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Rwanda: My Memories Regarding Pediatric Cardiology and More

Jacek Bialkowski, MD; Małgorzata Szkutnik, MD; Emmanuel Rusingiza, MD

My interest in the development of the field of pediatric cardiology in Rwanda has been growing since 2018, when I visited this country for the first time.[1-3] Rwanda is a small, beautiful, and mountainous Central African country **(Figure 1)** with a difficult and complex contemporary history and a population of 12.5 million people, with the highest concentration of inhabitants (mainly children) in this region of Africa.

The capital city of Rwanda, Kigali, which is located in the center of the country, has two cardiology centers: King Faisal Hospital (KFH), which is the national reference for cardiology interventions (cardiac surgery and catheterization), and has acquired a new catheterization laboratory (November 2020). This enables visiting humanitarian medical operators from abroad to perform surgeries. The second is Kigali University Teaching Hospital (CHUK), a major public tertiary level hospital, located in Kigali City and where the two pediatric cardiologists are based. Humanitarian missions organized by Chain of Hope Belgium Charity Foundation are still conducted in KFH twice a year, where simple Congenital Heart Diseases (CHD), like Atrial Septal Defect (ASD), Patent Ductus Arteriosus (PDA) and Pulmonary Valve Stenosis are treated percutaneously.[4] From 2008-2017, a cardiothoracic surgery program of ten international humanitarian missions (mainly by Brigham and Woman's Hospital from Boston, USA) took place in KFH, during which 200 valves were implanted in 149 patients with Rheumatic Disease (RHD).[5] However, although the majority of pediatric patients mostly with CHDs are treated in Rwanda during humanitarian missions, there are still a large number of patients with CHD and RHD being surgically treated outside Rwanda (in India, France, Israel and Egypt) with support of the Rwandan government and humanitarian organizations.

FIGURE 1 *Sunset in Rwanda*

This time, I was invited to Rwanda along with Professor Malgorzata Szkutnik, MD, by the Director of KFH, Professor Milliard Derbew, and Dr. Emmanuel Rusingiza, Senior Lecturer at the School of Medicine and Pharmacy, University of Rwanda and Pediatric Cardiologist at CHUK. This was possible with support from the Medical University of Silesia, Poland (our workplace). During this period, we gave several lectures in KFH and CHUK on our experience in percutaneous treatment of CHD. Special attention was paid to problems of ventricular septal defects closure, both congenital and postinfarction (PIVSD). Our experience with 28 patients with device closures of PIVSD indicates that such fragile defects should be treated with device closure after at least three weeks of initial septal rupture healing, when the procedure is much more effective (publication in preparation). We also participated in the outpatient clinic activities at CHUK with Dr. Rusingiza, where we saw the real and

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FIGURE 2 *Pride of impala antelopes in Akagera National Park, Rwanda*

FIGURE 3 *King bull in Nyanza, Rwanda*

enormous number of children with CHD and RHD needing proper treatment. Moreover, we were surprised by the high number of patients with genetic disorders coexisting with CHD (Downs, Noonan, Williams Syndromes, etc.). Rwanda developed quickly and is a well-organized and safe country, in which the worldwide conference of Commonwealth Heads of Government Meeting

FIGURE 4 *Center for Blind Children in Kibeho, Rwanda*

(CHOGM) was held in June of this year (53 countries participated in this event) in Kigali City.

During the weekend we visited several popular sites. The most impressive was a safari in Akagera National Park **(Figure 2).**

As Rwanda history is very interesting, we visited the King's Palace in Nyanza with famous traditional bulls with big white horns **(Figure 3).**

We also visited Kibeho, a pilgrimage site dedicated to Virgin Maria, where there is also a shelter for more than 150 children who are blind, some of them are albino **(Figure 4).**

The shelter, which was built by and continuously supported by the Polish government, is conducted by Catholic Franciscan Sisters. They deserve recognition as they are very well-prepared for this calling. This is a branch of a similar organization for people who are blind in Laski, Poland.

In conclusion, there is potential for development of Pediatric Cardiology in Rwanda. However, much has to be done, especially development of cardiac surgery and interventional cardiology of CHD. A call for advocacy to address the burden of pediatric heart diseases in Africa has been made for many years.[6]

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A Heads-Up to Our Readers: Do You Know What a Valuable Resource the Congenital Cardiology Today Program Directory Really Is?

John Moore, MD

Congenital Cardiology Today has published and posted a Program Directory of congenital and pediatric cardiac care providers in North America for more than a decade. We provide it to our readers without charge on Congenital Cardiology Today's website homepage, CongenitalCardiologyToday.com. The Directory provides current data as the Directory is updated annually in August.

