Canada-Israel Cardiovascular Innovation Forum

SUMMARY OF INNOVATIONS FOR PRESENTATION ON APRIL 25, 2021 (Register to Attend)

CANADIAN APPLICANTS:

Stephanie Buryk-Iggers, SPARKED, "Handheld, non-invasive device for early risk detection of cardiovascular disease" – E-mail Stephanie: stephanie.buryk@mail.utoronto.ca

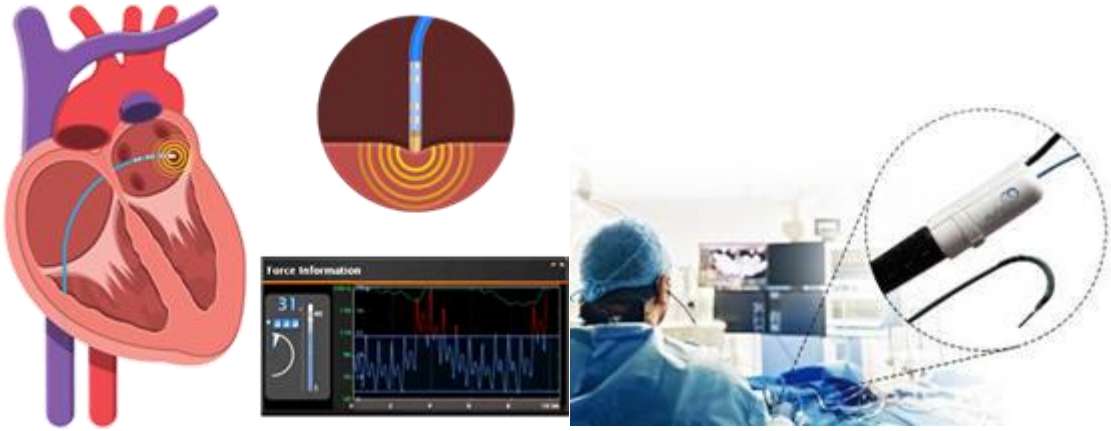
SPARKED offers a handheld device (SPARKED) for screening of cardiovascular disease (CVD) risk. It is non-invasive by using a saliva sample placed directly on the device. The application of microfluidics and nanotechnology allows SPARKED to put CVD screening into the hands of the customer. The device captures a protein biomarker and indicates the user's level of CVD risk as LOW, MED, or HIGH on a readout screen located directly on the device. SPARKED allows risk detection of CVD quickly with rapid results, painlessly using a non-invasive saliva sample, accurately with high sensitivity and specificity by employing microfluidic and nanotechnology; and thus eliminating the need for trained personnel, or a traditional laboratory.

Daniel Gelman, Aufero Medical, "Device to stabilize contact force during radiofrequency catheter ablation therapy for atrial fibrillation" – E-mail Daniel: dgelman@auferomedical.com

Summary. Aufero Medical introduces a much-needed product into the massive, fast-growing, highly profitable atrial fibrillation catheter ablation market. Our product solves a big problem that cardiac electrophysiologists face daily that dramatically reduces the procedure's success rate. Aufero Medical is developing an accessory device that stabilizes the physician's catheter to enhance therapy and drastically improve the procedure's success rate. We have developed proof-of-concept and commercial-stage prototypes, performed animal and lab-bench studies, generated IP, and will soon be conducting a first-in-human clinical study.

Problem. Atrial fibrillation (AF) – the most clinically significant form of heart arrhythmia – is an irregular heartbeat treated using ablation catheters to burn structures along the inside of the heart wall. Durable ablation relies on keeping consistent contact between the catheter tip and the moving heart. Inconsistent contact (demonstrated on the right) varies ablation quality, which results in AF recurrence, requiring another procedure. Overall medical expenses triple when a catheter ablation procedure fails, which occurs in up to 50% of patients (~30% average). The total economic burden of ablation failure to the US healthcare system is expected to amount to over USD3.5B in 2021.

Solution. Aufero Medical has developed the Catheter Contact-Force Controller to stabilize catheter contact to a set level. Our system includes an accessory device that attaches seamlessly to routinely used ablation catheters and gives the physician *on-demand contact stability for precise ablation production*. Our product is designed with input from several electrophysiologists, ensuring it is intuitive and can be used with little-to-no training. Our product is plug-n-play, has minimal impact on the regular procedure workflow, and can be easily incorporated into any existing EP lab.



