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Atrial assist device, a new alternative to lifelong anticoagulation?

Etienne Abdelnour-Berchtold[a], *Piergiorgio Tozzi*[a], *Giuseppe Siniscalchi*[a], *Daniel Hayoz*[b], *Ludwig K. von Segesser*[a]

[a] Cardiovascular Surgery Department, CHUV, Lausanne, Switzerland
[b] Department of Internal Medicine, Friburg Hospital, Friburg, Switzerland

Summary

Objective: Atrial fibrillation is a very common heart arrhythmia, associated with a five-fold increase in the risk of embolic strokes. Treatment strategies encompass palliative drugs or surgical procedures all of which can restore sinus rhythm. Unfortunately, atria often fail to recover their mechanical function and patients therefore require lifelong anticoagulation therapy. A motorless volume displacing device (Atripump®) based on artificial muscle technology, positioned on the external surface of atrium could avoid the need of oral anticoagulation and its haemorrhagic complications. An animal study was conducted in order to assess the haemodynamic effects that such a pump could provide.

Methods: Atripump is a dome-shape silicone-coated nitinol actuator sewn on the external surface of the atrium. It is driven by a pacemaker-like control unit. Five non-anticoagulated sheep were selected for this experiment. The right atrium was surgically exposed, the device sutured and connected. Haemodynamic parameters and intracardiac ultrasound (ICUS) data were recorded in each animal and under three conditions; baseline; atrial fibrillation (AF); atripump assisted AF (aaAF).

Results: In two animals, after 20 min of AF, small thrombi appeared in the right atrial appendix and were washed out once the pump was turned on. Assistance also enhanced atrial ejection fraction. 31% baseline; 5% during AF; 20% under aaAF. Right atrial systolic surfaces (cm^2) were; 5.2 ± 0.3 baseline; 6.2 ± 0.1 AF; 5.4 ± 0.3 aaAF.

Conclusion: This compact and reliable pump seems to restore the atrial "kick" and prevents embolic events. It could avoid long-term anticoagulation therapy and open new hopes in the care of end-stage heart failure.

Key words: cardiac assist device; atrial fibrillation; anticoagulation; nitinol alloy

Objective/Introduction

Atrial fibrillation (AF) is the most common abnormal heart rhythm encountered in medical practice. It is a rapid atrial arrhythmia also characterised by irregular or absent mechanical activity [1]. In the western world, 5% of the population is affected and long-term studies reveal that the mortality of these patients is twice that of persons with normal sinus rhythm [2].

AF is associated with a five-fold increase in the risk of cardioembolic strokes due to blood stasis and therefore clotting phenomena [3, 4]. These strokes are the most severe ones, with long transient ischaemic attacks, presumably due to embolisation of larger particles than in carotid disease. Cognitive defects may be detected together with asymptomatic embolic events on brain-CT, reducing the quality of life (QOL) [5]. Statistical significant fall in patient's activity and heart rate variability also occur. [6]. Finally, decreased ventricular filling time and loss of atrial contraction make AF an independent risk factor for chronic heart failure (HF) [7–9].

Based on these observations, we elaborated an experimental atrial assistance device that restores the missing mechanical support during AF. Further clinical aims could be:

– prevention of embolism, or at least be an overall physiological assessment of the problem of atrial stunning
– a better ventricular preload, that could become significant when preserving the little cardiovascular performance left, in patients with reduced ventricular function.

Until now, and because AF has detrimental sequelae, many therapeutic strategies have been developed. Actual treatments embrace two main

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alternatives that both require a challenging decision in clinical management. First, the use of palliative drugs such as negative chronotropes combined with lifelong oral anticoagulation (according to the CHADS2 score). Secondly, the only surgical or endovascular intervention that can potentially cure AF, known as the AFib radiofrequency ablation procedure.

The first Cox-Maze was performed in 1988 and is based on the fact that AF results from multiple microreentry circuits in the atria. The operator creates precise microlesions, using cryo- or thermo ablation, creating electrical blind alleys in which there are no longer sustainable multiple wavelets [10–12]. This extensive procedure has some negative effects on atrial mechanical work. Postoperative patients assessed by echocardiography showed, five years later, a significant loss in atrial contractility and an increase in atrial size [13]. Today, the AFib ablation uses radiofrequency (RF) after precise mapping and is reported to be effective in restoring sinus rhythm and preserving some atrial function. Ablation of the atrioventricular junction plus pacing "ablate and pace" as well as electrical isolation of pulmonary vein (PVI) are effective non-pharmacological therapeutic strategies in patients with refractory AF. In this case, the role of long-term anticoagulation after successful ablation is uncertain, since the embolic risk has not yet been well defined [14, 15]. A recent clinical trial provides very new information concerning the widely used routine strategy of rhythm-control, which does not reduce the rate of death from cardiovascular causes, compared with simple rate-control treatment [16].

