

MITrep: a mini-invasive, automated surgical solution to mitral valve insufficiency

Bernard Pain, the president of CMI'nov, introduces MITrep, an innovative surgical device set to transform the treatment of mitral valve insufficiency

Stress, malnutrition, alcohol use disorders and a rise in the ageing population are all impacting on the prevalence of heart conditions worldwide. Among these pathologies, mitral valve insufficiency (or mitral regurgitation) affects 10% of the population aged 75 and over in both Europe and the USA.¹ It is characterised by the leaking of blood out of the valves, which normally ensure its one-way flow through the heart. Blood goes from the heart's mitral valve from the left ventricle to the left atrium.

In its moderate form (3% in children, 19% of the population between 50 and 60, 80% of patients aged over 80), mitral valve insufficiency causes chronic fatigue and shortness of breath as well as palpitations or a racing heartrate that impair active life. But if the amount of leaking blood is severe (10% of people above 75), the patient dies

within five years from sudden death (5-6% of patients each year, approximately 18,000 people).

Mitral valve insufficiency is treated with open heart surgery (300,000 surgeries per year in the EU/USA) and on bypass followed by intensive care, which is hardly a bearable roadmap for fragile patients. Therefore, 50% of over-75-year-old patients are labelled 'inoperable' because of their age.² Less invasive repair and replacement procedures (annuloplasty, transfemoral surgeries) have been tested, but they all have resulted in additional problems for the patient (e.g. improper sizing of the annuloplasty rings, which requires a second surgery). Moreover, all these repair procedures are highly dependent upon the skill of the cardiac surgeon, and poorly or inaccurately placed sutures in valves of poor quality may affect the success of procedures.

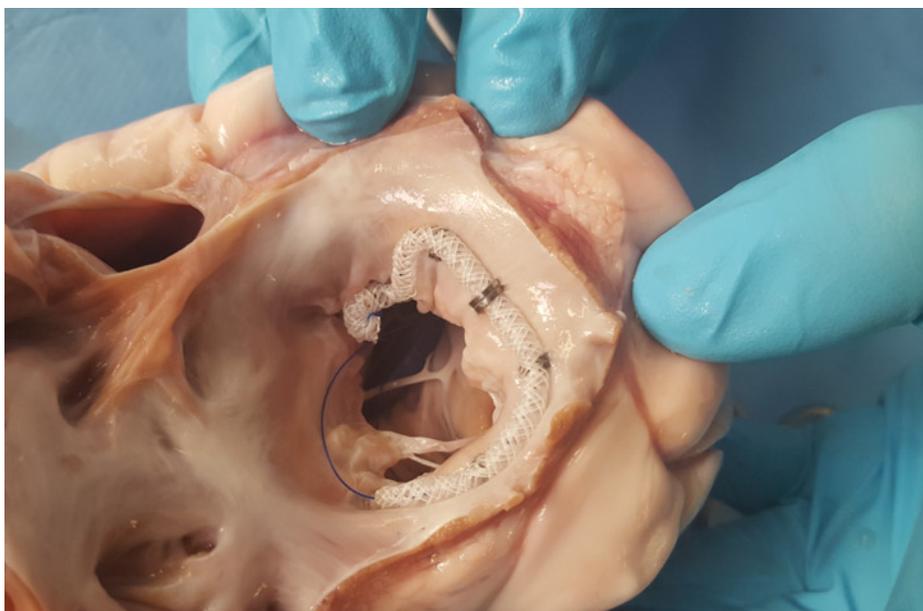
The surgeons must be highly skilled to perform mitral repair (the valve itself shows variable anatomy and is challenging to access). Specialisation of the cardiac surgeon is always required, and this is a limiting factor. New, accessible techniques must be found to expand the number of practitioners able to perform mitral repair and to answer an unmet need: the care of today's inoperable patients.

Introducing MITrep

In this context, CMI'nov has developed MITrep, the first mini-invasive automated surgical device that goes directly to the mitral valve with no trial and error to affix a leak-preventing ring onto the valve with robotised movements.

The patented device uses a transapical approach, i.e. the surgeon makes a small incision in the intercostal space to deliver and fix a textile ring (polyester) via a catheter through the apex of the heart.³ Once the ring is anchored with nitinol sutures, the mitral valve returns to normal activity. No heavy post-surgery effects are expected.

