**Transcript**

**Emmanuel Kattan, Host**: This is “Vis à Vis”, a new podcast series brought to you by the Alliance Program at Columbia University. "Vis a Vis" features conversations that challenge our understanding of key global, economic and social issues by casting them in a transatlantic perspective. I’m Emmanuel Kattan. I head the Alliance Program, a partnership between Columbia University and 3 French universities: Sciences Po, Paris 1 Panthéon Sorbonne and Ecole Polytechnique. Every episode, I sit down face to face – or as we say in French, “Vis a Vis” – with some of the most insightful thinkers on both sides of the Atlantic. I hope you enjoy our conversation.

(Theme music out)

**Kattan**: Every year, 1.3 million babies are born with congenital heart disease worldwide. One-third of them need an artificial valve implant. These complex heart surgeries save hundreds of thousands of babies' lives every year. But valve implants are not a perfect solution. There's an increased risk of blood clots, and as the baby's heart grows, the valve does not. New valves need to be implanted every few years, which requires multiple operations. These repeated surgeries have a deep impact on these children's quality of life. In today's episode of Vis a Vis, we will be discussing a pioneering technique currently being explored to improve operations on children's hearts. This technique involves the creation of artificial heart valves that expand as the child heart grows, which will significantly cut down the number of operations a child has to undergo. This innovation is being developed by David Kalfa, Florence Irving Assistant Professor of Surgery and Director of the Pediatric Heart Valve Center at Columbia University, and Abdul Barakat, CNRS Director of Research, AXA Professor at the Hydrodynamics Laboratory at École Polytechnique, and co-Chair of Biomedical Engineering at Institut Polytechnique Dubai. I have the pleasure and the honor to talk to them about their project today. Professor Kalfa is a cardiothoracic surgeon. Among his specializations is pediatric cardiac surgery. Over the past several years, he has performed cutting-edge studies that demonstrate the use of polymers in the design and development of novel artificial heart valves. Professor Barakat has a long standing interest in cardiovascular bioengineering. He's a recognized expert in experimental and computational biomechanics, with applications including computational modeling of vascular mechanics. Professor Kalfa, let me turn to you first. Could you provide us with the state of play concerning cardiac surgery for children today? How common is it for a child to need cardiac surgery? How common is it that these kids need repeated surgeries? And how does that affect their lives?

**David Kalfa, Guest**: Thank you very much, Emmanuel, thank you for this invitation. That, these are great questions. So I should say first that congenital heart defects are actually the most frequent malformation in children. In humans, I should say. Almost 1% of all the babies in the world have a congenital heart defect. So that's a huge number. And the vast majority of them will need an open heart surgery. In a center like Columbia, we do open heart surgeries between two and five times a day, just to give you, you know, an idea of how frequent this type of condition is, and how frequent an open heart surgery is needed in children. And these can go from one day of life to, to the adult, adulthood. Regarding you, your question of what kind of health condition can lead to cardiac surgeries, mainly malformation of the heart. And finally, you're asking me, how common is it that these kids need repeated surgery? Actually, that's very frequent, especially when we start working and on the valve zone. These patients need multiple operations. Why? Because first of all, we always try to repair the valve, which means that we keep the native tissue of the kid and then we try to improve the functioning of the valve. And if this doesn't work, then we have to replace the valve. In both options, you know, these patients need open heart surgery and repeat open heart surgery, either to improve the repair, or to replace the valve multiple times because of the lack of growth that we will be discussing very soon.

**Kattan**: Right, right. And could you, could you explain to us — for those like myself, who are laypersons — how exactly does, does a heart valve work? And you know, what, what's the specific challenge that you propose to address in the project that you're developing with Professor Barakat at Polytechnique?

**Kalfa**: So the valve is a structure inside the heart that allows the blood to go into one direction and not the other one. Promote the antegrade flow without having a retrograde flow. Okay, so we have four types, four valves in the heart, two on the left side, which are the mitral valve and the aortic valve, and then two valves on the right side, which are the tricuspid valve and the pulmonary valve. Three of these valves are made of three leaflets, which are, you know, these small components which open, right, during the ejection and then close during the diastole. And one of these valves is made, the mitral valve made of two leaflets only. So this is the way that these valves work. And the specific channel that we want to address is the fact that currently, none of the valve prosthesis that we have available right now have a growth potential. So what does it mean? It means that when you have to replace the valve, whatever valve it is, you know, you know, a neonate, for example, an infant, then this valve is obviously a small valve because you don't have enough space to put a large valve, obviously, and this valve will not grow. So you will have to reoperate multiple times on these children to change the valve once the valve is outgrown by the patient, or when the valve fails. Because some of these will also have a significant tendency to degenerate and calcify with time. And each of these open heart surgeries is a significant surgery. There's a significant amount of morbidity and mortality. Right? So this is what we, this is the unmet clinical need that we really want and we are working to, to address along with Professor Barakat.

