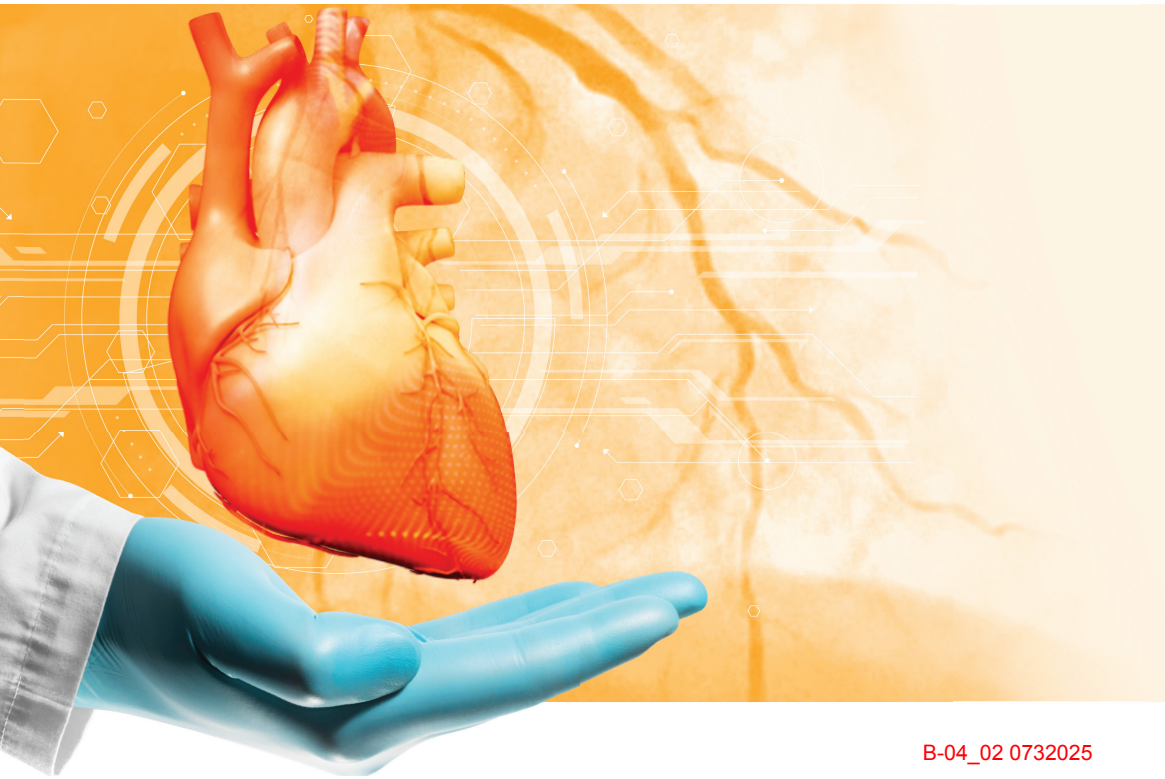
Clinical summary iVAC 2L pVAD

Percutaneous Ventricular Assist Device



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General Context

Today, Percutaneous Mechanical Circulatory Support (MCS) can be used to facilitate High-risk Percutaneous Coronary Interventions (HR-PCIs).
The in-hospital mortality rate of high-risk PCI patients is higher than usual, and may reach up to 28% after 30 days. To prevent this, the increasing use of prophylactic MCS in this setting aims to support the circulatory system from the first minutes of the intervention. This approach may reduce the risk of hemodynamic instability or circulatory collapse during coronary artery manipulation and provide sufficient time to achieve optimal and complete revascularization[1].

The main goals of Left Ventricular (LV) short-term MCS include:

- ✓ LV unloading.
- ✓ Reduction in Myocardial Oxygen Consumption (MVO_2).
- ✓ Increase in systemic pressures.
- ✓ Optimization of coronary flow and end-organ perfusion.
- ✓ Decongestion of the venous and pulmonary circulations.

Purpose of protected High-Risk PCI with pVAD

With prophylactic MCS in HR-PCI, operators can expect a reduction in major adverse events [1-9].

