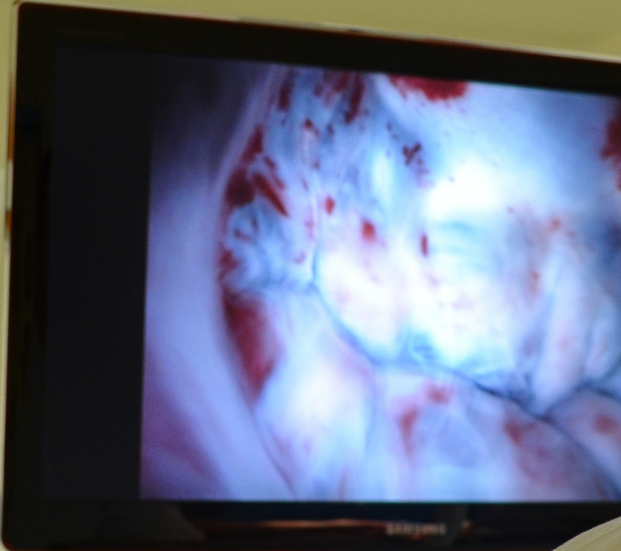


## Cardioscopy at IMMR : spectacular and insightful images



There are many ways to reach an answer in cardiovascular research. But there are few convincing ones. Imaging is definitely one of them. However imaging is only a representation of reality. Despite a formidable evolution of ultrasound imaging quality (3D, TEE, Intra cardiac echo) and angiography (biplane, 3D reconstruction, scatter radiation optimization), it is often difficult to actually “see” what we are doing inside the body, and particularly in the heart. In order to have direct vision of valves and interventional procedures, advancing a camera inside the heart was not the greatest challenge, but we had to find a way to see through blood. Replacing blood by saline was the best solution. We have worked in that simple manner for almost 10 years, on arrested hearts and sometimes on beating hearts. This approach has provided us with the capacity to see things that were impossible to visualize on the explanted open heart, thanks to the magnifying capability of the telescope, and even more importantly see it in situ with a fully loaded heart. But we had difficulties keeping the heart beat for more than a few minutes with solely saline or a Krebs Henseleit solution, albeit oxygenated. Instead of trying to reinvent the wheel, we simply found the world specialists of ex-vivo isolated beating heart platforms : LifeTec group. Our partnership makes a lot of sense as they have a unique know-how in ex vivo beating hearts and as we are specialists of preclinical validation of medical devices, in particular for structural heart disease.


Nicolas Borenstein, DVM, PhD  
Scientific and technical manager  
IMMR

In collaboration with



LifeTec  
Group





**M**arco Stijnen is a biomedical engineer and co-founder of LifeTec Group where he holds the position of Cardiovascular Group Manager. Sjoerd van Tuijl is Research Engineer and has largely been responsible for the development of the PhysioHeart Platform.

**IMMR :** Marco, can you share with us, in a few words, how your company was born?

During my PhD study there were many R&D requests from research groups in industry, clinics and institutions that could not be handled in an academic setting. An opportunity was identified to serve these groups and my colleague Jurgen de Hart, later to become our CEO, recognized the need for an independent organization to take up these requests. This led to creating a company specialized in MedTech R&D which would be able to cover those projects with dedicated researchers and readily available expertise in an accessible but professional environment. We started this company in 2004 at the University of Technology in Eindhoven ensuring an autonomous character, as we believed our independence to be very valuable to our clients. A few years later we were active on different clinical domains and a large portfolio was built up. A management buyout followed in 2012 and the company was named LifeTec Group. We are currently employing 15 people and provide applied research, consultancy and (development of) enabling technology as a service to our clients in different biomedical areas of expertise, such as cardiovascular, orthopedic, urology, imaging and so on.