MITrep's design and robotised use make it accessible to surgeons who are not necessarily mitral valve specialists. The surgeon will only have to hold the device, which automatically performs the straight-to-the-target surgical gesture. Simplifying the surgery in this way will make it possible to operate on fragile people. As MITrep disseminates, mitral repair will become a standard surgery addressing a wider spectrum of patients. It is expected to replace heavy, risky and discriminating open heart surgery. Mitral valve insufficiency will no longer be a chronic and life-threatening condition, no matter what the age of the patient or the severity of mitral insufficiency.⁴





Operation-wise, the MITrep concept has the potential to halve the operation time (from around five hours today to less than two hours with MITrep). Intensive care will no longer be necessary, and hospitalisation time will be reduced to three days (compared to 5-8 days today, including two days in intensive care). In addition, a MITrep operation (€30,000) will cost three times less than open heart surgery (€100,000). That means a dramatic cost reduction for healthcare systems and a significant improvement of the patient's pathway and quality of life.

The MITrep device and its complementary minimally invasive procedure for mitral valve repair will be applicable to other configurations of valvuloplasty involving the right/left ventricles (aortic valve repair, tricuspid valve repair).

This project will be a value driver for CMI'nov, which aims to contribute to the rise of a new operative gold standard in valvuloplasty, starting with mitral repair.

Objectives of the Phase 1 project: 'From semi- to full robotization'

The present project will validate both the technical and economic feasibility of mitral valve repair with

the MITrep device during simulations and beating heart surgeries on animals together with a renowned cardiac surgeon.⁵ This study will be instrumental in drawing the operational conclusions before launching the industrial scale-up of the fully robotised device (miniaturisation of the engines and robotisation of the remaining manual actions) followed by the multicentric clinical validation of the MITrep surgery prior to market uptake in a Phase 2 project.

Opportunities and challenges

This project will allow CMI'nov to seize significant business opportunities:

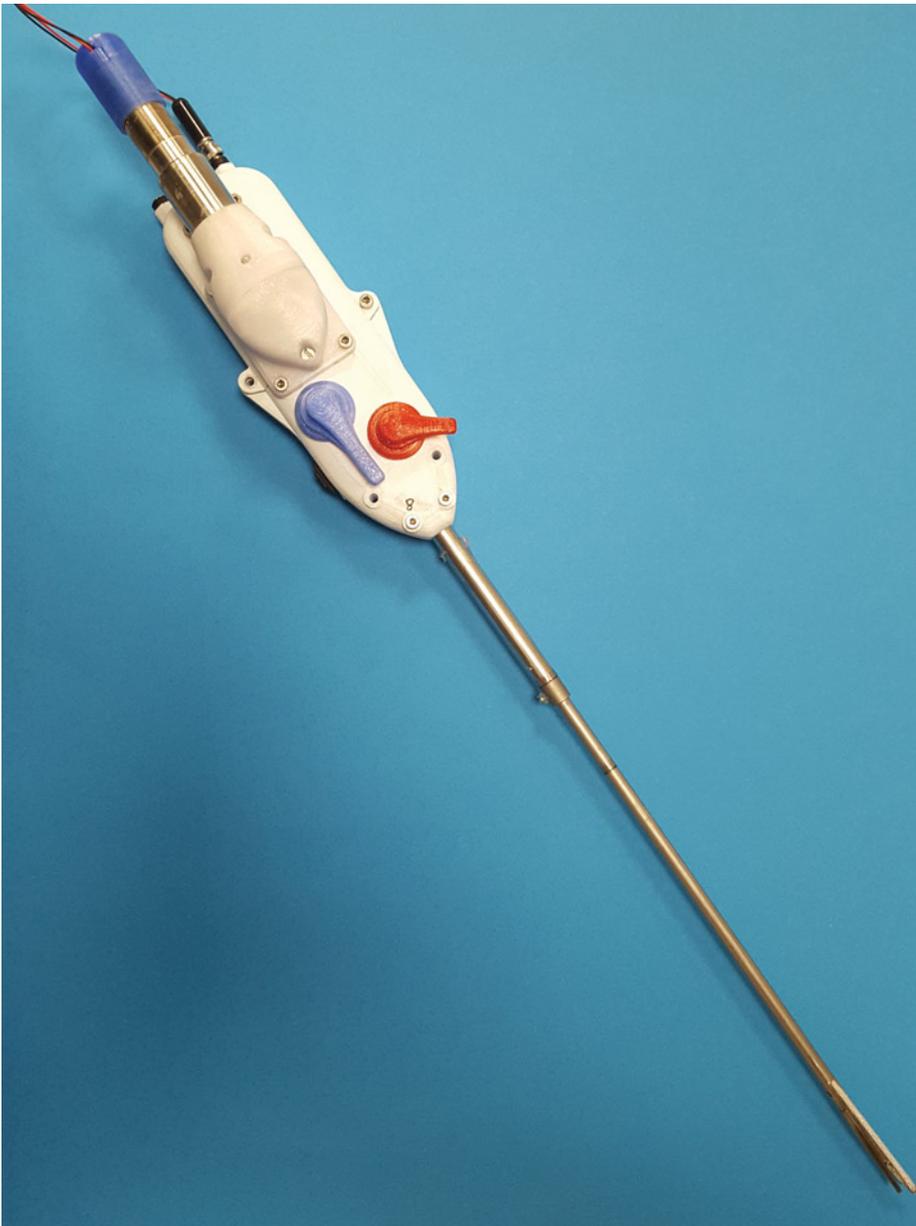
- The number of patients with mitral valve insufficiency is forecasted to double by 2030, reaching millions worldwide.⁶ The annual growth rate of the mitral repair market is exceeding 30% worldwide. This emphasises the huge dynamics in this market
- The ageing of the global population is boosting market opportunities for new inclusive approaches to treating heart conditions and new standards of care for the elderly in both Europe and the USA
- There is a real early adoption potential in other growing markets such as China, India and