Body of Evidence

The efficacy of MCS has been suggested by multiple comparative studies:

- Cardiopulmonary bypass reduced intraprocedural mortality in in patients with low ejection fraction undergoing high-risk PCI (4.8% vs 18%, $p < 0.05$)[8].
- In the BCIS-1 trial, hemodynamic instability occurred in 1.3% of the group assigned for planned IABP insertion (pre-PCI) versus 12% in the group with no planned IABP insertion ($p < 0.001$), In the latter group, patients received IABP only in case of instability. The IABP is the weakest modality of MCS available[9].
- In the SHOCK trial Registry, the use of IABP significantly reduced mortality among patients with acute myocardial infarction followed by cardiogenic shock (50% vs 72%, $p < 0.001$)[10].
- The PROTECT II trial showed a 22% reduction in the relative risk of Major Adverse Events with MCS vs IABP after 90 days and a significant increase in the Cardiac Power Output (CPO) intraprocedurally. The PROTECT II trial is the largest randomized controlled trial comparing MCS with IABP in high-risk percutaneous coronary interventions1.
- An analysis of 198 high-risk patients undergoing HR-PCI with MCS (n=69) or without MCS (n=129) at the Erasmus Medical Center (Rotterdam, NL) showed that MCS improved survival and reduced adverse events when compared with standard-of-care only[2].
- A prospective study conducted by the Erasmus Medical Center (Rotterdam, NL) documented increases in systemic pressures and reduction in pulmonary pressures when iVAC 2L was activated in elective cases of HR-PCI, with no major adverse events[6].
- A head-to-head comparison between iVAC 2L and Impella 2.5 in elective HR-PCI showed both devices are capable of significantly increasing the MAP[9].
- The PULSE trial shows LV unloading, increased mean arterial pressure (MAP) and lower myocardial oxygen consumption (MVO_2) with the use of iVAC 2L in high-risk PCI[3, 4].
- Recent experiment using porcine models of acute myocardial infarction with cardiogenic shock (AMICS) showed that iVAC 2L decreases the mean pulmonary capillary wedge pressure (mPCWP), and increases blood pressure and cardiac output at the onset of cardiogenic shock and after 12h of support[11].
- A recently published expert consensus recommends that MCS may be considered in highly selected patients undergoing HR-PCI in case of acceptable femoral access (> 6 mm in diameter of the common femoral artery with no severe tortuosity) and should be preferred instead of IABP and VA-ECMO[5]

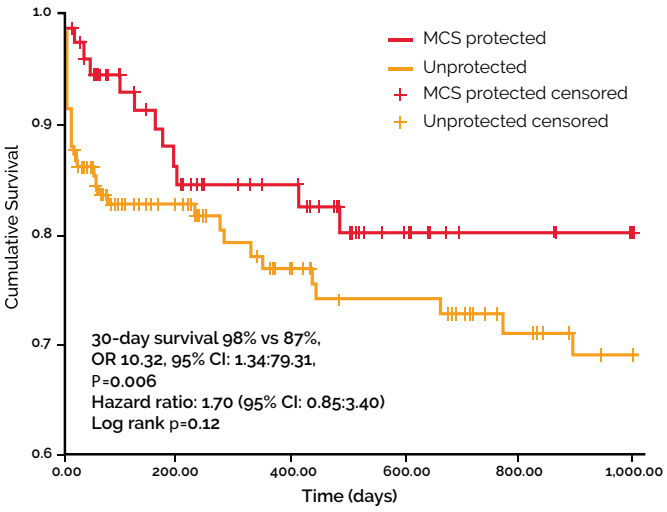

Figure 1. *Kaplan-Meyer survival curves showing that mechanically-assisted HR-PCI may have better survival compared to HR-PCI with no mechanical support. Adapted from Ameloot et Al, 2018.*