However, and even if new medication guidelines are still being developed, many patients continue to require anticoagulation therapy and up to 3% of them, according to foreign data are exposed to the risk of severe haemorrhagic complications and non-compliance problems [17]. In Switzerland, management of oral anticoagulation and its major bleeding complications are nevertheless lower (0.6%) [18, 19].

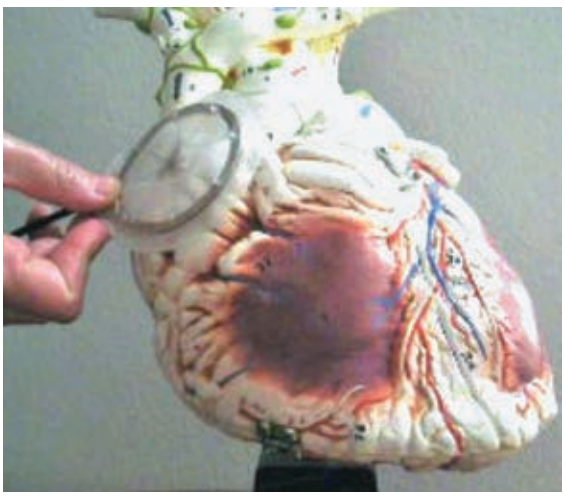
Atripump® introduces a completely new concept for treating AF. It is a motorless volume-displacing device based on artificial muscle technology that could restore the pump function of normal atrium. Actual shape memory alloys enable the construction of micro-actuators that move, and therefore work by changing their molecular structure when low voltage is applied to them. Positioned on the external surface of the atrium, they compress the heart chamber with the potential for avoiding chronic anticoagulation, and do not have other limitations of the current cardiac assistance devices such as intrusive tubes and a heavy power supply.

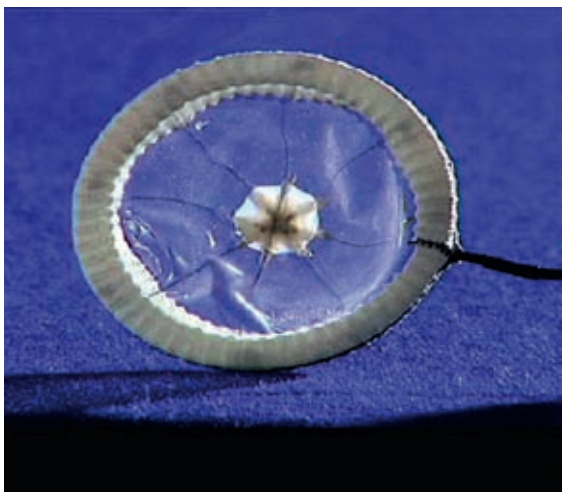
A first publication by our team has already demonstrated the atripump to completely reproduce haemodynamic performance in a bench model. It ran for three consecutive months without any technical failure. The Starling law was respected and temperatures were compatible with those of the human body [20]. As a continuation, the second aim was to assess these mechanical effects in an appropriately designed animal study.

Methods

Atripump® (Nanopowers SA, Lausanne, Switzerland) is a dome shape, silicone coated nitinol actuator 5 mm high, set on a plastic ring 40 mm in diameter. The thickness of this membrane is about 3 mm.

Stochiometric Nickel-Titanium alloys (nitinols) undergo a diffusionless martensitic transition at temperatures near 70 °C with marked changes in physical properties such as shape or hardness, and do so with great force.





Figures 1 and 2

Dome is made of nitinol fibers, linked up to a ring and covered with a double layer of silicon. It is then placed on the external surface of right atrium.

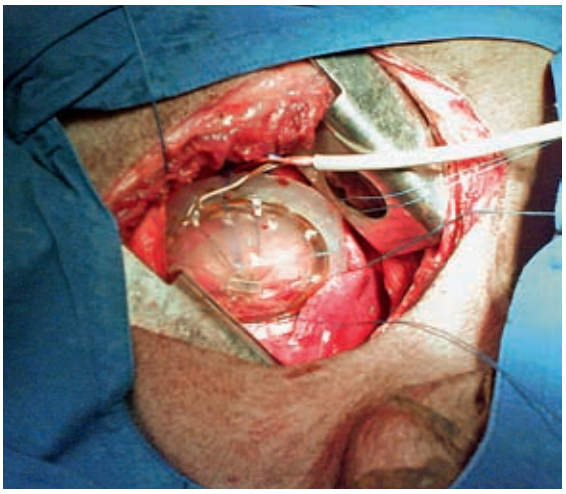


Figure 3

Intra-operative view of the dome, being sewed and connected.

