



# **VIRTUAL CARDIAC EXPEDITION TRANSPLANTATION & THE EX-VIVO ORGAN SUPPORT SYSTEM**

Questions & Answers with Dr. Jayan Nagendran





## QUESTIONS FROM VIRTUAL CARDIAC EXPEDITION:

### 1) Do you use donor blood for perfusion?

We use a combination of components from blood that includes packed red blood cells which we actually receive from the blood bank. We do not use portions of the donor blood during the lung perfusion protocols for the reason that sometimes there are pro-inflammatory cytokines inside that donor blood and part of the reason that the donor passed away somewhat causing a toxic milieu that may have the lungs not work as well as they could which is why we use components from the blood bank.

### 2) What physiologic markers are you using to make decisions on the device for use?

We use well established clinical physiologic markers including the lungs ability to oxygenate the perfusate or blood base solution that is flowing through it. This would be similar to us drawing a blood gas on a donor to see how well the lungs are working. We also look at how compliant the lungs are or how well they are able to distend when they are breathing. If the lungs are stiff, they won't distend as easily and that is a sign that they are damaged. The third parameter we use includes the vascular compliance of the lung, so that we can measure the vascular resistance in the lung vessels themselves and again to look for normal levels of resistance in the lungs. If the resistance is very high, it may indicate a problem with the lungs including things like a blood clot lodged in the lung.

### 3) Is the intent to expand this to pediatric donations?

At this time, we are focusing on adult lung transplantation. We are fortunate that there are very few pediatric lung transplants. There are many more pediatric heart transplants that occur. As such, the need for pediatric lung transplantation is very low. However, our device is scalable to be used as the only potential device that can address much smaller organs of a pediatric nature. We will have to perform future investigations to include pediatric donation. However, large children that are in their adolescence could certainly have their lungs supported on our current technology without any modifications.

### 4) Once the lungs are on your system, what kind of therapies do you do to improve them?

The type of therapies that we would use on our device are specific to the damage of those particular types of lungs. For example, if the lung had a pneumonia in it, we would then treat those lungs with the very high dose of antibiotics outside of the body. A dose that would be too high to give inside a donor and that is an example. Another example could be that if there was a blood clot lodged in the vessels of the lung we could give a clot busting drug like we do during heart attacks to help melt away that clot and then show that the lung continues to work well outside of the body which we have previously done.



**5) In one of the slides it mentioned Dragon's Den presentation. How did that go?**

We presented to the Mazankowski Alberta Heart Institute Dragon's Den and this was in the setting of the Maz Innovation Fund. We are very pleased that we were successful in this pitch and attained \$900,000.00 in secure funding to allow for clinical use of the EVOSS system which we hope to start in the Fall of this year.

**6) After my surgery on Nov. 23rd of open-heart surgery of replacing aortic valve I have poor circulation in my fingers when outside. Is this related?**

The circulation you may feel since your open heart surgery at the end of November is likely related to a combination of some of the new medications you would be on including antihypertensive medications at varying doses as well as the fact that after open heart surgery all patients experience a little lower level of hemoglobin and in such that anemia which will improve over time may also be sensed as a feeling of poor circulation in the first 6 months after surgery. Rest assured this is a common feature that many patients experience after open heart surgery.

**7) What substance runs through the lungs' vessels when you have it on EVOSS?**

There are components of blood that are run through the lungs include packed red blood cells. We also have a high concentration of Albumin which is a component of blood, it is a protein in blood. It also helps maintain the oncotic pressure in the vasculature as it flows through the lungs. It is also buffered to maintain a normal PH like the blood to allow for a more physiologic or normal functioning of these lungs outside of the body. We also add a blood thinner called Heparin as well as steroids to help block inflammation and antibiotics to help treat infection outside of the lungs.

**8) Is the EVOSS system going to be presented to the stock market? The world would really benefit from this fabulous technology. It would not take long to get this word out, and then more research money would be available to enhance this tech even more.**

The company that was cofounded by Darren Freed and myself, TEVOSOL, has merged with Bridge to Life. Bridge to Life is still a privately held company out of Illinois and we plan for a future liquidity event over the next 2-3 years by either acquisition of a publicly traded company or by our own company and Bridge to Life reaching an IPOE.

