IMMREVIEW

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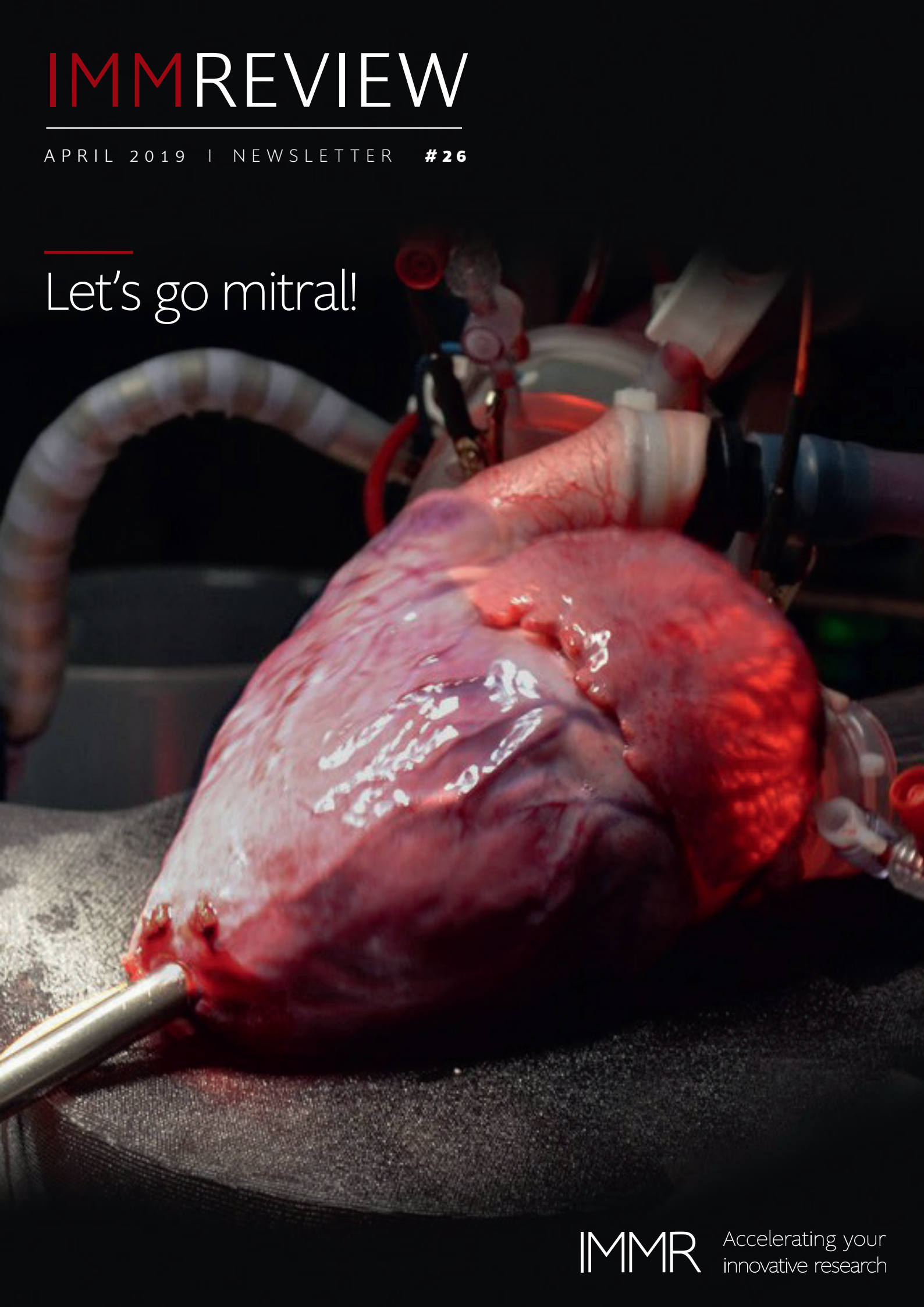
Let's go mitral!



