

Concept and first experimental results of a new ferromagnetic assist device for extra-aortic counterpulsation

Christoph T. Starck^{a,*}, Jakob Becker^a, Roland Fuhrer^b, Simon Sündermann^a,
Jan Wendelin Stark^b and Volkmar Falk^a

^a Clinic of Cardiac and Vascular Surgery, University Hospital Zurich, Zurich, Switzerland

^b Institute for Chemical and Bioengineering, Swiss Federal Institute of Technology Zurich, Zurich, Switzerland

* Corresponding author. Clinic of Cardiac and Vascular Surgery, University Hospital Zurich, Raemistrasse 100, 8091 Zurich, Switzerland.
Tel: +41-44-2553298; fax: +41-44-2554467; e-mail: christophthomas.starck@usz.ch (C.T. Starck).

Received 17 May 2013; received in revised form 17 July 2013; accepted 19 August 2013

Abstract

OBJECTIVES: Based on a ferromagnetic silicone cuff for extra-aortic counterpulsation, a new assist device concept was developed. The driving force is generated by an external magnetic field, which leads to contraction of a soft magnetic cuff. The force generation capacity of the device was tested in a silicone aorta model.

METHODS: Magnetic elastomers can be constructed through dispersion of micro- or nanoparticles in polymer matrices and were designed to act as soft actuators. Two magnetically active silicone cuffs were produced with a nanomagnet loading of 250 wt% (Cuff 1) and a micromagnet loading of 67 wt% (Cuff 2). The magnetic cuffs were applied on a silicone aorta model and contracted against hydrostatic pressure.

RESULTS: A full contraction of Cuff 1 was possible against a maximal hydrostatic pressure of 30 cmH₂O (22 mmHg) at a magnetic flux density of 0.4 T (Tesla) and 65 cmH₂O (48 mmHg) at a magnetic flux density of 1.2 T. A 50% contraction of Cuff 2 was possible against a maximal hydrostatic pressure of 80 cmH₂O (59 mmHg) at a magnet-cuff-distance (MCD) of 0 cm. At MCDs of 1 and 2 cm a 50% contraction was possible against 33 cmH₂O (24 mmHg) and 10 cmH₂O (7 mmHg), respectively.

CONCLUSIONS: Combining the advantages of magnetic elastomers with the principle of extra-aortic counterpulsation in a new assist device concept avoids the need for anticoagulation (no contact with bloodstream). With regard to the magnetic principle of action, no intra- to extracorporeal connection is needed. More experimental work is needed to further increase the force generated by the silicone cuff and to transfer the device concept into an *in vivo* setting.

Keywords: Assist device • Heart failure • Extra-aortic counterpulsation

INTRODUCTION

There are several assist devices that can be implanted as bridges to recovery, transplantation or as destination therapy. Volume displacement pumps are driven by pneumatic or electric mechanisms. Rotary flow devices work with constant radial, axial or mixed flow produced by a centrifugal pump [1]. These devices can be used either for full or for partial support.

Another class of assist devices works by the principle of counterpulsation support. These devices provide partial circulatory support. Intra-aortic balloon pumps (IABP) are well established in clinical use and work by electrocardiogram-triggered inflation and deflation of an intra-aortic balloon resulting in an afterload reduction and diastolic augmentation with increase in coronary blood flow [2]. IABP support is usually limited to short periods. Other counterpulsation devices are designed for long-term support. The C-Pulse device (Sunshine Heart, Inc., Tustin, CA, USA) works as an extra-aortic balloon (EAB) counterpulsation device with similar haemodynamic effects as those of the IABP [3]. It is a polyester-coated polyurethane

balloon cuff, which is installed circumferentially around the ascending aorta. Another concept is represented by the Symphony Counterpulsation device (SRC Inc, Louisville, KY, USA). It functions by counterpulsation with a peripheral capacitance chamber in a subcutaneous pocket in the right infraclavicular region. Blood is removed from the right subclavian artery in systole and returned in diastole [4].

Two major drawbacks of actual assist devices are (i) contact of blood with foreign material with the risk of thromboembolic complications and (ii) the intra- to extracorporeal connection with the risk of infectious complications. The C-Pulse device eliminates the problem of blood contact resulting in the fact that anticoagulation is unnecessary. The problem of an intra- to extracorporeal connection still remains. The proposed assist device concept aims at avoiding blood contact and the need for an external drive-line.