This Directory lists over 130 programs including all of the major ones in the United States and Canada. For each program, the Directory provides: the address, phone number and fax; the director's name and contact information; names of affiliated pediatric cardiologists and congenital heart surgeons; as well as information about available training programs. If there is a pediatric/congenital cardiology ACGME fellowship program, the program director's name and contact information is provided. Programs in the United States are organized according to the city and state where they are located. Canadian Programs are listed alphabetically by location.

The Directory is useful for making patient referrals, locating and contacting colleagues, identifying training programs for young physicians, etc. If you know about it, you will probably print it and refer to it on a daily basis. Take a look. You'll be glad you discovered this valuable resource!

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FIGURE 1 *The Program Directory's Cover as it appears on the CCT website homepage, CongenitalCardiologyToday.com*

United States

Alabama

Birmingham

Children's of Alabama/
University of Alabama at Birmingham
Pediatric and Congenital Heart Disease Center of Alabama
1700 6th Ave, S, Ste 9100
Birmingham, AL 35233
www.childrensal.org/heart
Division Chief of Pediatric Cardiology
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Pediatric Cardiologists
Waldemar F. Carlo
Leslie Collins
Marc Cribbs
Camden L. Hebson
Walter H. Johnson
Austin M. Kane
Yung R. Lau
Mark Law
William S. McMahon
F. Bennett Pearce
Robb Romp
Khalisa Syeda
Hayden Zaccagni
Congenital Heart Surgeons
Robert J. Dabal, Director of Surgery
David Cleveland
Robert Sorabella
Pediatric Cardiology Fellows
3 ACGME
1 CVICU

Arizona

Phoenix

Phoenix Children's Hospital
Children's Heart Center
1919 E. Thomas Rd.
Phoenix, AZ 85016
www.phoenixchildrens.com
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Craig Cohen
Damon Dixon
Erik Ellsworth
Wayne Franklin
Byron Garn
Joseph Graziano
Ryan Johnson
Christopher Lindblade
J. Carlos Macias
Erika McLaughlin
Neda Mulla
Todd Nowlen
Andrew Papez
Robert Puntel
Edward Rhee
Arash Sabati
Bethany Wisotzkey
Steven Zangwill
Congenital Heart Surgeons
Mohammad Alaeddine
Roosevelt Bryant
Javier Gonzalez
Daniel Valle
Pediatric Cardiology Fellow
9 ACGME

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Andrew Hoyer
Scott E. Klewer
Ricardo Samson
Mike Seckeler
Congenital Heart Surgeon
Kenneth Fox

Arkansas

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Josh Daily
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Pediatric Cardiologists
Michael Angtuaco
Sylvia S. Angtuaco
Lindsay Arthur
Thomas H. Best
Rupal Bhakta
Tanmay Bhamare
Elijah Bolin
Renee A. Bornemeier
Harrison Cobb
Tyler Cunningham
Joshua Dailey
Srikant Das
Amy Dossey
Brian K. Eble
Eudice E. Fontenot
Elizabeth A. Frazier
Xiomara Garcia
Scott Gatlin
Kevin Hinkle
Kenneth Knecht
Sam Lee
Shane Merves
Michele M. Moss
Pankaj Pradhan
Aruna Qasim
Markus Renno
Paul M. Seib
Dala Zakaria
Cardiac Surgeons
Lawrence Greiten
Brian Reemsten
Pediatric Cardiology Fellows
6 ACGME
2 CVICU
1 Advanced Imaging

California

Loma Linda

Loma Linda University Children's Hospital
11234 Anderson St, Rm 4433
Loma Linda, CA 92354
https://lluch.org/locations/loma-linda-university-childrens-hospital
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Pediatric Cardiologists
Erik Frandsen
Upinder Jodhka
Gregory Jutze
Ahmed Kheiwa
Michael Kuhn (Chief)
Jesse Lee
Jennifer Lo
Ravi Mandapati (EP Director)
Shireen Mukadam
Steve Nageotte
Natalie Shwaish
Jade Tran
Sonia Voleti
(Continued on p. 6)

FIGURE 2 *Typical page from the Directory listing programs in Alabama, Arizona, Arkansas and California.*

Lymphatics and So Much More

Kamel Shibbani, MD

We recently had the pleasure of sitting down with Dr. Yoav Dori, MD, PhD, Director of the Jill and Mark Fishman Center for Lymphatic Disorders at Children's Hospital of Philadelphia. Our conversation very nicely summarized the state of the field of lymphatics at the moment. Dr. Dori highlighted the importance of lymphatics and Congenial Heart Disease, the options for lymphatic imaging at the moment, and available treatments for lymphatic disease.