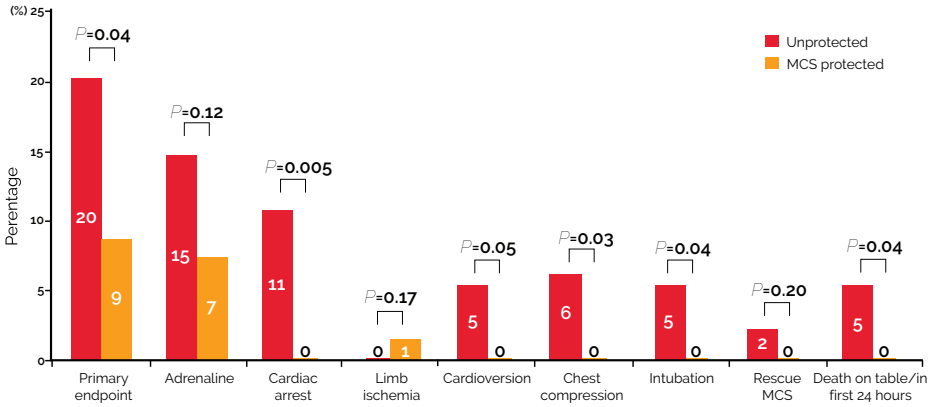

Figure 2. *Severe procedural adverse events related with the use of mechanical support during HR-PCI. The primary endpoint of the study (composite of cardiac arrest requiring resuscitation, hypotension with need for vasopressor support, need for rescue MCS, limb ischaemia with need for surgery and need for endotracheal intubation) occurred in 20% of the unprotected patients and in 9% of the MCS protected patients (OR: 0.38, 95%CI: 0.15-0.97, p = 0.04). Adapted from Ameloot et al, 2018.*

PULSE Trial[3]

- Design: prospective single-arm two center prospective cohort.
- Study population: patients undergoing HR-PCI with MCS.
- Objective: to understand the hemodynamic changes produced by iVAC 2L.
- Primary endpoint: reduction in pressure-volume area (PVA).
- Secondary endpoints: clinical endpoints at 30 days.

Investigators: Prof Nicolas Van Mieghem MD PhD (PI)[1], Dr M. B. Bastos MD MHSc[1], Dr J. Daemen MD PhD[1], Dr J. Schreuder MD PhD[1] and Dr S. Redwood, MD, PhD[2].

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(2) St. Thomas Hospital, London, United Kingdom

Main results

- LV unloading with reduction of pressures and volumes in the LV chamber.
- Significant reduction in MVO_2 as demonstrated by a fall in PVA.
- Reduction in LV afterload.
- Decrease in mechanical dyssynchrony.
- Increase in MAP.