By crosslinking metal nanoparticles into the polymer backbone of hydrogels, a contracting polymer can be formed [5]. Combining the advantages of this material with the principle of extra-aortic counterpulsation led to the development of a ferromagnetic cuff

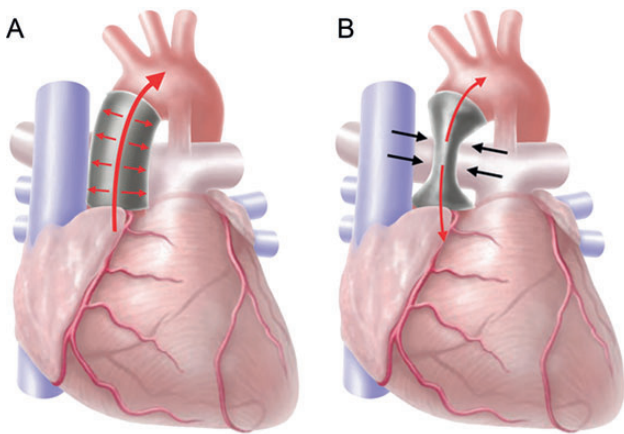


Figure 1: Principle of function of the ferromagnetic cuff as extra-aortic counter-pulsation assist device. (A) Relaxed position. (B) Contracted device.

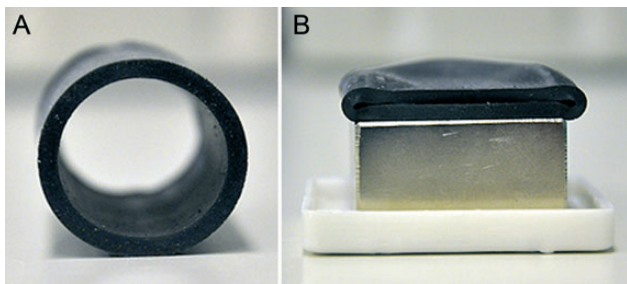


Figure 2: (A) Magnetic active assist device in relaxed position (diameter: 2.5 cm). (B) Silicone magnetic cuff with full contraction provoked by an external magnetic field.

(Fig. 1). The driving force for its assist function is generated by an external magnetic field, which avoids an intra- to extracorporeal connection.

In this feasibility study, we investigated the force generation capacity of the device in a silicone aorta model.

MATERIALS AND METHODS

Ferromagnetic cobalt nanoparticles or carbonyl iron microparticles were cross-linked into the polymer backbone of silicones. This resulted in a material with high mechanical stability and shape memory effect without losing flexibility. These magnetically active silicone cuffs were produced with a nanomagnet loading of up to 250 wt% (Cuff 1) or a micromagnet loading of 67 wt% (Cuff 2). The cuffs were produced as tubes with a diameter of 2.5 cm and a length of 8.0 cm, but can be produced in any desired shape and diameter (Fig. 2). The fluid displacement volume at full contraction is 39 ml.

The magnetic cuffs were applied on a silicone aorta model and contracted against hydrostatic pressure. For provoking contraction of Cuff 1, two different types of magnets were used: (i) a U-shaped permanent magnet with a magnetic flux density of 0.4 T (Tesla) and (ii) a neodymium-based permanent magnet with a magnetic flux of 1.2 T. The silicone aorta model was filled with water. For both magnets, the maximal pressure, at which a full contraction of the ferromagnetic cuff leading to a complete displacement of the entire volume of the silicone cuff (39 ml) was achieved, was measured (Fig. 3).

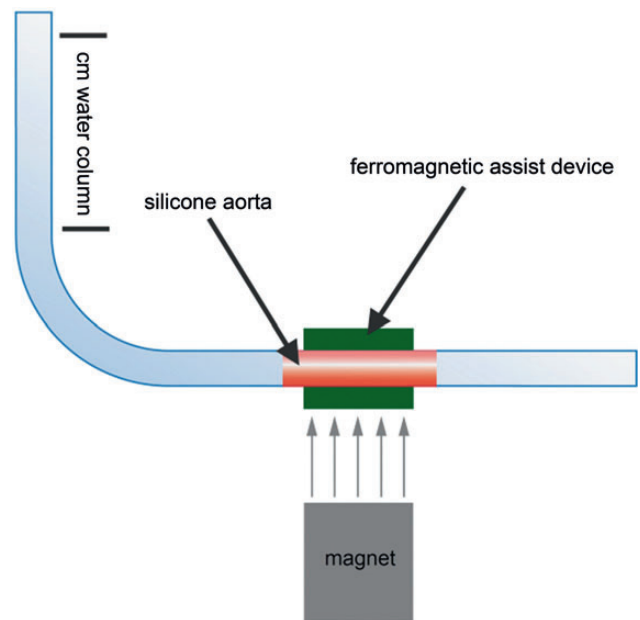


Figure 3: Experimental set-up of the silicone aorta model.