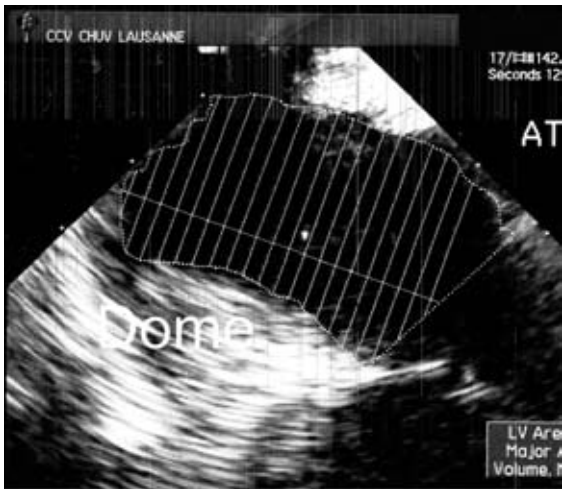


Figure 4

ICUS (intra cardiac ultra sound) assessed measures. All data were gathered and sored using dedicate softwares.

The underlying explanation is a crystal structure that cooperatively moves to another one at a specific temperature. It is a reversible phenomenon that can be endlessly repeated without any permanent damage. When the nitinol wires are electrically heated, they provide a replicative contractile function reminiscent of normal myocardial contractility, therefore pulling down the apex of the dome. When the electricity is cut off, the wires quickly elongate and get back to their rest length. The outcome of such a cycle in changing the dome's concavity is volume displacement. Our atripump has a pacemaker-like control unit that senses ventricular activity and delivers the electrical kick following a dedicated algorithm. The trigger comes from a lead placed on the epicardium and connected to the control unit. The control unit senses ventricular activity just like standard pacemakers (QRS or ventricular depolarization) and after a given delay (from 200 to 500 ms) activates the wires. It can also work in a fixed mode without triggers, just like standard VVI pacemakers. In preliminary experiments this homemade control unit was placed outside the body.

Five adult sheep (weight 65 ± 4 kg) were anaesthetised and ventilated to maintain a $PaCO_2$ of 35–45 mm Hg. Throughout the procedure, analgesia was maintained and mean arterial blood pressure monitored. The surgical approach was right thoracotomy in the 4th intercostal space after sterile preparation. The right atrium (RA) was exposed and the dome sutured onto the epicardium in order to provide the mechanical support for blood circulation. AF was induced using rapid epicardial pacing (600 bpm, Biotronik, Germany). Animals did not receive any anticoagulation treatment.

A Swan-Ganz catheter was inserted in the left jugular vein to measure the central venous and pulmonary pressure. A flowmeter was set around the pulmonary artery and computed ejection fraction (EF) of the RA was obtained with an intracardiac ultrasound (ICUS) inserted in the right jugular vein. That also allowed calculation of systolic and diastolic surface areas of the RA. A temperature probe was placed in, between the inner silicone membrane and the epicardium, right in the middle of the dome. All the major parameters were acquired under 3 conditions: baseline, AF and atripump assisted AF (aaAF). The experiment ran successfully for two consecutive hours in all animals and data acquisition occurred for 20 min in each haemodynamic situation (baseline, AF and assisted AF). All the devices were correctly sewn and their contractions were supplied with a power of 12 V, 400 mA for 200 ms. State ethics committee, in accordance with the Helsinki declaration, approved the animal procedures. Sheep were sacrificed at the end of the experience.