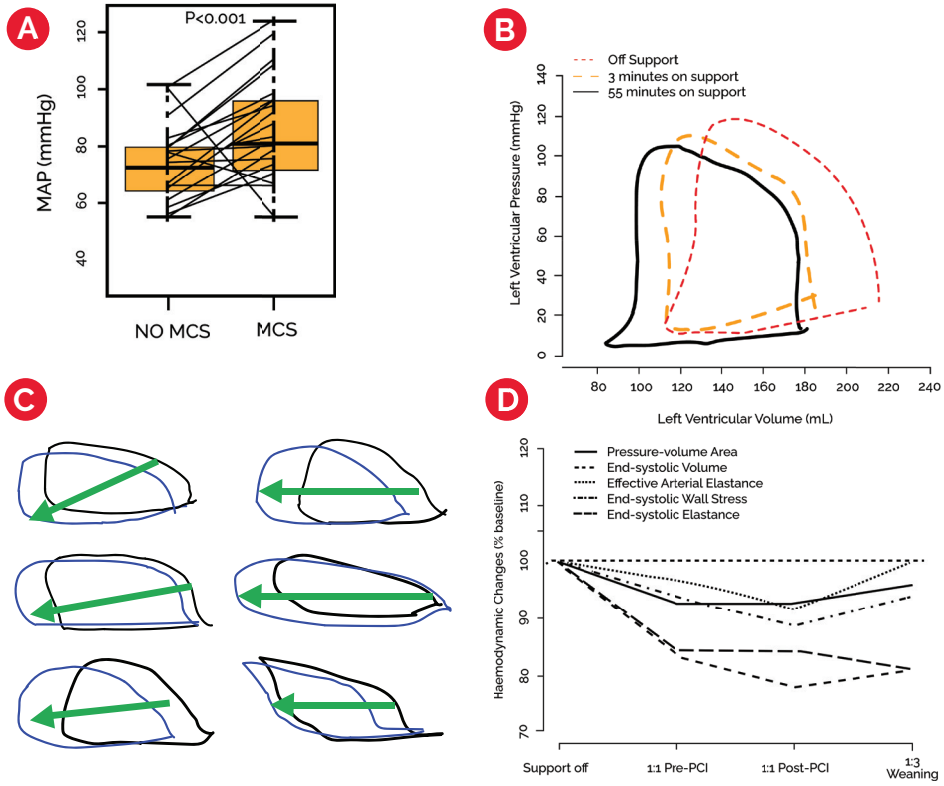

Figure 3. *(A) MCS with iVAC 2L significantly increased the mean arterial pressure (MAP) when activated. (B) Pressure-volume loops show progressive unloading of the left ventricle during the period iVAC 2L is active. (C) Pressure-volume loops from separate individuals showing left ventricular unloading with iVAC 2L activated (blue loops) as opposed to baseline (black loops) with iVAC 2L in stand-by. (D) Progression of hemodynamic markers during use of iVAC 2L show a gradual reduction in the Pressure-volume Area (MVO2), Effective arterial elastance (afterload), wall stress and in chamber volumes. Additionally, a partial return to baseline levels can be observed at weaning.*

Conclusion

The efficacy of iVAC 2L is demonstrated by its capability to provide:

- Left ventricular unloading.
- 17% increase in the Mean Arterial Pressure and in the left ventricular afterload.
- 23% increase in the Cardiac Power Output.
- 7-8% reduction in myocardial oxygen consumption.
- 30-days mortality rates similar or better compared to other devices.
- Low rates of intraprocedural hemodynamical instability.
- Low rates of major bleeding if operated by qualified hands.

PulseCath iVAC 2L Post-Market Surveillance Registry

PulseCath maintains retrospective registry that includes data from patients receiving iVAC 2L-assisted interventions with a variety of indications. The data derives from published studies, medical records and from reports provided by operators.

The current version of the registry includes data from 293 cases that originate from 116 different centers across 37 different countries worldwide. The results show low rates of Major Adverse Events at 30 days in elective cases of HR-PCI which are comparable or lower than those observed with Impella in several other studies. iVAC 2L also improved hemodynamics in stable and shocked patients. However, more data on 30-days endpoints is needed in order to validate these findings. This is also observed on the in-hospital outcomes, where mortality was similar to that observed in the EUROPELLA registry.

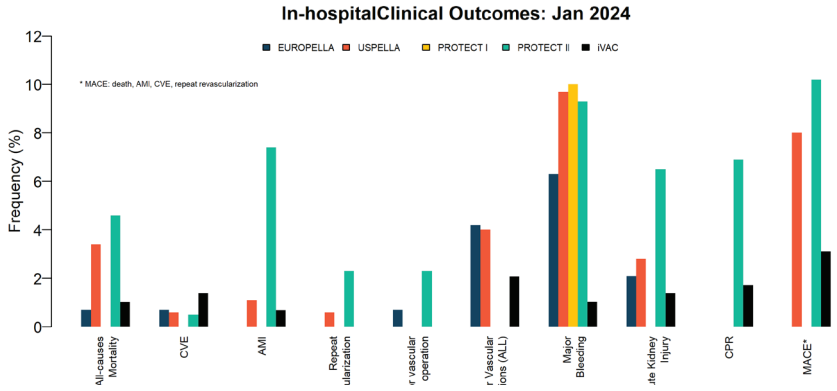

Figure 4A. *In-hospital rates of major adverse events on the use of PulseCath iVAC 2L compare favorably with previous studies with similar devices and the IABP.*

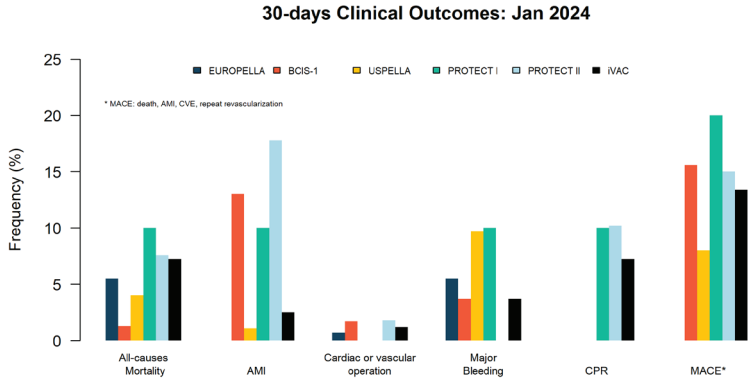

Figure 4B. *Rates of major adverse events on the use of PulseCath iVAC 2L at 30 days suggest equivalent results compared to other relevant studies on short-term mechanical circulatory support.*

IVAC 2L overview

iVAC 2L is a short term, fully percutaneous, 17Fr trans-femoral LVAD that effectively generates blood flow up to 2.0 L/min. By actively unloading the LV, the iVAC 2L provides critical haemodynamic support during high-risk revascularization procedures, in cases of acute myocardial infarction and in cardiogenic shock[11].