KS: Dr. Dori, thank you so much for the opportunity to chat about this growing and exciting field! Can you tell us a little bit why is it important to understand lymphatics, in particular when talking about patients with Congenital Heart Disease?
YD: Until now, most cardiology trainees did not get much exposure to lymphatics. There's a reason why this was called the forgotten circulation. However, it plays a very important role in everything we do! In the past, it was difficult to image the lymphatic system and to intervene upon it, so people just ignored it. We have, however, an entire population of patients with severe lymphatic dysfunction. I got into this field because we had a patient with plastic bronchitis, a disease that was historically considered to have a 50% mortality. Early on, there were hints of lymphatic involvement in the development of plastic bronchitis, so we started looking into the possibility of using MRI to better study this system. However, traditional imaging alone was not enough.

We did animal studies at Hopkins and developed the technique called intranodal dynamic contrast MR lymphangiography. When dealing with a circulatory system, you need to define anatomy, flow, and hemodynamics - or in this case lympho-dynamics. Dynamic contrast lymphangiography allowed us to study anatomy and flow, and we had the techniques to enter the lymphatic ducts and understand hemodynamics. We were able to start developing more selective procedures to understand how the lymph system plays a part in different diseases. This allowed us to better understand its role in PLE, chylothorax, and plastic bronchitis, as well as its role in heart failure, ascites, edema, and many other diseases.

KS: Where do we stand now with disease process like plastic bronchitis with respect to prognosis?
YD: We're submitting a paper about plastic bronchitis that shows that survival for patients is now between 90-95%. In reality, we are now at a point where we expect to be able to treat almost all patients with plastic bronchitis. That is a complete paradigm shift in the disease. The same applies for chylothorax, where we can fix almost all of those as well. PLE (protein losing enteropathy) is proving to be more difficult. Though even for PLE, we are looking at close to 70-80% ability to control and even resolve it. The one disease that is a little more complicated is multi-compartment lymphatic failure. And while it is more difficult to treat than isolated lymphatic dysfunction, we have multiple treatment options that have significantly reduced mortality even in these most complicated patients.

KS: You mentioned intranodal lymphangiography as a turning point in the field of lymphatics. Can you talk to us about the role that other imaging modalities have played in the understanding of the lymphatic system?
YD: Imaging has been integral in discovering the pathology of the lymphatic diseases in CHD. Imaging of both flow and anatomy was absolutely key in this. The main streams that are supplying the thoracic duct are the liver, lungs, and the mesentery. The liver contributes about 40% of lymphatic flow in healthy patients, though that can increase significantly in patients with heart failure. Liver lymphatics can now be visualized through intra-hepatic dynamic imaging, and that is what allowed us to understand the the etiology of PLE to a large extent. The mesenteric lymphatics, which play a big role in ascites, had historically never been imaged. We have developed a method of imaging mesenteric lymphatics through the use of intra-mesenteric lymphangiography.

Kamel Shibbani, MD

Yoav Dori, MD, PhD

"Plastic bronchitis was historically considered to have a 50% mortality [...] Survival for patients with plastic bronchitis is now between 90-95% [...] That is a complete paradigm shift in the disease process"

Yoav Dori, MD, PhD

KS: What is the prognostic value of understanding different lymphatic disorders and lymphatic anatomies in patients with CHD?
YD: As our understanding of lymphatics grew, we started classifying lymphatic disorders of the chest based on T2 imaging and dynamic contrast lymphangiography. What we found is that T2 imaging proves to be an excellent predictor of which patient will have a successful Fontan based on the location of the lymphatic abnormalities in the lungs. This is something we now use to classify patients into those at high risk of Fontan failure. As far as the dynamic imaging, we use that as a guide to understand what interventional procedures these patients would potentially benefit from after they undergo surgical palliation. We have also started categorizing the liver lymphatics as well to help guide post-surgical management.

KS: What is your screening protocol for single ventricle patients?
YD: We screen our patients twice, once before the Glenn and another time before the Fontan. At a minimum, each and every single-ventricle patient should have a screening done before the Fontan with a T2 weighted MRI scan.

KS: Is there a process in place of helping other centers perform some of the lymphatic work that your group has pioneered?
YD: We have taken the approach that our job is to make sure that this knowledge is disseminated, and we've put in a huge amount of effort to do that. Anyone who wants to come to our center is welcome, and we have made it a point to start training people from all over the world. People come for a week or two, learn the techniques, and after they go back home, we set up regular zoom conferences where we discuss the patient images and what needs to be done next. Some people have come here to train on interventional techniques, and in other cases we have travelled to centers to train people if they cannot come to us. Typically, someone can learn to do the basic imaging techniques in a few weeks.

KS: Can you talk to us about some of the interventions that can be offered to patients in whom a lymphatic disorder has been identified?
YD: This is another area where the field is evolving rapidly. In the beginning, there was only thoracic duct embolization. And while this is a simple procedure and could be helpful in some, it can be very harmful in a single-ventricle patient. This led to the development of tools to allow us to do selective procedures. Today, with the exception of placing valves, we've been able to do the same types of interventions in the lymphatic system that we do in the cardiovascular system; we've stented vessels, ballooned vessels, occluded vessels, embolized vessels, etc. We've also developed tools to decompress the lymphatic system in the cath lab, something that was originally done surgically by Dr. Hraska. So, interventions are much more focused nowadays and tailored to the problem.