**Kattan**: Right. That's fascinating. And, and on, on your side of the equation, Professor Barakat. So, could you describe the kind of valves that you are trying to develop, and why they are called "polymeric valves"? And what is the polymeric valve? How does it work? And how do these valves differ from the ordinary valves that Professor Kalfa just described are being implemented on children's hearts?

**Abdul Barakat, Guest**: So thank you, Emmanuel, for the invitation. So the polymeric valves are basically valves that are made of polymeric materials, as opposed to mechanical valves or biological valves, right? So there's basically synthetic materials. If you put biological valves into kids, for example, biological valves that are derived from animals, for example, they've been shown to have limited durability. And so polymeric valves are supposed to be superior in that respect. And with the ability to control the com- the composition of polymers, we're able to make them biocompatible, and also hemodynamically very attractive, so they're able to basically accomplish their, their task, which is what Professor Kalfa mentioned, the idea of having forward flow, but not retrograde flow. If you design the polymer correctly, you should be able to meet that objective. Now, you asked, how are, what's specific about these types of valves that we're developing in collaboration with Professor Kalfa? Well, this goes back to what Professor Kalfa mentioned, that you don't have room to put a large valve in a small child. So what we're trying to do here is, since we need more surface area, basically, because as the child grows, we need to be able to accommodate the growth of the vessel that develops is inserted in. We’re using the third dimension, right? So instead of something that is completely flat to begin with, we're actually making a structure that has some height to it. You know, as the child grows, this thing becomes flatter and flatter. So by the time the child becomes an adult, ideally, your valve is flat just like an adult's native valve is. And so the key thing is to try and add surface area while trying to maintain optimal performance.

**Kattan**: And these valves would last when they're made in polymer. What is their life expectancy? I mean, do they last 10 years? 20 years? Do you have an idea? Are you able to test that?

**Kalfa**: Our data show that the durability of this valve is very, very promising. Let's remind that the currently used porcine or bovine valve that Professor Barakat just mentioned usually lasts for 12 to 15 years in adults. But the rate and, the rate of degeneration and degradation in children is much, much faster. When you implant a porcine or bovine valve in, let's say, a three month old infant, it lasts sometimes only nine to 12 months. Right? So it degenerate very, very quickly. These valves, the durability of these valves seems to be very promising, and they can last up to 10 to 15 years, which is a huge, a huge benefit for this patient when you know how quickly the animal-derived valve can degenerate.

**Kattan**: Right, right. And then the valves themselves, so that's the part of this surgical procedure to actually implant these valves. But are these valves sewn on to the heart? Or is there a process whereby you make tissue grow around the valve so that it actually gets implanted?

**Kalfa**: Yeah, so very good question. So when we do, you know, because we are working specifically on the pulmonary valve, right, which is the valve which is located between the right ventricle and the pulmonary arteries, which are the arteries going to the lungs. When we do this operation on a daily basis — I do this one yesterday, and I will do another one today — we have to actually reconstruct completely the connection between the right ventricle and the pulmonary artery. So we have to implant not only a valve, but actually a new vessel, right, which is a kind of a tube, basically, a new vessel with a valve inside. So, in our project, we hypothesize that biohybrid design will be the most effective. What does it mean, "biohybrid"? We mean that the valve that Doctor Barakat was mentioning, the valve is made of polymer, which is biostable, which means that the polymer will stay here forever. It will not degrade with time. Right? But the tube that we will implant at the same time, which is the future vessel, where the valve will be, is made of biodegradable polymer. So, the concept behind the vessel is actually a concept of regenerative medicine and tissue engineering. So we use a biodegradable polymer to create this tube. This polymer is designed to degrade with time and being replaced by your new tissue made of the cells coming from the host. Cells coming from the patient. And the cells will lead to the formation of new autologous and living tissue. And because it's autologous and living, it can grow. So the vessel, or the tube will grow, because at the end of the day, it will be made of the patient's own tissue. And then the valve itself is made of a biostable polymer. So it will not be replaced by your new tissue. But thanks to the design that Dr. Barakat just mentioned, with the extra length of height, then these valves can accommodate the growth of the tube once the tube grow. So that the whole concept.