**9) Are there any other prototypes in trial or used in the world?**

There are no other EVOSS prototypes used in the world. So far, they have all been used at the University of Alberta. However, we plan to have an International multi-center clinical trial starting in 2022 including centers in the United States which would include Baylor College of Medicine, Methodist Hospital, Duke University, Emory and the University of California and San Diego.



### 10) How is the training for students and other doctors around the world to properly use the technology?

The goal of this technology is to make the user experience extremely friendly and very simple. As such we do not plan to have increased people included in the donor procurement process because of this technology. In fact, we plan the opposite, where it is so simply used that the current team including donor coordinators and our current surgical Fellows could run the device easily on its blue tooth iPad system without extensive training. There will be some training though this will be relatively simple given all the automation and safety features of the device inherently.

### 11) Nova Scotia recently changed their organ donor laws as of January 2021. People who don't register to be a donor and are eligible will be seen as having consented to donating their organs and tissues after death. Do you think this would be helpful in Alberta?

Thank you for bringing this very important issue forward with regards to donation. I strongly believe this would be beneficial everywhere in the world including Alberta and I hope to see a similar change as preceded by our colleagues in Nova Scotia to have an increased potential donor pool to save lives of patients with end stage organ failure. It is very clear the biggest reason for a lack of transplantation is a lack of donors through the EVOSS program we hope to use more of the precious few donors we have. However, legislation that was passed in Nova Scotia if it was widely adopted would help at all levels as well.

### 12) Have transplant surgery continued with COVID?

Yes, we have continued to perform transplantation of all solid organs during Covid-19. There was a slow down for a few months before the summer. However, we have gone back to near normal rates and I fear that there will be an increase need for lung transplantation given the chronic lung disease that may occur in patients who have recovered from Covid-19 though still exhibit symptoms of respiratory distress.

### 13) What inspired you to pursue medicine and this project specifically?

I can't remember exactly what inspired me to pursue medicine. I think my parents certainly wanted me to pursue medicine. However, once I entered medical school my interest in heart surgery drove me to become a heart surgeon and transplantation was my greatest interest within heart surgery. We are fortunate at the University of Alberta that the heart surgeons are extensively involved with both the heart and lung transplant programs. After my training at Stanford University in heart and lung transplantation I have been very fortunate to come and join a very collegial and growing group with great results at the University of Alberta Lung Transplant Program.



**14) What is use able from my 77-year-old body? I am in good shape. Not anything cut up. Will B. S. I am a silver pickle ball player.**

That is great to hear your willingness to consider donation at any age. As I said during the talk, there are different forms of donation that do not just include organs, but also include tissue and bone. As such, all ages are welcome for donation and as we improve these technologies to consider organs outside of the body and show viability then we may certainly increase the age of donation in lung transplant donation to include people like yourself. We currently go to the age of 70 for lung transplant donors. However, my colleagues in liver transplantation have used older donors even at the age of 80, so I encourage you to sign your donor card and thank you for your support.

**15) I am transitioning into post-secondary and am interested in following a career path towards cardiac surgery. Any advice?**

I am glad to hear you have an interest in cardiac surgery. I would start by taking all the undergraduate pre-requisite courses required to getting into medical school and performing very well in those courses as well as on your MCAT exam. The next biggest step in your early education would be to get an interview for medical school and hopefully get accepted to a medical school within Canada. I should note that every medical school in Canada is a good medical school, so I would encourage you to apply broadly. That would be the first important step in your career path.

**16) Who is responsible for the transportation and delivery of the lungs?**

The transportation and delivery of lungs is coordinated by our organ procurement organization here at the University of Alberta. That is the HOPE program. The Human Organ Procurement program. They have donor coordinators who are on call 24 hours a day who will be notified of an appropriate donors for the consideration of donation and then they will start an in depth process to see if donors are at all suitable for donation and then my team would get involved if there are suitable lungs for donation and we would work with HOPE team throughout the process including travelling to the donor site and procuring the organs and the HOPE coordinators will be working with us all the way back until the organs are at my hospital and ready for me to transplant.