Surath Gomis, Arma Biosciences, "A handheld device for rapid, continuous remote monitoring of biochemical markers in patients with heart failure"
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Remote monitoring devices with the capability of biochemical monitoring of disease biomarkers remains an unmet need which could significantly improve patient outcomes with cardiovascular conditions such as heart failure (HF). Over 65 million patients are diagnosed with HF worldwide, where in Canada over 600,000 people live with HF and 50,000 more people are diagnosed each year. HF is the leading cause of hospitalizations and re-hospitalizations due to the challenge of managing discharged patients who can decompensate quickly, leading to 3-4 rehospitalizations per year per patient with average costs of >$10,000 per patient for 5-10 day mean stays, costing more than $2.8B per year. Remote monitoring of HF patients would allow patients and their physicians to obtain more data on how their health is trending, enabling early interventions such as with pharmaceutical regimen changes, to avoid re-hospitalization.

We have developed a new sensing strategy which permits molecular analytes to be detected in situ without any external reagents or sample processing, making this technology amenable to a remote monitoring format since it is self-contained, is a single-step measurement for the user, and is portable. Our sensing strategy, called a molecular pendulum (MP), measures the presence and concentrations of molecular biomarkers of disease in just a drop of biofluid, such as blood, saliva, urine, tears, or sweat, using an antibody tethered to the MP. Under an electric field, the MP falls, and we readout sensor motion using as an electric current correlating with protein concentration. For patients with HF, many biochemical markers including B-type natriuretic peptide (BNP), N-terminal (NT)-pro hormone BNP (NTpro-BNP), C-reactive protein (CRP), or cardiac troponin I (cTnI) increase in concentration if patents are decompensating, and we can detect these proteins in blood or saliva. We have already demonstrated detection of BNP in vitro, and cTnI for continuous monitoring in situ in mouse models (Das, J., Gomis, S. et al. Nature Chemistry, 2021).

Currently, HF remote monitoring includes assessment of physical symptoms, and a few externally accessible measurements such as heart rate and blood pressure. Blood tests for biomarkers are generally done during regular doctor visits (every two weeks to every six months depending on the

patient's HF severity). Our technology would enable the addition of biochemical measurements of BNP and other biomarkers which are a direct response of heart health and mortality in HF patients to be done remotely as frequently as needed, to improve patient outcomes by enabling early intervention. Funding from the Canada-Israel Cardiovascular Innovation Competition would allow us to translate our technology into a remote patient monitoring platform, including the development and scaling up of our sensors as disposable test strips and the handheld measurement device to take the measurements on the test strips. With cardiology collaborators at the Ted Rogers Centre for Heart Research and a strategic partner identified to help with industrial sensor scaling, we are confident in the capabilities of our technology to greatly benefit HF patient outcomes. The support of the CI2 Forum will be instrumental in our preclinical studies.

Ali Tavallaei, Magellan Biomedical, "A novel catheter allowing for accurate localized steering and tracking of endoluminal devices" – E-mail Ali: ali.tavallaei@magellanbiomedical.com

It is estimated that more than 2.14 million deflectable catheters are used globally for various cardiovascular interventions. All deflectable catheters are remotely manipulated from outside the body and rely on the same old method of pulling on wires integrated within the catheter to deflect the softer distal end of the catheter. These devices have 3 degrees of freedom (DOF): axial push-pull, rotation, and deflection of the distal end. The user inputs are applied manually from outside the patient body. The remote manipulation of these lengthy and flexible catheters, together with their extensive engagement with the more rigid anatomy along their length, significantly limits the precise navigation and control of these devices. To address these limitations, we have developed an entirely novel approach to catheter steering and tracking that promises to overcome many of the limitations of conventional deflectable catheters. Our proposed solution consists of an expandable Nitinol frame, which is initially constrained within an outer sheath. When we approach the vicinity of the target anatomy using the sheath, then the frame is expanded and anchors to the anatomy of interest. Once the frame is expanded, it acts as a relatively rigid frame of reference that allows for local manipulation—and tracking—of a catheter tip relative to the frame and hence the anatomy to which it is anchored to. As the catheter is manipulated with a number of cables, it is mechanically over-constrained and is not free to move or buckle when under excessive axial force. As the cables are mechanically tracked, using the geometric constraints of the system, the device's position can be tracked with high accuracy relative to the frame and hence the anatomy. The tracking relative to the frame is presented for the user in real-time to provide 3D visualization of the device's position in conjunction with conventional fluoroscopy/US imaging. The proposed platform technology has numerous applications and can be used for therapeutic and diagnostic purposes or both. The manipulated catheter accommodates other devices through its lumen, such as guidewires, needles, ablation catheters, etc., or it can accommodate imaging sensors such as US transducers allowing for forward-looking imaging and a complete image-guided navigation platform.