What is the labeled indication for the iVAC 2L system?

iVAC 2L is intended for use in patients with impaired left ventricular function which require mechanical circulatory support for up to 24 hours. This includes left ventricular support in the following situations:

- Elective or emergent HR-PCIs for Coronary Heart Disease.
- Cardiogenic shock of various etiologies.
- Acute Decompensated Heart failure.
- High-risk electrophysiological procedures.

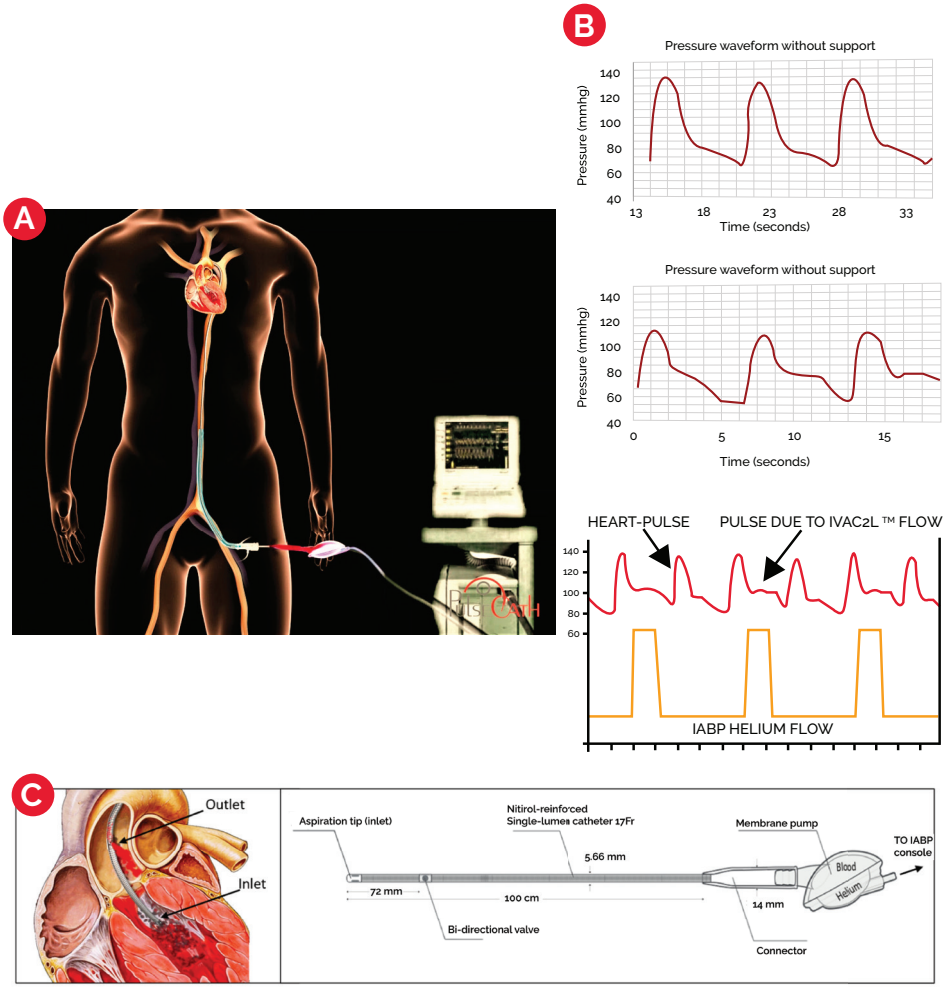

Figure 5. *(A) Implantation of iVAC 2L. The catheter is introduced through the common femoral artery and positioned with the tip inside the LV. The catheter is connected to a membrane pump which is in turn connected to a conventional IABP console. (B) Effect of iVAC 2L on the aortic pressure waveform showing diastolic augmentation and additional pulsatility in the diastolic descent. (C) Schematic view of iVAC 2L showing its main working components. Effective length of catheter as indicated by the arrows is 920 mm*