IMMR Accelerating your innovative research

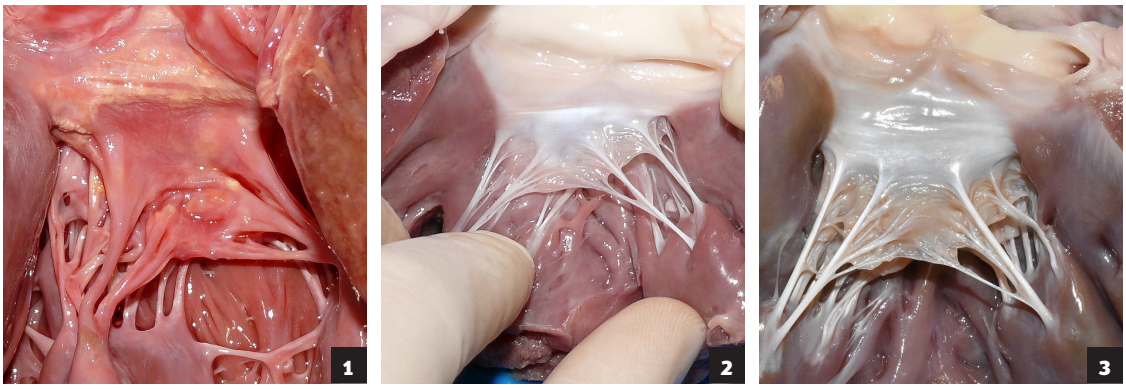
Stented valves and the advent of structural heart devices were a revolution in human interventional cardiology as of the early 2000's. We have been very much involved with this development and have been one of the leading labs in that particular field. Finding the proper animal model for the best experimental set-up is a real challenge for preclinical laboratories.

Now that transcatheter aortic replacement (TAVR) has become one of the key pieces in the armamentarium for the treatment of aortic stenosis, other endeavors arise, such as the mitral valve and the tricuspid valve. More particularly on the mitral front, the anatomy is a lot more challenging and complex than that of an aortic valve.

Let's go mitral!

One of our veterinary surgeons / study directors, Dr Alexis Morlet, DVM, PhD, has been working for the past 4 years on that very subject at IMMR: comparative anatomy of the mitral valve.
Not only from a strictly dimensional standpoint but also functionally with very novel approaches such as cardioscopy.
His work allowed us to strengthen our expertise in that particular anatomic environment, in all clinically relevant animal species.
His work is soon to be published but we use this body of knowledge on a daily basis, trying to fine-tune the animal models used, understand better which is more appropriate all the while understanding that these models bear limitations.
This newsletter is the opportunity for Alexis to tell us more.

Nicolas Borenstein, DVM, PhD
Scientific Director - Founding Partner - Board Member



Comparative anatomy of the mitral valve in Humans **[1]**, Ovine **[2]** and Porcine **[3]**

Alexis, can you tell us what was the objective of your research?

Anatomy has obviously been a strong suit of IMMR and for many years. It is very logical that Nicolas suggested that I entered a PhD program to come up with a comprehensive approach of the mitral valve of different animal species, classically used in MedTech research for the mitral valve. Nicolas wanted me to deepen our knowledge in the specifics of mitral anatomy such that animal mitral valves would become very much our territory, so to speak. This was aimed at being able to help our research groups, start-ups and large players alike, to understand which model was best for their valve and the limitations of each model. We get that question every day, sheep or pig? We now have robust data to support what were mostly hunches or experience.

What are the specifics of mitral anatomy?

The mitral valve is a complex structure, far more than one would believe. There is an annulus, and the so called sub-annular apparatus, i.e. two (more or less) scalloped leaflets (anterior and posterior), cords and papillary muscles. There is a lot of interspecies variability but also quite a bit of intraspecies variability in each of these elements. The annulus is not symmetric. It has a 3D saddle-like shape and is more fibrous on its anterior part and is more muscular on the posterior aspect. The leaflets themselves have a rough zone (where coaptation occurs) and a smooth zone. This is strictly descriptive but the functional aspects are also fascinating and for a large part not fully understood. Not to say that the aortic anatomy or function is a walk in the park but the mitral valve is indeed a complex structure.

What animal species did you choose and why?

We chose the relevant animal models for preclinical validation of novel mitral devices, sheep and pigs mostly, and also added dogs. We compared all three species to humans.

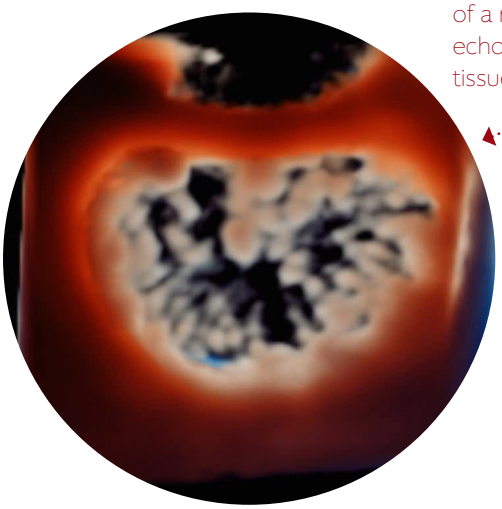
Dr Alexis Morlet, DVM, PhD

Did you focus on descriptive anatomy only?