In addition, there's also advancements with medical interventions. As more research is getting done and as more people get involved, we will get better at understanding the problem and at developing more targeted treatments.

KS: Dr. Dori, if you would allow us to switch gears a little bit, I was wondering what advice you have for early career interventionalists who are looking to do meaningful research. This does not have to be specific to lymphatics. In general, how do young interventionalists interested in research ensure that they are doing impactful work? How do you create a niche for yourself? When you look at the scope of what your group has done in lymphatics, achieving something similar seems like an impossible task…
YD: It is absolutely not an impossible task. The only "impossible" part is that your mind is already projecting the outcome and thinking "this is impossible, how can I get there?!" If you start by allowing your mind to project the enormous task at hand, the need to develop or create an entirely new field of research, for example, you've already lost.

Marlys Witte, one of my favorite people on the planet, started the Ignorance University. What she's done in the latter part of her life is to teach students how to just ask questions, how to be comfortable with not knowing, and how to ask questions about things you do not know. And that is the single most important aspect of this whole process. And with the ability to ask questions comes humility, which is absolutely needed for this process also. If you look at the world from the correct perspective, you will see that ignorance is infinite, and knowledge is nothing in comparison. Every single thing we do is based in ignorance, it starts from a complete lack of understanding of a phenomenon.

So to create a niche, the only thing you need to do is to have humility and ask questions. Understand that you don't know everything and just start investigating. Don't take things for granted, and, maybe most important, don't fixate on a specific result. It is perfectly fine to have a vision but fixating on a result that must happen will almost never work out.

KS: This reminds me a little bit of the advice that Kary Mullis, the chemist who discovered polymerase chain reaction (PCR), gives in his book "Dancing Naked In The Mind Field". He says that instead of setting up an experiment that tries to solve the entire problem from the get-go, start by solving for a small question. Come up with any reasonable hypothesis to a simple question that relates to the problem, then try to disprove it. Make adjustments to your hypothesis and repeat the process. And keep doing that until you get to a point where you can't disprove your hypothesis anymore. And that process might open some doors that allow you to think of the bigger problem.
YD: That will absolutely open doors. But you have to be willing to listen and to be humble. That is the beauty of some of the other practices that I do, along with other people who spend an entire lifetime trying to live in the present. It is the exact same process that you are doing with your mind.

Think of it this way, you read about someone who makes a discovery or a significant achievement. In your mind, you translate that to "I, too, need to do something that's going to be huge". And now, you have already limited yourself because if you don't get to the huge achievement you imagined, it'll be a problem. And then fear kicks in because the task is so big, and suddenly you're not willing to try.

But everything you imagined about this great achievement you're supposed to accomplish, it's all in your mind. It doesn't exist the way you think it does. All you have to do is just start moving, in any direction! Be curious, ask questions. Forget about this movie you've created in your mind about big achievements, even if you end up writing only two articles. If you do that with joy, then you've already done something good. What's interesting though is that in almost all cases, you will find that when you are genuinely curious, doors will start opening because you will be present to see the opportunities.

KS: That's sounds deceptively easy! How do you simply change the way your mind approaches these problems?
YD: There's a book that I highly recommend: it's called *Altered Traits*. It is a summary of the scientific investigation into what happens to your mind when you do certain types of practices like meditation. There are parts of the brain that have been scientifically proven to be modifiable through these practices. You can teach people to be humble, how to have values, how to be curious, how to be happy. And what's crazy is that we don't do this regularly!

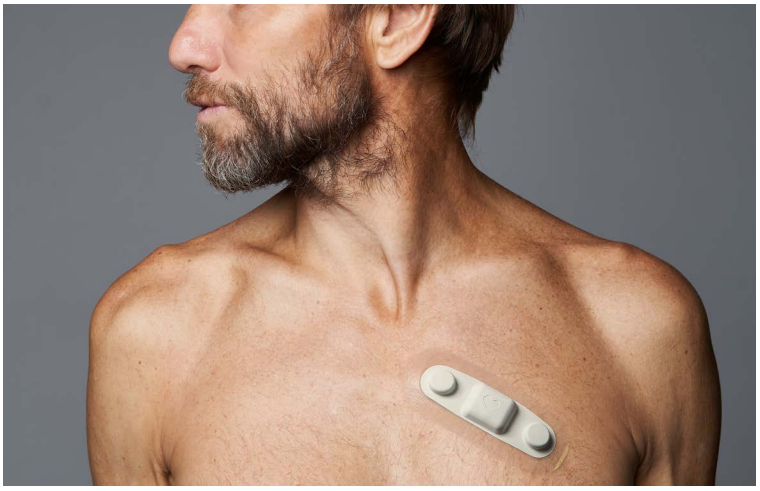
KS: Even though we've moved away from our original topic of lymphatics, this is a fascinating conversation that I feel we need to spend a few more hours on!
YD: (laughing) That sounds good to me actually!