This technology provides a passive (manually operated) and inexpensive solution that overcomes the intrinsic limitations in steering, tracking, and navigation of conventional cardiovascular devices. **This solution offers localized, accurate, and reliable control** of the catheter position **relative to the anatomy of interest rather than a random trial and error approach** that exists with many conventional devices.

Ryan Tennant, No named company, "A novel re-entry device for angioplasty of coronary and peripheral chronic total occlusions" – E-mail Ryan: ryan.tennant@uwaterloo.ca

Coronary artery and peripheral artery chronic total occlusions (CTOs) remain a therapeutic challenge for interventionalists. Success rates are approximately 50%-70% for most operators in carefully selected cases. The most common reason for failure is inability to cross the occluded segment with a guidewire into the distal true lumen of the artery. In many of these cases, the guidewire actually crosses the occlusion but has been advanced into the subintimal space and unable to re-enter into the true lumen. Current devices to redirect the guidewire are limited by cost, size/bulkiness of the device (peripheral CTOs), and the requirement for advanced skill set to operate the device (coronary CTOs).

Our innovation is a re-entry device, which is a microcatheter fitted with a micro balloon within the distal end of the device. Inflation of the balloon redirects the guidewire out of the microcatheter at the precise angle required to re-enter the lumen beyond the occlusion. The microcatheter size and function are similar to conventional microcatheters currently used in CTO angioplasty procedures in the coronary and peripheral arteries, and therefore very familiar and comfortable for operators. The proximal end of the microcatheter contains a separate port for an inflation device that is connected through a hypotube inside the catheter lumen to the distal balloon. To confirm orientation of the microcatheter under fluoroscopy, the device has a uniquely shaped radio-opaque marker around the distal tip that appears as a different shape under two 90-degree apart fluoroscopic images. The device kit also contains a realignment rod that can be inserted into the microcatheter to permit rotation of the microcatheter into the desired position for re-entry into the true lumen.

A provisional USA patent application (US 62/566,610) was filed on September 11, 2017. A PCT application, International Publication Number WO 2019/046976 A1, has a filing date Sept 11, 2018. National entry applications have been submitted. The patent is currently in the final stages of being reassigned from the institution (Sunnybrook Health Sciences Centre) to the inventors. Several prototypes have been developed and device freeze is expected in fall 2021.

ISRAELI APPLICANTS

Lihu Avitov, Revamp Medical, "The Doraya Catheter - a novel temporary intravenous flow regulator" – E-mail Lihu: lihua@revampmedical.com

Revamp Medical has developed an innovative medical device designed to address the indication of Acute Heart Failure (AHF), a common condition that carries a high morbidity and mortality. Acute heart failure is a sudden worsening of the signs and symptoms of CHF (congestive heart failure), primarily caused by fluid congestion. AHF is a complex systemic disease that causes organ damage and can cause death if not quickly treated.
Fluid decongestion is key in the treatment of AHF patients, where diuretics form the primary decongestive treatment for this condition. 15-30% of ADF admitted patients suffer from Diuretic Resistance, defined as failure to achieve effective congestion relief despite appropriate or escalating diuretic doses.

The leading contributing factors to diuretic resistance are **Increased Central Venous Pressure (CVP) & Renal Venous Pressure (RVP)**. The Doraya is a temporary (up to 12 hours) intervention to reduce CVP/RVP with the goal to improve diuretic responsiveness and improve congestion signs and symptoms.The Doraya Catheter is a temporary intravenous flow regulator that is percutaneously positioned in the inferior vena cava below the level of the renal veins. The catheter distal frame creates a modulation of venous flow, resulting in reduced CVP at the outlet of the renal veins. By creating an optimal hemodynamic environment, the Doraya enables diuretic efficiency to relieve congestion and restore organ function following AHF, reducing prolonged hospital admissions and readmission rates.Revamp completed a 9 patient FIH study in Europe and Israel, with promising results. The initial data demonstrated safety (no device related SAE, stable hemodynamics, 100% successful deployment and removal) and signs of improvements (2.6X improvement in Urine output rate, >30% CVP/RAP reduction, improvement in dyspnea and edema at 48 hours). Based on these results, FDA granted the Doraya a Breakthrough Device Designation in mid 2020.