In a second series of measurements, contraction of Cuff 2 was achieved by a neodymium-based permanent magnet with a magnetic flux of 1.2 T. In this series, a 50% contraction (19.5 ml fluid displacement volume) was provoked against hydrostatic pressure in the silicone aorta model. At different distances of the magnet to the cuff with a soft tissue barrier (gelatin spacer), the maximal pressure at which a 50% contraction of the ferromagnetic cuff was achieved was measured.

In a final series of measurements, contraction of Cuff 2 was achieved by a neodymium-based permanent magnet with a magnetic flux of 1.2 T at different distances with a soft tissue barrier (gelatin 10%). In this series, the cut-off distance was determined at which a loss of cuff-contraction against a water column with a pressure of 33 cmH₂O was observed.

RESULTS

For Cuff 1, both magnetic fields were able to induce complete contraction of the ferromagnetic cuff. The U-shaped permanent magnet (0.4 T) was able to produce a contraction against a maximal pressure of 30 cmH₂O, which is equivalent to 22 mmHg. The neodymium-based permanent magnet (1.2 T) still generated a full contraction of the cuff at a maximal pressure of 65 cmH₂O or 48 mmHg (Table 1).

Regarding the results of Cuff 2, a 50% contraction with the neodymium-based permanent magnet (1.2 T) at a magnet-cuff-distance (MCD) of 0 cm was possible against a maximal hydrostatic pressure of 80 cmH₂O (59 mmHg). At a MCD of 1 cm, a 50% contraction with the neodymium-based permanent magnet (1.2 T) was achieved against a maximal hydrostatic pressure of 33 cmH₂O (24 mmHg) and at a MCD of 2 cm against a maximal hydrostatic pressure of 10 cmH₂O (7 mmHg) (Table 2).

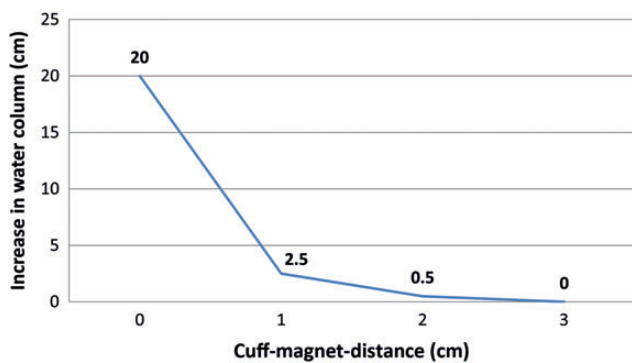
The third series of measurements (neodymium-based permanent magnet (1.2 T), water column 33 cmH₂O) revealed an increase of 20 cm water column in case of direct contact of the magnet with the cuff (distance 0), at a MCD of 1 cm an increase of 2.5 cm

Table 1: Summary of the results of Cuff 1 (cobalt nanoparticles 250 wt%)

Magnet type	Magnetic flux density (T)	Maximal hydrostatic pressure (cmH ₂ O)
U-shaped permanent magnet	0.4	30
Neodymium-based permanent magnet (51 × 51 × 25 mm)	1.2	65

Table 2: Summary of the results of Cuff 2 (carbonyl iron microparticles 67 wt%)

Magnet-cuff-distance (cm)	Maximal hydrostatic pressure (cmH ₂ O)
0	80
1	33
2	10

**Figure 4:** Magnetic force efficiency on cuff contraction against a water column with a pressure of 33 cmH₂O versus cuff-magnet-distance.

water column was noted and at a distance of 2 cm, an increase of 0.5 cm water column. The cut-off distance for loss of contraction of the ferromagnetic cuff was found to be at 3 cm (Fig. 4).

DISCUSSION

The results of the experiments have demonstrated that a nano-magnetic soft-pump concept is feasible under *in vitro* conditions.