KS: (laughing) Dr. Dori, thank you so much for a wonderful conversation about lymphatics and so much more!

Cuffless Blood Pressure Monitoring – Remote Devices are Changing the Research Landscape

Jiang Li

No one disputes that blood pressure (BP) is one of the critical basic human vital signs, but high blood pressure detection and diagnosis has not significantly changed in decades. The inflatable cuff was invented over 100 years ago, yet it is still the standard basis for measuring blood pressure. The frequency of monitoring is also relatively unchanged; it's still the occasional doctor's office visit.



The Status Quo

The traditional scenario is for patients to have their BP checked in the physician's office or clinic, then perhaps take a few measurements at home and communicate that information back to the clinician. But significant errors and subsequent misdiagnosis can occur. The American Heart Association, ahajournals.org/doi/10.1161/HYP.0000000000000087, cites multiple sources of measurement error: patient-related, device-related and procedure-related issues.

"White coat hypertension" refers to a condition where patients experience persistent high blood pressure when it is measured in a clinical setting. And the opposite effect, though less frequent, can also occur. A Penn Medicine study, pennmedicine.org/news/news-releases/2019/june/people-untreated-white-coat-hypertension-twice-likely-die-heart-disease, found that people with untreated white coat hypertension are at greater risk and are twice as likely to die from heart disease. Some people who don't have high blood pressure in their daily lives, are prescribed unnecessary medications because of the situational high reading. Others have readings within an acceptable range on the day of the office visit, but have masked hypertension that goes undiagnosed. Either way, the single or occasional point in time reading is not an accurate representation of the patient's real condition resulting in an incorrect baseline for diagnosis.

The Evolution

An obvious solution to white coat hypertension is a more robust, non-invasive measurement method that doe not place undue stress on the patient, yet produces quality results. Ambulatory BP monitoring devices are available and produce accurate systolic and diastolic measurements, but they still use inflatable cuffs which are cumbersome and effectively discourage patients from following through with the protocol and is not practical to wear for an extended time.

With the increased adoption of wearable sensors, other devices are being introduced to continuously monitor BP through new technologies. These include wristbands, mobile phone apps, finger sensors and more. Photoplethysmography (PPG) is used in finger cuff monitors but this vascular unloading technique raises concerns about digital ischemia and isn't practical for frequent use.

There is a relatively new class of BP devices that use optical sensors on a wristband - blood pressure is estimated from the pulse arrival time (PAT) which measures the time for a pulse wave to move between two arterial points. Photoplethysmography (PPG) uses optical sensors to detect blood flow volume change by measuring the amount of light either transmitted or reflected. However, the accuracy of optical sensors is dependent on many factors such as the patient's body mass index (BMI), skin tone, movement, and correct device adherence since exposure to other sources of bright light can affect the precision.

Another new option is an advanced multimodal continuous signal processing patch that leverages electrical ECG and mechanical signals to capture BP. Multiple measurements take the patient's activity level into consideration so the excess "noise" can be filtered out to ensure quality data. In the case of the Vivalink rechargeable wearable ECG patch, a continuous stream of data is wirelessly uploaded to a biometric data platform in the cloud where advanced AI algorithms calculate the BP.

The Potential

Cardiovascular or cardiopulmonary studies strive to attain accurate ongoing measurements without placing an undue burden on patients. And physicians need comprehensive data to improve diagnosis and therapeutics. It is key to obtain contextual data to offer a full perspective on what the patient is doing before and during the BP measurement. With sensors that collect multiple vitals, the provider or researcher can better understand the context. For example, an EEG measurement showing high brain wave activity could indicate stress and affect the BP reading.

Myriad physical and functional factors figure into obtaining an accurate measurement. All the elements must work together for optimum performance. Like so many standard-use tools and methods, that cumbersome inflatable BP cuff is not the only game in town anymore. Innovators are designing and implementing technology that will bring about real change for both patients and clinicians. Both the wrist band and the patch are convenient options, but neither is fully verified compared to cuffless BP monitoring - not yet. The point is that progress is being made. Wearable sensors are available for research and development, which is both novel and promising. The concept of measuring blood pressure from a single ECG patch is revolutionary. The remote factor opens the door to test with a diverse population which will be necessary for clinical use and groundbreaking for research. There is still a lot of work to be done, but there are steps proceeding in the right direction.