**IMMR :** Sjoerd, what is the concept of the PhysioHeart?

Like several other platforms we have developed, LifeTec Group is striving to provide al-

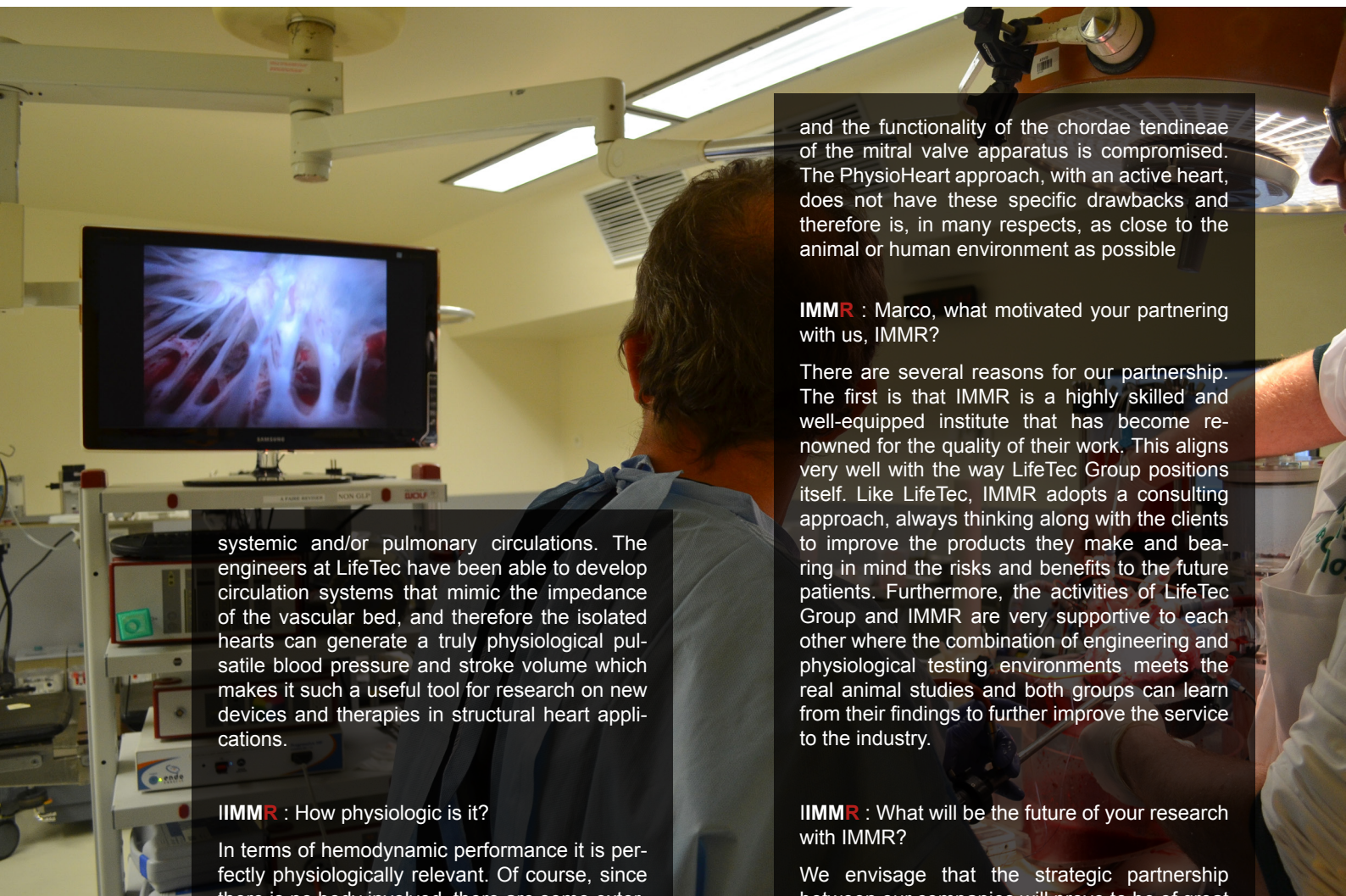
ternatives to animal testing in the early phases of R&D on new medical devices, therapies and pharma, and therefore we need physiologically relevant environments such as bioreactors and ex-vivo tissue platforms. The concept of ex-vivo platforms in general is that we can harvest tissues that were not meant for human consumption from slaughterhouse animals, and keep these tissues alive for a while such that they are valuable tools to conduct research with, but without the need to sacrifice animals specifically for this purpose. The PhysioHeart is one of these platforms, where a heart is treated like a transplant organ and can be revived in our perfusion system. Once the heart is reactivated, we can make it work on a physiological level again and use it to test and assess for example the functionality of new medical devices or interventions in a real environment, while being able to use measurement techniques that are not clinically applicable such as endoscopic video registration in a normally working heart. These experiments will allow our clients to learn more about their prototypes as well as the intervention required, such that they will be much better prepared for the subsequent animal studies that are necessary for long-term follow up.