**Kattan**: I see. And Professor Barkat: So, when you're creating, developing these valves, obviously, you have to be able to test them. So first of all, where are these, these polymer valves developed? Are they developed in, in the lab, or or do you have at Polytechnique itself, the, the wherewithal to design and produce these vials and then test them?

**Barakat**: Yeah, so so that's, that's a very good question. We – the development and the testing is actually done in collaboration between Dr. Kalfa’s group and ours. So, we at École Polytechnique are primarily spearheading the computational part of the design, implementation, and testing. And Professor Kalfa's group is primarily conducting the experiments. And so, the idea is we're doing this approach, kind of highly interdisciplinary approach, where we're using computational simulations to optimize the design. And, you know, whenever you're doing computational simulations, you need to also validate the simulations experimentally. And so that's why we need to also run experiments that show that the computational models are valid and accurate.

**Kattan**: I see. And how does computational modeling work, essentially? I mean, you, you take data from the polymeric valve itself in terms of its size and different data points, you basically create a program, you enter them into the program, and how does the testing work?

**Barakat**: Computational modeling of the performance of, say, engineered systems has been around for many, in many different industries for a while, right? You know, cars often are designed computationally before they're built. Airplanes and wings are designed computationally before they're built. There are many, many industries that actually start with computational design, at least in order to narrow down the choices that you're going to eventually test experimentally, right? Computational modeling is a very robust and powerful tool to try and play around with parameters. So, you know, you start with some basic design, and then you say, "Well, what if I change this parameter? What if I tweak this, the material properties of this design? What if I change the dimensions? What if I change the angle with which it's oriented?" Things like that. And these are things — if you have confidence in your computational model — then these are things that you can test much more easily and in a less expensive manner, than having to run an experiment every time to try and, and get the results. In the specific case of the valves that we're working on, we started dreaming up what these designs might look like. And we then drew the design on a computer. And then we entered that design into what's called a "meshing program." And meshing program means you convert your drawing into a computational mesh on which you can actually make computations at every point in the design. And then that computational mesh is then entered into another software in order to know how this design is going to respond to external stimuli. So in our case, for example, we say, “Well, we need a certain amount of flow to go through this valve.” And we control the mechanical properties, as well as the thickness of the valves' leaflet leaflets. And we try and see what the computational prediction is on how the valve is going to open, what dynamics — how, is it going to be fully open? Is it gonna be only partially open? And then when it closes, does it close fully? Does it close only partially and then leak? You know, there's all, these are very important considerations, right? And then we, in this particular case, we want to make sure that the designs work for a child as well as for an adult, right? Now, we do these simulations, but at some point, we have to validate them experimentally. And that's where the collaboration with Professor Kalfa's group becomes essential. So we tell them, for example, "These are some designs that we think have the potential to work, can we validate them?" And then they measure the performance, the opening, the closure, the, what's called the regurgitation, meaning the leakage of the valve, if there is any. And we then verify that the experiments give you the same thing as the computations. And when we get agreement, then we have confidence in the computational modeling, and we can go back to the computational models, and use them to try and optimize the design even further. That's kind of the idea of iterating between experiments and computations.

**Kattan**: Right, so there's a feedback loop, in a way, between the testing, the computational testing, and the design, or the fixing, or the tweaking, of the design of the valves that is being done in your lab, also, David Kalfa. And and, Professor Kalfa, so, in terms of testing, what, what do you do? Because then, you know, these valves have to work in, in real life, as it were, not just as a computational model. How do you test them in real life?