Jiang Li is founder and CEO of Vivalink. His passion and extensive experience in bringing innovative technology and products into the marketplace positions him as an innovative thought leader in virtual healthcare. An executive with more than two decades of experience across multiple disciplines, including global healthcare IT, medical device, cloud software, and sensor and IoT industries, he is a regular contributor to leading edge media including Forbes and an established industry speaker. Prior to joining VivaLNK, he was responsible for new product and technology development as the VP of engineering at Kovio and Thinfilm Electronics, leading printed electronics companies. Prior to that, he worked at AMD and the joint venture between AMD/Fujitsu, Spansion. As the VP of product engineering at Spansion, Jiang managed the major new product launches at Spansion. Jiang holds 22 US patents, and a PhD degree from the University of Wisconsin-Madison.

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3D Printed, Bioinspired Heart Valves

Scaffolds Created by Melt Electrowriting Aim to Support New Tissue Formation

Prof. Dr. Petra Mela, Technical University of Munich, Chair of Medical Materials and Implants

Researchers have developed 3D printed artificial heart valves designed to allow a patient's own cells to form new tissue. To form these scaffolds using melt electrowriting – an advanced additive manufacturing technique – the team has created a new fabrication platform that enables them to combine different precise, customized patterns and hence to fine-tune the scaffold's mechanical properties. Their long-term goal is to create implants for children that develop into new tissue and, therefore, last a lifetime.

In the human body, four heart valves ensure that blood flows in the correct direction. It is essential that heart valves open and close properly. To fulfil this function, heart valve tissue is heterogeneous, meaning that heart valves display different biomechanical properties within the same tissue.

A team of researchers working with Petra Mela, Professor of Medical Materials and Implants at the Technical University of Munich (TUM), and Professor Elena De-Juan Pardo from The University of Western Australia, have now, for the first time, imitated this heterogeneous structure using a 3D printing process called melt electrowriting. To do this, they have developed a platform that facilitates printing precise customized patterns and their combination, which enabled them to fine-tune different mechanical properties within the same scaffold.

Melt Electrowriting Enables the Creation of Precise and Customized Fiber Scaffolds

Melt electrowriting is a comparatively new additive manufacturing technology that uses high voltage to create accurate patterns of very thin polymer fibers. A polymer is heated, melted and pushed out of a printing head as a liquid jet to form the fibers.

During this process, a high-voltage electric field is applied, which considerably narrows the diameter of the polymer jet by accelerating it and pulling it towards a collector. This results in a thin fiber with a diameter typically in the range of five to fifty micrometers. Moreover, the electric field stabilizes the polymer jet, which is important for creating defined, precise patterns.

The "writing" of the fiber jet according to predefined patterns is conducted using a computer-controlled moving collector. Similar to moving a slice of bread below a spoon dripping with honey, the moving platform collects the emerging fiber along a defined pathway. The user specifies this pathway by programming its coordinates.

In order to considerably reduce the programming effort associated with the creation of complex structures for heart valves, the researchers developed a software to easily assign different patterns to different regions of the scaffold by choosing from a library of available patterns. Furthermore, geometrical specifications such as the length, diameter and thickness of the scaffold can easily be adjusted via the graphical interface.

The Heart Valve Scaffolds are Compatible with Cells and Biodegradable

The team used medical grade polycaprolactone (PCL) for 3D printing, which is compatible with cells and biodegradable. The idea is that once the PCL-heart valves are implanted, the patient's own cells will grow on the porous scaffold, as has been the case in first cell culture studies. The cells might then potentially form new tissue, before the PCL-scaffold degrades.

The PCL-scaffold is embedded in an elastin-like material that imitates properties of natural elastin present in real heart valves and provides micro-pores smaller than the pores of the PCL structure. The aim is to leave enough space for the cells to settle, but to seal the valves adequately for blood flow.

The engineered valves were tested using a mock flow circulatory system simulating physiological blood pressure and flow. The heart valves opened and closed correctly under the examined conditions.

Nanoparticles Allow for Visualization Using MRI

The PCL-material was further evolved and evaluated together with Franz Schilling, Professor of Biomedical Magnetic Resonance, and Sonja Berensmeier, Professor of Bioseparation Engineering at TUM. By modifying PCL with ultrasmall superparamagnetic iron oxide nanoparticles, the researchers could visualize the scaffolds using magnetic resonance imaging (MRI). The modified material remains printable and compatible with cells. This might facilitate the translation of the technology to the clinics, as the scaffolds can thus be monitored upon implantation.

"Our goal is to engineer bioinspired heart valves that support the formation of new functional tissue in patients. Children would especially benefit from such a solution, as current heart valves do not grow with the patient and, therefore, have to be replaced over the years in multiple surgeries. Our heart valves, in contrast, mimic the complexity of native heart valves and are designed to let a patient's own cells infiltrate the scaffold", says Petra Mela.