Mechanism of action

The operating mechanism of the iVAC 2L is a patented 2-way valve integrated in a 17Fr single lumen and bi-directional, 1000 mm long catheter. This catheter is connected to an extracorporeal membrane pump. The system is compatible with a standard IABP console and does not require dedicated hardware. When the heart is in the **systolic** phase, blood is aspirated from the ventricle through the tip of the catheter and transported via the lumen into the membrane pump. During the **diastolic** phase, the membrane pump (with the IABP console as a driver) directs the blood back through the catheter to the ascending aorta by opening the 2-way valve.The pulsatile synchronization between closing of the aortic valve and the opening of the catheter valve ensures that the aortic valve function is not impaired, but supported.

General features:

- ✓ Trans-aortic insertion from the femoral artery.
- ✓ Designed for percutaneous use.
- ✓ Actively ejects left ventricular blood into the ascending aorta at rates
- ✓ up to 2.0 L/min (average: 1.5 L/min).
- ✓ Diastolic augmentation that elevates the mean arterial pressure through increases in the diastolic blood pressure, with potential benefits to the coronary flow.
- ✓ Driven by any conventional IABP consoles.

Advantages

- ✓ Pulsatile support, leading to more effective left ventricular unloading.
- ✓ Fast and easy implementation through the femoral artery.
- ✓ Fully percutaneous approach.
- ✓ Highly flexible catheter.
- ✓ Cost effectiveness: iVAC 2L has a universally adaptable design that fully integrates with a standard IABP console, but provides up to four times the support provided by the IABP.

Advantages of Pulsatile flow

Continuous flow reduces the motility of the aortic valve and has been related to worse end-organ perfusion. It may also increase the aortic impedance reducing its effectiveness in protecting the myocardium. In contrast, synchronized pulsatile flow preserves pulsatility and cyclic strain in the peripheral vasculature, potentially improving end-organ perfusion. iVAC 2L may also optimize coronary blood flow thus increasing oxygen delivery to the myocardium while sparing it by reducing the left ventricular afterload[3, 4].