**Kalfa**: We have basically three ways to validate it. The first one is to use what we have here in my lab. A heart valve pulse duplicator, which means basically, that it's bench test setting that, where we can put a valve and that we will mimic the circulation of the blood as it will through the, the heart, basically. And we can measure and quantify the functioning of the valve. We also have a durability valve tester, which means that's another machine that we can put a valve, which will open and close the valve in a very accelerated fashion. To see how much cycles of opening and closing this valve can endure, can support basically, before failing from a mechanical standpoint. And finally, at the end of the day, obviously, we will implant it in a large animal model, right? So, we will implant it in growing lab model. So we take your lab, and then we'll implant the valve in the primary position. And then we can then dilate these valves, a few hours or a few days after the surgery, and then repeat an echocardiography or a catheterization to assess the degree of obstruction and regurgitation before dilation, which will correspond to the diameter of of a young baby, and after dilation, which would correspond to the diameter of an adolescent or an adult. So this is the way that we use all these experimental data, basically, to work in a very collaborative and multidisciplinary fashion with Dr. Barakat's team.

**Kattan**: That's really fascinating. That's fascinating. You were mentioning this collaboration. And I was wondering, Professor Barakat, in terms of the collaboration that you've established with David Kalfa's team, how, you know, how crucial is it for an institution like yours, for for École Polytechnique, for Institute Polytechnic Dubai, to create these collaborations? And also, perhaps, you know, how, how often do these collaborations happen, specifically on cardiac research? I mean, are there a lot of these international collaborations? Or do labs basically work more often on a national basis? How important is it, really, to create these international collaborations? And, and, and also, you know, what incentives are needed? I mean, what what are the challenges? Are they financial challenges, or logistical challenges? How can we encourage more of these international collaborations that lead to, you know, such constructive and promising results?

**Barakat**: I've thoroughly enjoyed the collaboration with with Professor Kalfa's group. It's been a very, very gratifying experience overall. Now, you mentioned how much international collaboration occurs in cardiac research. Research is becoming, or has become, very international. And we have all sorts of tools to collaborate across the world. And I think, in this particular case, I mean, I think Professor Kalfa's team has unique expertise that I think we couldn't have found in too many other places. So that, it, that collaboration needed to be international. You asked also about what the hurdles are. Well, the last two years it's been COVID. That's been one hurdle. But other than that, I mean, you know, there are all sorts of hurdles. Certainly financial, in terms of limiting what you can do. And that's where, for example, the Alliance grant, the the seed grant that we got through Alliance Program has been very, very important. Because it has allowed us to actually do the experiments and the, and the simulations that we're doing, to get things going. And now that we have these results, we're actually writing a paper now to describe these results. That's going to allow us to then go to a bigger funding source and say, "Let's build on this seed grant with you know, something that would, that would allow us to continue the collaboration."

**Kattan**: Yeah, thank you. Thank you so much. And this is a fascinating conversation for me and such admirable work that you're doing. My last question to both of you is a very simple one, you know, what, what drives you, basically to do this work? And, you know, where where do you find your, your motivation? Professor Kalfa, do you want to start?

**Kalfa**: I would say passion, passion for what I'm doing primarily in the operating room, right. It's a challenging job, very highly demanding, for me and for you know, my family as well. And for the whole team who is working along with me. So passion to improve the quality of care, and the quality of the outcomes and the quality of life of these children with congenital heart defects. To give them a normal life. Right? Without even talking about trying to decrease the costs related to the healthcare system, actually, right? Which is another, another important point to mention. That's the reason why, you know, we operate during the day and we do research during the night and during the weekends.

**Kattan**: Right. And, and I won't ask you when you, when you sleep, because I'm sure you sleep very little. Professor Barakat, how about you? What, what drives you to do this work and, and all the work indeed, that you do in terms of cardiovascular, computational testing and computational modeling?

**Barakat**: You know, David sees, of course, these young patients in a very real and concrete way every day. I don't, but I can only imagine how it is. But you know, I think if we're able to contribute a tiny bit towards improving the lives of these kids, I think it would be just absolutely amazing. So, so and, you know, this is one project we work on, we work on other projects, as well. And the driving force, I think, for any biomedical engineer, is always let's try to make a little contribution to improving human life.

**Kattan**: Wonderful, thank you so much. Thank you, thank you both for your contribution, for this fascinating conversation. I've learned a lot. I'm in awe of, of what you, both of you are doing. And we will be following, very closely, the development and the results of your project together. Thank you both so much, and have a lovely day.

**Barakat**: Thank you.

(Theme music in)

**Kattan**: “Vis A Vis” is brought to you by the Alliance Program, a partnership between Columbia University, Paris 1 Panthéon Sorbonne, Sciences Po and Ecole Polytechnique. This podcast is produced by Monica Hunter-Hart and Abdibasid Ali, and I’m Emmanuel Kattan.

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