The next step on the way to the clinic will be pre-clinical studies in animal models. The team also works on further improving the technology and developing new biomaterials.

NEONATOLOGY TODAY
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US to See a Staggering Number of Cardiomyopathy Cases by 2031 According to GlobalData

- *2.3 million cardiomyopathy cases expected in the US by 2031, representing 83% of total cases in the 7MM (The US, Japan, France, Germany, Italy, Spain and the UK)*
- *Lack of epidemiology data and poor lifestyle choices contributing to US numbers*
- *US 'acquired cardiomyopathy' cases are double that of 'inherited cardiomyopathies', significantly higher than any other 7MM country*

Research by GlobalData has highlighted the startling difference between the forecast number of diagnosed cardiomyopathy cases in the US, compared to other countries in the 7MM*.

The leading data and analytics company's report, 'Cardiomyopathies Epidemiology Analysis and Forecast, 2021-2031', notes that the US will have the highest number of diagnosed prevalent cases of cardiomyopathies in 2031, at over 2.3 million. This represents 83% of the total cases in the 7MM**, with the next closest countries being Germany (5.7%) and Spain (2.9%).

Cardiomyopathy is a general term for a collection of diseases that affect the heart muscle. The walls of the heart are thickened or stretched, reducing its ability to pump blood around the body and can lead to heart attack. Risk factors range from family history to diabetes, alcohol consumption, obesity and high blood pressure.

Walter Gabriel, MPH, Epidemiologist at GlobalData, explains: "Even if we compensate for the differences in population size, as in **Figure 2**, the US is still miles ahead when it comes to total cardiomyopathy cases. In a way, this is no surprise. The number of Type II diabetes cases in the US is expected to annually rise by 1.8% to over 20.8 million cases by 2028, while high blood pressure is also expected to annually rise by 0.95%, to over 65 million diagnosed cases in 2027. These are key risk factors for cardiomyopathy. While it is not new to say that the US has challenges with obesity, visuals like this can often be useful to highlight the impact that those with unhealthy lifestyles are having on the healthcare industry."