**17) Can a second lung transplant be done if damage is brought on by COVID?**

There are cases where we perform a re-transplantation or a second lung transplantation years after a first lung transplantation. We do this very rarely and out of the over 70 lung transplants we do a year we may perform this operation once a year. However, in a few select individuals that have early failure of their lungs after transplantation in the first few years due to either infection or rejection, we may consider and successfully perform a re-transplant or second transplant operation. In the setting of COVID-19 we would not transplant anyone who has an active Covid-19 infection. They would have had to have cleared the virus to be acceptable for transplantation.



### 18) Are we able to oxygenate the lungs while using during negative pressure ventilation with this portable device?

Yes, the lungs will oxygenate the fluid or the perfusate going through the lungs because that is the function of the lungs is to take the oxygen from the air we are breathing and deliver it to the blood. In fact, on our device the blood that comes out of the lungs that now has oxygen in it which the lungs delivered to it will then be deoxygenated where we remove oxygen from the lungs so that we can continue to test that when the blood then goes back into the lungs with the same low level of oxygen that the lungs are used to seeing as it comes back from our body that the lungs can continue to oxygenate as well. Indeed, it is the ability for the lungs to oxygenate this blood as it goes through with a low level of oxygen to a normal level of oxygen after it passes through the lungs that indicates to us that these lungs are usable. All of this is done on our portable device.

### 19) Do the anti-rejection drugs with transplant surgeries become an issue?

Yes Dave. All patients after transplantation from any solid organ will require anti-rejection drugs and that is individually tailored to the individual patient. The anti-rejection drugs do have significant side effects and as such they are an issue. Some of the side effects include chronic damage to the kidneys and the overall effect to the body of decreasing its immunity which is what anti-rejection drugs do increases your risk of developing infections as well as our immune system is very important in recognizing pre-cancerous and cancerous cells within our body. As such, when we chronically treat people with anti-rejection medications they are at much higher risk of developing cancer over their lifetime. We hope that with our technologies that eventually we can modulate these organs outside of the body to decrease their immunogenic burden as such decrease the need for immunosuppressive therapy and with the hope that some day to completely avoid immunosuppressive therapy if enough EX VIVO manipulation can happen to make these organs non-immunogenic after transplantation.

### 20) Would this technology have to be modified if it is to be used for pediatric lungs?

As Alanna previously asked about pediatric lungs, we would not need to modify our current organ to use adolescent lungs. We would have to scale it to treat truly pediatric lungs in much smaller children. However, we are very lucky that very few children require lung transplantation though we have the capability of scaling our technology down to the size of very small lungs including pediatric lungs if needed.

### 21) Is there an age limit for donation of organs?

As previously asked by Elsie, there is no age limit for donation. We are continuing to expand the use of organs including in advanced age donors and with the increase use of our technologies we should be able to expand the use of older organs with greater safety knowing that the organs are functioning well in an objective environment outside of the body.



## 22) How many of these machines are being used? Currently at the hospital and what is the cost of one of these machines?

During the clinical trial where 12 patients underwent transplantation with marginal donor organs, we had two machines available and we plan to have two machines available in the future as well with our portable type device that we plan to start using in the fall. The cost of these devices are based on different models of funding for the program in that the devices will be on a service contract to the hospital and the cost to the individual hospital will be the cost of the individual disposal sets which will be used with every transplantation. The current cost of those disposable sets are around \$25,000.00 per transplant. However, based on the efficiencies and better outcomes using this type of technology we have added an economic analysis to our registry to hopefully show a cost savings by not having surgeries performed in the middle of the night by cancelling less operations the next day due to overtime use of staff and by having better outcomes for patients with reduced time on the ventilator and in the ICU and in hospital which would all be cost savings. In the longer term follow up we will also follow for rates of infection and rejection and readmissions to hospital and if all of these areas are also positively impacted by having better donor organs at the time of transplantation due to use of these technologies there will surely be a cost saving to the system with better outcomes for patients

## 23) How many EVOSS's are being used across Canada or North America?

Currently EVOSS has only been used at the University of Alberta and as I previously spoke about, we plan to have an international clinical trial with 6 centers in the United States starting this year and after completion of that trial we hope to have international expansion throughout the rest of the United States, Canada, and to Europe in 2023