**IMMR :** How is it different from a classic Langendorff system?

The concept of hearts beating outside of a body is not new, as it was already conceived in 1897. In a Langendorff perfusion, however, aortic blood pressure is generated by an external pump which perfuses the coronary system directly. The Langendorff perfusion does not include the ventricles in the circulation and therefore the heart does not generate a cardiac output – except for the right ventricle that can pump the venous return of blood that has gone through the myocardial tissue. In a Working Heart mode, the ventricles are allowed to pump fluid through



# Looking inside the beating heart in physiologic conditions is now possible !



systemic and/or pulmonary circulations. The engineers at LifeTec have been able to develop circulation systems that mimic the impedance of the vascular bed, and therefore the isolated hearts can generate a truly physiological pulsatile blood pressure and stroke volume which makes it such a useful tool for research on new devices and therapies in structural heart applications.

**IMMR :** How physiologic is it?

In terms of hemodynamic performance it is perfectly physiologically relevant. Of course, since there is no body involved, there are some external influences that are missing such as hormonal responses and the effect of kidneys and liver on blood. But recent studies have shown also the benefits of this. Compared to other experimental approaches the PhysioHeart performs very well. In mock-loop systems comprised of artificial flow generators and circulation systems it is often hard to work with blood, and the fixation of the device will usually not be done in a material that resembles tissue and therefore not provide the same loading on or interaction with the prototype device. Delivery or implantation of prototype devices will also not be as they would be in animal or clinical trials, thereby excluding part of the normal procedures. To solve those issues several passive heart platforms have been developed, one of them by ourselves. These passive heart platforms involve a dead heart which is mounted to a pump to generate flow and a circulation that can be used to tune blood pressure. Although this approach allows for anatomical correctness, the material properties of dead tissue are still slightly different from living tissue. In these passive hearts, the myocardium does not contract and as a result for example the deformation of the valve annulus

and the functionality of the chordae tendineae of the mitral valve apparatus is compromised. The PhysioHeart approach, with an active heart, does not have these specific drawbacks and therefore is, in many respects, as close to the animal or human environment as possible

**IMMR :** Marco, what motivated your partnering with us, IMMR?

There are several reasons for our partnership. The first is that IMMR is a highly skilled and well-equipped institute that has become renowned for the quality of their work. This aligns very well with the way LifeTec Group positions itself. Like LifeTec, IMMR adopts a consulting approach, always thinking along with the clients to improve the products they make and bearing in mind the risks and benefits to the future patients. Furthermore, the activities of LifeTec Group and IMMR are very supportive to each other where the combination of engineering and physiological testing environments meets the real animal studies and both groups can learn from their findings to further improve the service to the industry.

**IMMR :** What will be the future of your research with IMMR?

We envisage that the strategic partnership between our companies will prove to be of great benefit to our clients, and will improve the expertise and know-how of both our companies. For example, LifeTec's advanced research platforms are ethically very well-considered and improve the success rate of subsequent animal studies. Before our collaboration it was only possible to perform studies during and immediately following implantation. Now, it is also possible to harvest the hearts from the animals following IMMR studies and revive them in the PhysioHeart platform. This will allow detailed functional studies of devices and tissue responses after several months of functioning in the animal model. In the future, the PhysioHeart platform will also be applied to study the hearts of different species that have been used in an animal study, which is currently not possible for species that are not used for consumption. Our combined expertises will also allow us to improve existing and create new models for structural heart disease and exploit them as a service to the biomedical community. Summarizing, the future of our collaboration will be exciting ! ♦





**F**ollow [this link](#) to view some remarkable videos on cardioscopy at IMMR.

**W**e are very enthusiastic about this new tool. We have used it in both healthy and pathologic conditions. It is true that there is a bit of show business involved, and it cannot hurt to convince investors and opinion leaders, as the videos are just superb and rare. But it is true also that our endeavour here is mostly scientific insight and in situ visualization, for everyone to understand (valvular motion, prostheses of all sorts, interactions between the anatomy and the device, etc.).

**W**e strongly suggest that you took the time to watch the [videos](#) we posted on our website to fully comprehend the potential of this unique approach to gain insight in cardiac physiology, cardiac dysfunction and in situ medical device assessment. ♦

**IMMR**  
Accelerating **your**  
innovative research

#### Our know-how

Early R&D studies  
Good Laboratory Practice studies  
Surgical Physician training  
Complete pathology services

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