Certainly not; once we had validated the comparative anatomy of those 4 species, we moved on to intracardiac visualization with so called cardioscopy, a technique whereby we introduce a camera inside the heart and replace the blood by saline. The images are simply spectacular and extremely insightful. We also added a CT scan study as well as a histological approach. All of this is or will shortly be published in peer-reviewed journals.

Apical view of a porcine mitral valve during cardioscopy.

atrial «surgeon eye's view» of a mitral valve with echocardioscopy and tissue rendering modality



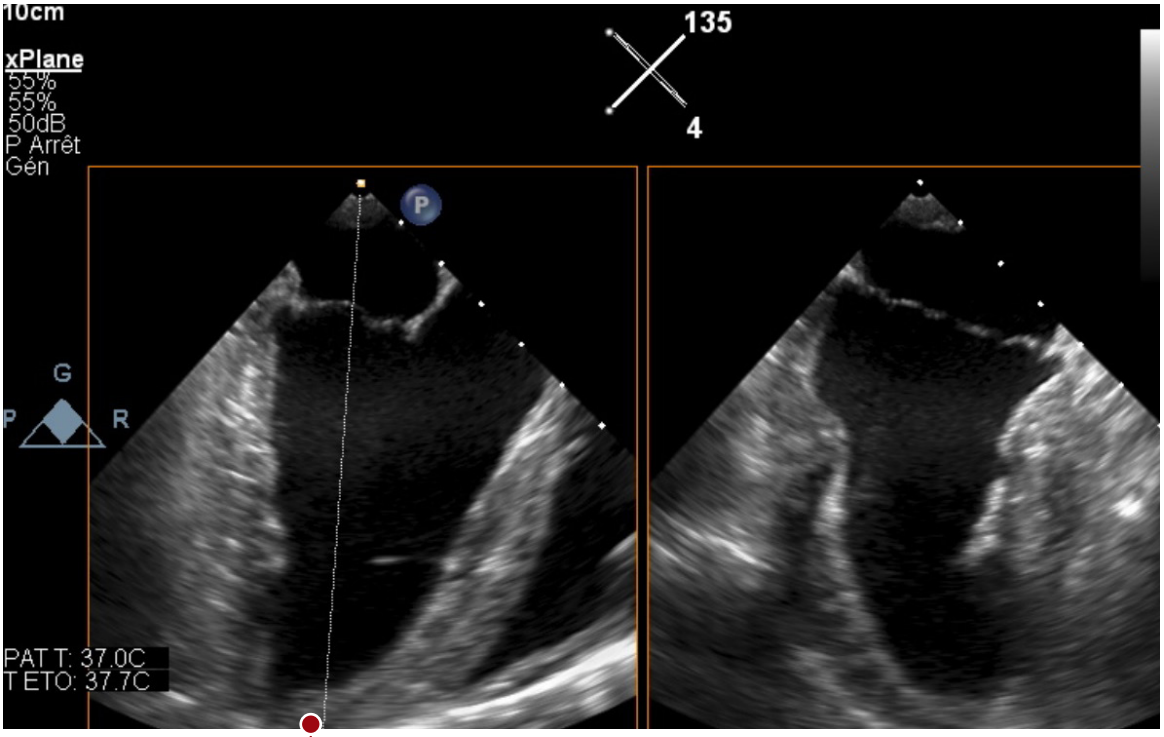
How does this help the research groups that work with IMMR?

Most of our studies start with a thorough reflection upon what best animal model we should use as regards sizing, specific anatomy, ease of sourcing of animal models, etc. The mitral groups we work with have the same basic needs, sheep or pig, what age, what size, what problems we may encounter with each model (anatomically speaking, functionally speaking and biologically speaking, not to mention regulatory aspects). We have a tremendous body of knowledge to address their questions.

Apical view of an ovine mitral valve during cardioscopy.

What kind of collaborations did you have for this beautiful endeavor?

My PhD allowed me to work with many different people (that's one of the great aspects of such a project), the Ecole doctorale MTCI (Sorbonne Paris Cité), Pr. Christian Latrémouille, head of the cardiac surgery department at the Georges Pompidou Hospital in Paris, the Anatomy Laboratory URDIA with Paris V, the LifeTec group from Eindhoven for functional beating heart cardioscopies, Dr Jean-François Paul from the imaging department at IMM, Dr Laurence Fiette, IMMR's chief of Pathology, and everyone at IMMR!



Long axis echocardiographic view of the mitral valve

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Editor: Nicolas Borenstein
Photos: © Nicolas Borenstein

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