requires much time and gives a good bit of trouble both to the patient and the practitioner; because its hue and character are foreign and opposed to all our habits and associations.'' René-Théophyle-Hiacinthe Laënnec published the basic form of the stethoscope in 1819. And his book was translated by the physician John Forbes in 1821, where he stated the above quote in the introduction.[14]

As the above statement proved wrong, it is not only used as famous example of wrong prediction but also the expert opinion of Forbes is sometimes described as wrongheaded and even foolish. This however is not the entire truth. In fact, it is not even half of the truth. Because the quote above is incomplete. Having a look at a longer excerpt clarifies that Forbes recognized the stethoscope as ''one of the greatest discoveries in medicine'' and at the same time stated a far-sighted vision for future high technology assessment namely the fundamental principle of fair trial. Quote: ''I have no doubt whatever, from my own experience of its value, that it will be acknowledged to be one of the greatest discoveries in medicine by all those who are of a temper, and in circumstances, that will enable them to give it a fair trial.''

Much of our daily research and publications will—at least in part—base on previous knowledge, and most publications are not providing groundbreaking novelties. Some highly ranked journals, which mainly accept large randomized controlled trials claim the novelty aspect among the most important selection criteria for publication. Very nicely, Forbes describes the disruptive nature of a novelty, namely ''foreign and opposed to all our habits''. However, the novelty aspect of trials is limited to confirmation of a previously developed novel hypothesis in a large patient population. Thus, not every piece of newly generated knowledge can be groundbreaking. However, most of it deserve that we give it a ''fair trial''. As editorial office, we try to make sure that all submissions get such a fair trial. This is of general importance, but becomes even more important when reviewing manuscripts for a Journal dedicated to a single method (nuclear) and a single organ (cardiology). New and highly innovative or controversial developments may find the way into daily routine through such a specialized journal long time before its application may be evaluated in a large trial. Therefore, I believe that an editorial team of a highly specialized Journal such as the Journal of Nuclear Cardiology must be particularly open to new ideas for which we can serve as door openers. We should not be disappointed by the fact that the credit of high citation numbers will go to landmark publications of large trials. We should rather be proud of the fact that techniques originally investigated in a specialized Journal are so well received and established in daily routine that the original work is not even cited any more when using this technique in publications. I welcome the fact of having clinical impact—rather than aiming at the impact factor as calculated metric.

For a novelty with an inherent importance occult to a majority of a non-specialized general audience a publication in our Journal may be the famous first small but important step in the path of 10,000 miles. Moreover, sometimes even to experts the novelty may not appear evident. If we have a second look at the Figures 1 and 2 of this article, it may still appear evident, that the major novelty and advancements happened during the decades between Figures 1 and 2. This, however, is not the entire truth. In fact, it is not even half of it. In reality, what has been often claimed the most important novelty and advancement of Cardiology in the 20iest century lies occult in the day between the left and the right panel of Figure 1. i.e., the day of September 16th 1977. That magic date—exactly 45 years ago these days—will be forever bound to the ''dies mirabilis'' when Andreas Grüntzig performed his famous first percutaneous transluminal coronary angioplasty (PTCA).[15] The disruptive innovator Grüntzig intuitively used nuclear MPI as the then most promising technique to assess the extent and location of ischemia in the territory subtended by the stenotic left anterior descending coronary artery and for guiding and monitoring the success of the first intervention. Nuclear MPI scanning was just been introduced at our institution supported by his interest and was far from being established or validated. Thus, the planar nuclear MPI scan in Figure 1 illustrates the formidable success of the first PTCA ever performed in a human patient (still doing well 45 years later) but also

documents the very first steps in Nuclear Cardiology at the University Hospital Zurich, Switzerland. Despite the lack of any body of evidence in the literature, Grüntzig generously gave it a fair trial, as it appeared evident to him that this was the path to follow on his way of interventional cardiologist. Thus, Andreas Grüntzig—the founder of Interventional Cardiology—was also the strongest promotor of Nuclear Cardiology and has triggered decades of fruitful developments in this field at our institution and elsewhere.

Grüntzig not only pioneered the modern use of nuclear MPI as a method for ischemia assessment before PTCA but also anticipated the importance of discussion between the interventional cardiologist (the singular is appropriate as he was for quite some time the only one in Zurich and worldwide) and imagers for joint team decision making of the treatment strategy. With this modern multidisciplinary approach—much ahead of time—a gap between imaging and intervention could not even begin to arise. There was no room for discordance between MPI results and subsequent clinical management. Because decisions where drawn by consensus (personal communication from Urs M. Lütolf, then at the Department of Nuclear Medicine and Radio-Oncology, now retired Chair of the Department of Radio-Oncology, who acquired and discussed with Grüntzig the MPI scans in Figure 1 and many subsequent patients undergoing PTCA in Zurich). Forty-five years later, empowered by formidable technical advancements and evidence supported from large clinical trials we start closing a gap which was not even thinkable at the begin.

Thus, step by step we now seem finally to moving forward – back to the future.

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