The company is now preparing for an Early Feasibility Study in the US (5 sites, all in the NY area) to start enrollment late 2021, and is looking to expand its clinical work to Europe and Canada as well, with the goal of obtaining a CE mark.

Nitai Hanani, Paragate Medical, "Implantable Peritoneal Ultrafiltration Device (IPUD), for continuous & active fluid decongestion in heart failure patients"
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Paragate Medical aims to improve clinical condition of fluid overloaded patients by **continuously removing extracellular fluids** with a unique fully implantable peritoneal ultrafiltration device, operating non-aggressively and independently of the kidneys' function.

The Paragate device breaks the hospitalization cycle for the chronic overloaded patients. Instead of receiving acute and aggressive diuresis treatments that do not prevent recurrence of the overload episodes, the Paragate device offers an active 24/7 out-of-hospital solution that goes beyond the monitoring.

Elon Reshef, Invatin Technologies, "A Novel Continuous Stroke Prevention Device"
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INVATIN developed the SYNAXIS, a first in class permanent aortic implantable apparatus for diversion of thromboembolic materials from the brain. The device was developed to address the large population of patients with atrial fibrillation (AF), high stroke risk, and high bleeding risk. Patients that cannot be treated with other measures are the ultimate candidates for the SYNAXIS. Accordingly, it may be used in patients with intra-cardiac thrombi and in patients who are at risk for non-left atrial auricle (LAA) related cerebral embolization. The device confers a new approach towards stroke prevention, and poses several advantages as compared with available technologies and drugs.

The INVATIN's SYNAXIS is a novel one-piece cylindrical endovascular graft consisting of Nitinol frame and detachable filtering unit components. The stent graft is constructed of woven polyester

fabric sewn to self-expanding nitinol stents with braided polyester and monofilament PTFE suture. The filter unit is made of PTFE foil fenestrated with 1X1 mm pores, positioned 100 micrometers apart, designed and reinforced to sustain a high shearing forces and provide sustainability. The filter unit is positioned to protect all 3 branches emerging from the aortic arch. Its design enables minimally invasive removal of the filtering apparatus with an intra-vascular biopsy forceps as a bailout procedure, and future application of replacing the filtering unit.

Animal studies have been completed, demonstrating both safety and preclinical efficacy in acute and chronic swine models of cerebral embolism. Cerebral and aortic pressures were continuously measured prior to and following device implantation. Filtration effectiveness was tested by a controlled embolization of >100 particles of radiopaque thrombi. Patency was evaluated after 4 weeks, and development of thrombi and neointimal growth were tested with scanning electron microscopy (SEM). Long-term follow-ups of implanted devices are underway.

INVATIN has filled 2 US and PCT patents and an additional provisional patent application is currently drafted. The company is in preparation for its pre-IDE meeting with the FDA, scheduled for Q3-2021. The SYNAXIS is going through its final animal validation study, and product launch is planned for Q1-2026. A FIH study is scheduled for Q2-2023 in EU leading centers.

The SYNXIS addresses the expanding 11.5 B$/year market of stroke prevention.

Ariel Weigler, Cuspa Ltd, "Transcatheter artificial cusp for repair of valve insufficiency" – E-mail Ariel: ariel@cuspamedical.com

Cuspa Medical (Nazareth, Israel) Developer of an artificial cusp designed to eliminate the regurgitant orifice in cases of valve insufficiency while maintaining normal valve function. The Cusper device offers a minimally invasive repair option for valve insufficiency, specifically targeting aortic insufficiency in a simple, intuitive procedure expected to benefit a patient population with very few alternatives. with no percutaneous solution for aortic regurgitation, the surgical approach proposed to these patients involves great risks due to open heart surgery. Transcatheter aortic valve implantation is ill-advised due to lack of calcification, necessary for the prosthetic valve anchoring.

A percutaneous device for the treatment of aortic regurgitation will benefit this patient population by eliminating the risks associated with open heart surgery and substantially reducing patient discomfort. Although we chose to target Aortic Regurgitation as a first indication, our platform technology can also be adapted to the Tricuspid and Mitral valves as well.

For more information, visit https://www.cicvinnovation.com/

For any questions regarding the Canada-Israel Cardiovascular Innovation Forum or regarding any of the innovators, please contact Liz Thuo at hsrl.centre@utoronto.ca.