So far, a full cuff contraction is possible against a maximal pressure of nearly 50 mmHg. This may not be enough to guarantee sufficient contraction in a patient with heart failure. *In vivo* the cuff needs to contract against pressures of ≤ 95 mmHg, given a maximum systolic pressure of the patient of 120 mmHg [6]. These pressure values assume that the beginning of the cuff contraction is timed at the diastolic notch. A recent study performed by Zhang *et al.* [7] on optimal timing algorithms of a para-aortic counterpulsation device in a sheep model of acute ischaemic heart failure concludes that the optimal timing of ejection of the para-aortic counterpulsation device is at the end of the

isovolumetric relaxation phase. This would transfer to a post-diastolic notch contraction-start of the ferromagnetic cuff.

Our first measurement series measured the maximal hydrostatic pressure at which a full contraction of the ferromagnetic soft pump was achievable. Davies *et al.* compared in an acute porcine model the haemodynamic effects of intra- versus extra-aortic counterpulsation. A 7 ml EAB was compared with a 25 ml intra-aortic balloon. The coronary blood flow augmentation was better in extra-aortic counterpulsation despite smaller volume displacement. Both methods performed comparably in diastolic pressure augmentation, afterload reduction and augmentation of cardiac output [8]. With regard to these results, it has to be assumed that a mild contraction as opposed to the complete cuff collapse induced might be sufficient to generate comparable haemodynamic improvements as intra-aortic counterpulsation. Therefore, we performed a second series of measurements with merely provoking a 50% contraction. In this second series, it could be shown that a 50% contraction is possible against a maximal pressure of nearly 60 mmHg. These results show an improvement in contractile strength, but still may not be enough to guarantee sufficient contraction in a patient with heart failure, given the assumption that counterpulsation has to be achieved against maximal pressures of ≤ 95 mmHg.

Two possible solutions can further improve the generated power: (i) increasing the magnetic flux by the use of stronger magnetic fields and (ii) increasing of the nano- or micromagnetic load of the soft actuator.

In our experiments (Fig. 3), the distance between magnetic field and ferromagnetic cuff was zero in the first series of measurements. In the second test series, the contractile strength of the magnetic cuff with increasing MCD (0, 1 and 2 cm) using a soft tissue barrier (gelatin spacer) was investigated. The results revealed a very strong decrease in the generated force by the magnetic cuff. This was confirmed with the third series of measurements, in which the cut-off distance for a loss of cuff-contraction was determined to be 3 cm under the given experimental set-up (magnetic field, ferromagnetic load of the silicone cuff). For *in vivo* studies, the magnet will have to be located extracorporeally, which means an even greater distance between the magnet and the assist device as tested in this series. This will lead to a decrease in the strength of the magnetic field at the required location and most likely require stronger magnetic fields. In addition, design improvements (for example, asymmetric ferromagnetic particle load) might be required to improve cuff contraction at greater distances.

When the silicone cuff is brought into a magnetic field, it will contract on its full length (given the magnetic field covers the full length of the cuff). This could lead to high shear stresses of the aortic tissue at both ends of the cuff with resultant damage. Therefore, a cuff with a maximal load of magnetic nanoparticles concentrated in the middle part will be developed. This would allow for a more 'thumb-printing'-like contraction, reducing wall stress at each end of the cuff and minimizing possible aortic wall injury comparable with the C-Pulse device (C-Pulse; Sunshine Heart, Inc., Tustin, CA, USA) [3, 9].

This new assist device concept will have a number of limitations. As other (extra-aortic) counterpulsation devices, it will be contraindicated in patients with severe ascending aortic atherosclerotic disease, aortocoronary bypass grafts or aortic regurgitation [10]. Unfortunately, it will not be possible to bypass these mentioned limitations with changes in design. The performance of coronary artery bypass grafting will be possible if proximal anastomoses to the ascending aorta can be avoided. Another limitation will be the presence of medical devices that are susceptible to electromagnetic

interference. On the other hand, magnetic resonance imaging-compatible pacemaker and implantable cardioverter-defibrillator devices have been developed and are available, which address this problem of electromagnetic interference. Further improvements in this sector can be expected in the future, which will positively influence this limitation.

This new assist device concept has two major advantages: risk elimination of infectious complications due to percutaneous drive lines and abolishment of anticoagulation because of the avoidance of direct blood contact.