South Africa. The Asian-Pacific mitral valve repair and replacement market is growing rapidly, registering annual growth of over 34% since 2016 (with China representing a 25% share of the total region).⁷ Therefore, in these markets, there is an opportunity to introduce MITrep as a gold standard and multiply CMI'nov's potential market by three (from 300,000 to 900,000 potential mitral surgeries worldwide)

- The automation features in MITrep are unrivalled today. It will take time for the 'manual' competition to develop an equivalent offer to the patented MITrep system: there is no automation on offer and the latest competing innovation (the transfemoral annuloplasty device Cardioband from Edwards Lifesciences) requires at least ten different surgical gestures (compared to only three using MITrep).

The MITrep project also addresses major EU-wide challenges, including:

- **Inclusive access to care (whatever the age of the patient):** Mitral valve insufficiency is associated with unbalanced access to care, where age is an exclusion criterion. In turn, MITrep makes no distinction



between a young and old heart and will allow a five-fold increase in the number of patients included in surgery. It is a technology designed for ageing well

- **Cardiac surgery 2.0:** MITrep contributes to automating the gesture of cardiac surgeons. Starting with mitral repair, the technology has the potential to automate more gestures in cardiac valve repair. The direct consequence is the multiplication of the number of surgeons who will become capable of performing mitral repair. The patient flow will thus be much improved
- **Improved psychological care of female patients:** Open heart surgery leaves a visible 20-25cm scar on the chest of the patients. For women, this scar can be a stigma, and female patients tend to feel isolated. MITrep will result in a five-fold shorter scar (5cm incision for trocar entry).

Transapical approach

MITrep is an automated surgical device for mitral valve repair, aimed at performing a transapical beating heart surgery without extra corporeal circulation.

The transapical route is the best solution to go directly to the apex of the heart. Many solutions have been proposed to achieve less invasive annuloplasties, avoiding both pharmacologic cardiac arrest (ischaemic) of the heart muscle and extracorporeal circulation. Among the known processing devices to perform annuloplasty, it is possible to use a navigation in the left atrium or retrograde, i.e. from the femoral artery, or antegrade (by venous trans-septal route). However, these solutions (i.e. MitraClip and NeoChord) remain difficult to use, make tracking of the mitral annulus a painstaking process, and result in a relatively large time investment.

Surgeons are trying to combine several methods and techniques to try to address more and more

mitral repair in the future. However, many challenges and needs have still not been met (namely safety and efficiency). For example, difficulties may arise for the attachment of the prosthetic implant at the native mitral annulus. The literature pinpoints the limitations of the 'one-valve-fits-all' principle, which has been followed by device manufacturers so far. There are many systems being assessed to obtain market acceptance or in preclinical tests. But all these technologies show important concerns of durability, safety and interaction with adjacent cardiac structures. End users (cardiac surgeons) also underline the issues of effectiveness, user-friendly reproducibility, and recapturability in case of inappropriate deployment.