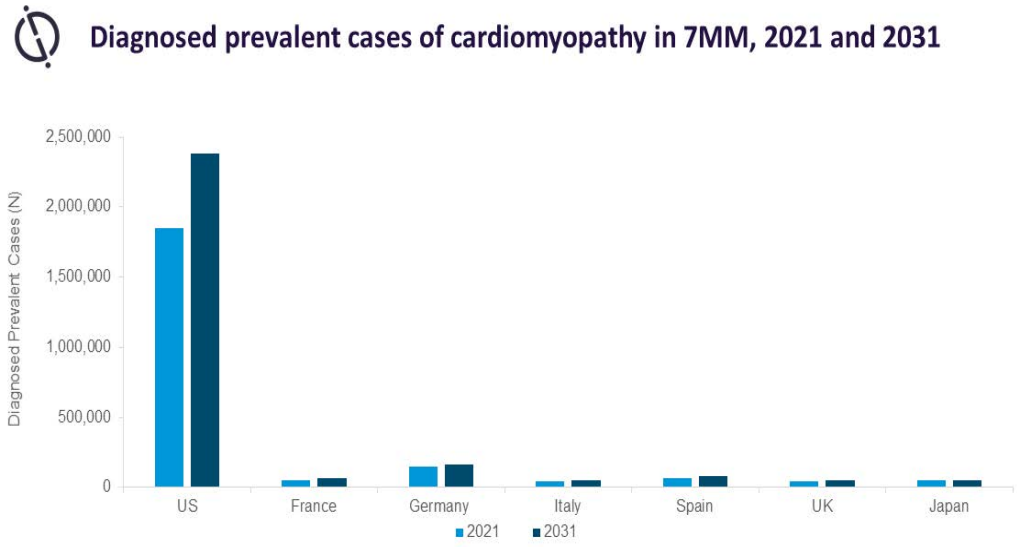

FIGURE 1

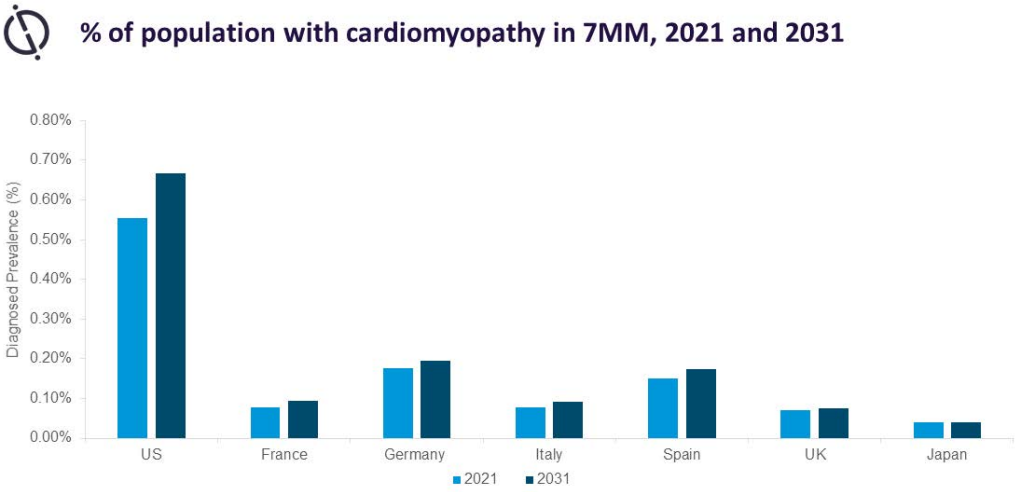

FIGURE 2

Another contributing factor to the US's high numbers is the lack of robust epidemiological data. The main forms of cardiomyopathy are dilated cardiomyopathy (DCM),

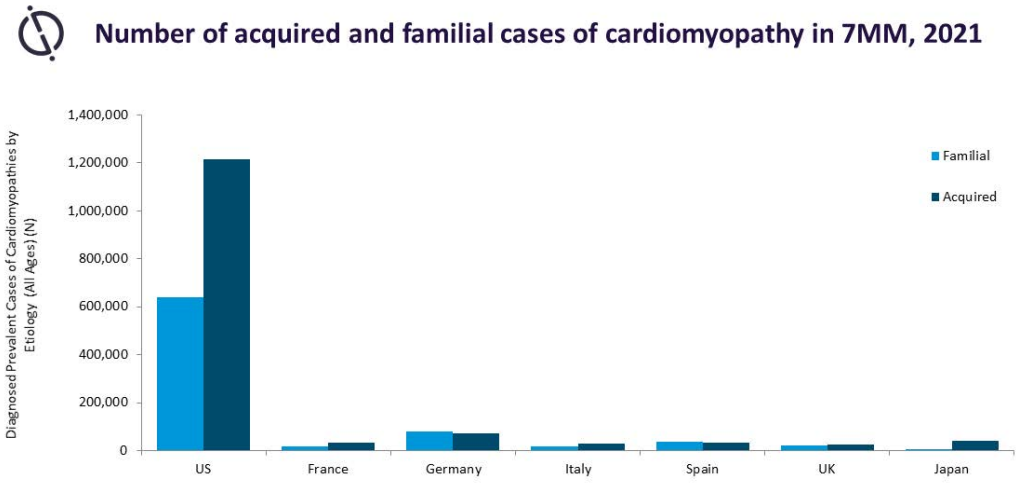

FIGURE 3

hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy (RCM), and arrhythmogenic right ventricular cardiomyopathy (ARCM).

Gabriel continues: "When forming our report, we found that epidemiological data pertaining to these specific forms of cardiomyopathy were incomplete for many markets; therefore, we had to assume that the ratio of cardiomyopathy subtypes were similar between markets with missing data. This resulted in the US having many additional cases of cardiomyopathy due to its high prevalence of HCM. The lack of market specific data make it difficult for countries to predict the burden of cardiomyopathies, and, thus, our report helps to fill a critical knowledge gap."

Another metric, the split between familial (inherited) and acquired cardiomyopathies (where the patient develops cardiomyopathy as a result of another condition or factor), also places the US figures in stark contrast to nearly every other country in the 7MM. The US proportion of acquired cardiomyopathies is double that of inherited, whereas in the rest of the 7MM is broadly an even split.

Gabriel concludes: "The high proportion of acquired cases of cardiomyopathy in the US may be attributed to a high number of individuals engaging in lifestyle factors that place them at a higher risk of developing cardiomyopathy. These factors include but are not limited to diet, drinking alcohol, and a lack of exercise. On an individual basis, cardiomyopathy increases the risk of sudden cardiac death, and, thus, it is important for individuals with these risk factors to be assessed for potential cardiovascular complications frequently."

* 7MM: The US, Japan and the 5EU (France, Germany, Italy, Spain and the UK)
** Research conducted on the 7MM - dilated, hypertrophic, restrictive, or arrhythmogenic cardiomyopathy types included
*** 5EU: France, Germany, Italy, Spain and the UK

MEETING CALENDAR

OCTOBER

27-29

CATCH 2022: Caring for Adults and Teens with Congenital Heart Disease
Kapolei, Hawaii, USA
https://web.cvent.com/event/ba10cbbd-9a74-4ce8-b81f-e1796fb5ca66/summary

NOVEMBER/DECEMBER

27-01

RSNA 2022
Chicago, Illinois, USA
https://www.rsna.org/annual-meeting

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