Approximately 15–30% of the patients with assist devices suffer from a drive line infection [11]. Of note, 30–40% of deaths among assist device patients are related to serious infections [12]. Hayward *et al.* performed a pilot study using the C-Pulse in 5 patients. Three of them (60%) suffered infections of whom 1 patient had late infectious complications related to the percutaneous drive line [9]. Therefore, the missing intra- to extracorporeal connection due to the magnetic principle of action of our assist device concept is a clear advantage to existing assist device systems.

Due to the extra-aortic placement, the ferromagnetic cuff pump does not interact with the blood itself. This may favourably affect patient outcomes by decreasing the incidents of thromboembolism, haemorrhage, and device-related coagulopathy and abolishes the need for anticoagulation [4].

Another positive aspect of the described ferromagnetic soft-pump assist device concept is that after possible recovery of the patient due to a missing intra- to extracorporeal connection, the device can stay in place. This leaves the opportunity to make use of it again in case the patient suffers a relapse and needs circulatory support again.

Because biocompatibility issues typically limit IABP therapy to short durations of hours to days [4], this could indicate extra-aortic counterpulsation as a serious alternative in patients with moderate-to-severe heart failure.

Because of the mentioned advantages of the magnetic polymer cuff pump, we consider it as a potential alternative in patients in need of temporary partial cardiac support.

CONCLUSION

In this *in vitro* feasibility study, the concept of contracting an aortic model by a polymer cuff loaded with ferromagnetic nano- or

microparticles was proved. However, more experimental work has to be performed with the goal to further increase the force generated by the soft pump, to determine what degree of contraction is required for adequate support and to transfer the device concept into an *in vivo* setting.

Conflict of interest: none declared.

REFERENCES

- [1] Timms D. A review of clinical ventricular assist devices. *Med Eng Phys* 2011;33:1041–7.
- [2] Scheidt S, Wilner G, Mueller H, Summers D, Lesch M, Wolff G *et al.* Intra-aortic balloon counterpulsation in cardiogenic shock—report of a cooperative clinical trial. *N Engl J Med* 1973;288:979–84.
- [3] Sales VL, McCarthy PM. Understanding the C-pulse device and its potential to treat heart failure. *Curr Heart Fail Rep* 2010;7:27–34.
- [4] Bartoli CR, Dowling RD. The future of adult cardiac assist devices: novel systems and mechanical circulatory support strategies. *Cardiol Clin* 2011; 29:559–82.
- [5] Fuhrer R, Athanassiou EK, Luechinger NA, Stark WJ. Crosslinking metal nanoparticles into the polymer backbone of hydrogels enables preparation of soft, magnetic field-driven actuators with muscle-like flexibility. *Small* 2009;5:383–8.
- [6] Hébert JL, Lecarpentier Y, Zamani K, Coirault C, Daccache G, Chemla D. Relation between aortic diastolic notch pressure and mean aortic pressure in adults. *Am J Cardiol* 1995;76:301–6.
- [7] Zhang GW, Wen T, Gu TX, Yu Y, Zhao Y, Zhang YH *et al.* Optimal timing algorithms of para-aortic counterpulsation device: an animal study. *ASAIO J* 2012;58:115–21.
- [8] Davies AN, Peters WS, Su T, Sullivan CE, Perkidides T, Milsom FP *et al.* Extra-ascending aortic versus intra-descending aortic balloon counterpulsation—effect on coronary artery blood flow. *Heart Lung Circ* 2005;14:178–86.
- [9] Mitnovetski S, Almeida AA, Barr A, Peters WS, Milsom FP, Ho B *et al.* Extra-aortic implantable counterpulsation pump in chronic heart failure. *Ann Thoracic Surg* 2008;85:2122–5.
- [10] Hayward CS, Peters WS, Merry AF, Ruygrok PN, Jansz P, O'Driscoll G *et al.* Chronic extra-aortic balloon counterpulsation: first-in-human pilot study in end-stage heart failure. *J Heart Lung Transplant* 2010;29:1427–32.
- [11] Holman WL, Park SJ, Long JW, Weinberg A, Gupta L, Tierney AR *et al.* Infection in permanent circulatory support: experience from the REMATCH trial. *J Heart Lung Transplant* 2004;23:1359–65.
- [12] Lietz K, Long JW, Kfoury AG, Slaughter MS, Silver MA, Milano CA *et al.* Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: implications for patient selection. *Circulation* 2007;116:497–505.