References

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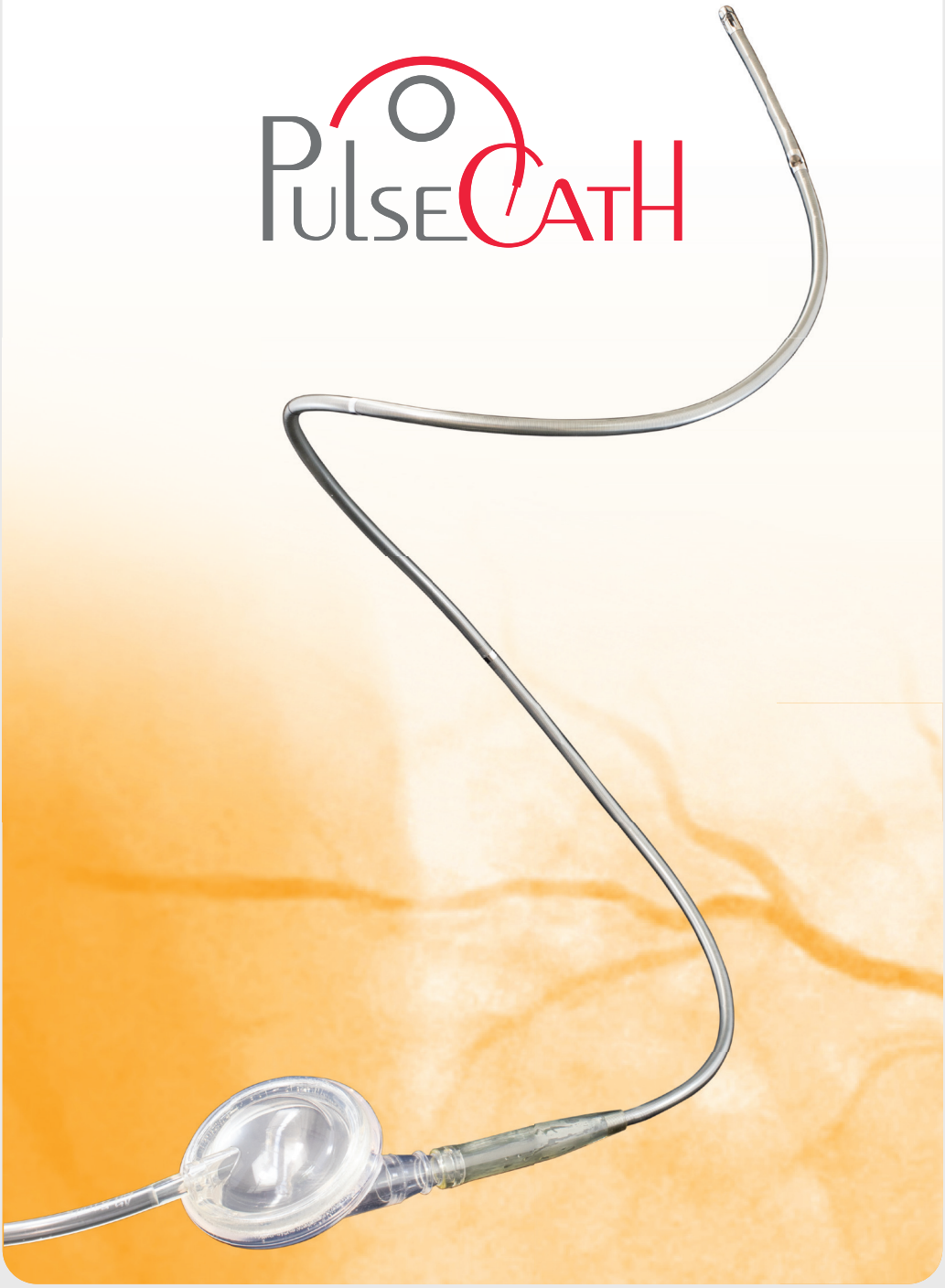
PulseCath



Facts and figures

Registrations
> 50 countries approved registrations

Cases
> 175 shared cases on LinkedIn;
> 400 reported cases

> 1.300 iVAC 2L sold
> 35 distributor agreements

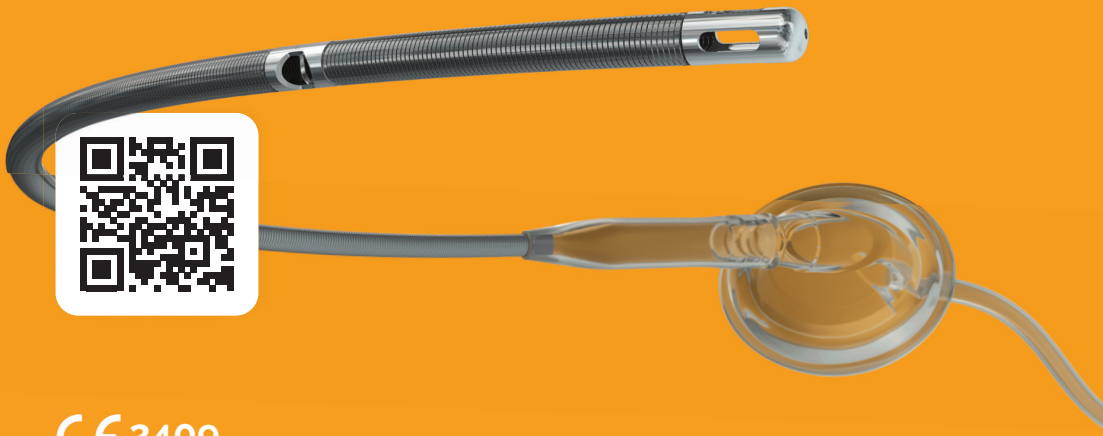
Hospitals
> 45 hospitals use iVAC 2L on a regular base;
> 9 Centers of Excellence.

Patients
> 600 patients world wide treated by iVAC 2L

Indication
The iVAC 2L is intended for use in patients with impaired left ventricular function which require left ventricular mechanical circulatory support for up to 24 hours

Clinical evidence
> 30 publications

PulseCath



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