These limitations appear because regurgitant mitral valve poses unique challenges for successful transcatheter valve deployment since it is frequently subject to anatomical variations. This presents a real challenge in terms of both new product design and surgical technique.⁸

Very often with these systems, attempts are made to obtain a good fixation with the aim of overcoming these drawbacks in a safe, simple, effective and efficient way.

Annuloplasty is the prior basic intervention for any operation on the mitral valve for the cordae repair or replacement of the valve. To date, there is no transapical solution available for the treatment of the mitral regurgitation. Our MITrep device will supplement the actions of devices like NEOCHORD for cordae repair or SAPIEN for the mitral valve replacement.

Innovation and improvement potential

Five innovation types are championed to assess the innovation potential of MITrep:⁹

- 1) **Core process:** The automated suturing and closing system is patented and active worldwide. The core process stems from both an automation engineer and a cardiac surgeon, which gives it its uniqueness and direct applicability to cardiac valve surgery
- 2) **Product performance:** MITrep allows a full repair of the mitral valve in two minutes, with no risk of damage to the valve or of hooking of the sutures. It initiates a leap forward in transapical surgery, which is in turn applicable to all cardiac valves (not only to aortic surgery)
- 3) **Service:** CMI'nov will offer training services to surgeons delivered by referring surgeons (i.e. surgeons who have been trained by

CMI'nov's co-founder Professor Marco Vola). This will accelerate the learning curve

- 4) **Practitioner experience:** The surgeons will define new patient pathways and new recovery patterns in cardiac medicine. No intensive care will be needed
- 5) **Brand:** CMI'nov will use the brand 'Straight to the heart' to express uniqueness and value to the users and patients.

Over time, the improvement potential of the MITrep device will reside in the extension of the indications to other valves and in its use as a complementary device to other surgical equipment to perform an edge-to-edge operation (i.e. to edge the leaflets of a valve). Hence, MITrep will grow its market potential as time goes by (first in Europe and the USA, then Asia, then the entire heart valvuloplasty market).

Our biggest successes and our biggest hurdles

Our start-up has been a three-time national innovation winner and has recently been awarded the first European innovation prize under Phase 1 of the SME Instrument.

The device is Class III, i.e. with maximum risk. The start-up's main difficulty for the development of the device is to respond correctly to the new regulatory requirements which have been strongly reinforced since 2016.

Despite these awards, the development of such a complex device in terms of both technology and its field of application (cardiac surgery) requires a lot of time and a lot of money. Potential investors only commit themselves if animal trials are successful. However, before the start-up can reach this stage, the development costs are also very

CMI'nov

CMI'nov was created in August 2015 following a meeting between Bernard Pain and Professor Marco Vola in November 2012.

Pain is a born inventor and his career has been punctuated by 20 patent applications; Vola is a renowned cardiac surgeon who in 2010 was awarded the 'Victoires de la Médecine' in cardiology.

Pain's wife, Corinne Pain, has since joined the two founding members, bringing her managerial and organisational skills to the team.

CMI'nov is specialised in the design and development of medical devices in mini-invasive cardiac surgery. Its ambition is to become the European leader in this activity thanks to its engineering staff and complementary skills.

important and it must be able to finance the project. Thanks to its good management and thanks to the relevance of its project, CMI'nov has successfully raised seed funds of €1m. This fundraising will allow it to achieve the animal trials.

CMI'nov plans to quickly recruit clinical and regulatory research engineers to carry out all the steps up to CE mark.

References

- 1 Burden of valvular heart diseases: a population-based study. Nkomo VT, *Lancet* 2006;368: 1005-1011
- 2 What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? Mirabel M *et al. Eur Heart*
- 3 At a reduced distance to the valve: only 20-25cm
- 4 From functional mitral insufficiency in infants to rheumatism and severe cases in adults
- 5 Professor Marco Vola
- 6 Source: Frost & Sullivan
- 7 This is attributed to their rising healthcare expenditure and increased awareness regarding mitral valve diseases. For instance, in some states of India, the presence of favourable government initiatives and reimbursement policies provide coverage for the transcatheter heart therapies
- 8 Transcatheter mitral valve replacement: still a long way to go! Thierry Carrel, *Ann Transl Med* v.5(17); 2017 SepPMC5599293
- 9 How hot is your next innovation? Geoff Tuff, *Harvard Business Review*, May 2009



Bernard Pain
President
CMI'nov

+ 33 6 81 15 56 62
+ 33 6 09 47 10 53

Bernard.pain@cmi-nov.com