Results

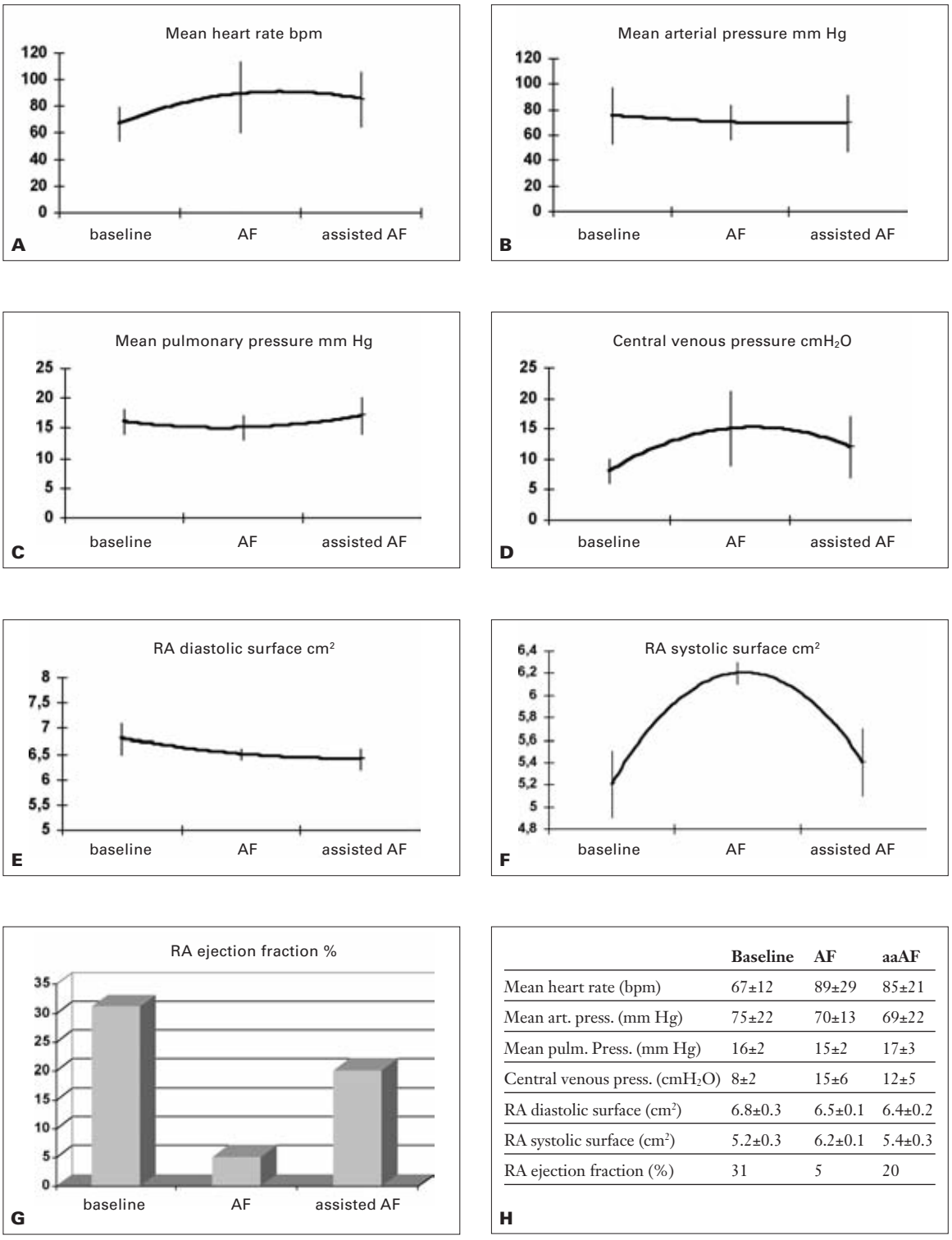
In two animals, after 20 min of AF, a small thrombus appeared in the right atrial appendix (ICUS assessed) and was washed out once the pump was turned on.

Mean heart rate (bpm) increased from 67 ± 12 (baseline) to 89 ± 29 as soon as AF was induced and stayed at 85 ± 21 under atrial assistance (aaAF).

Concerning the two arterial pressure records, mean arterial pressure (mm Hg) showed the following values; 75 ± 22 (baseline), 70 ± 13 (AF), and 69 ± 22 (aaAF). For mean pulmonary pressure (mm Hg) we observed the following: 16 ± 2 (baseline), 15 ± 2 (AF) and 17 ± 3 (aaAF). Central venous pressures (cmH_2O) rose from a 8 ± 2 baseline value to 15 ± 6 during AF and went back to 12 ± 5 after atrial assistance started running.

Right atrial surface area (cm^2) presented the following pattern: in diastole 6.8 ± 0.3 (baseline), 6.5 ± 0.1 (AF) and 6.4 ± 0.2 (aaAF), whilst in systole the surface area started at 5.2 ± 0.3 (baseline), then reached 6.2 ± 0.1 (AF) and declined, 5.4 ± 0.3 with assistance (aaAF). A statistically relevant change was observed for the right atrial ejection fraction (%). Baseline values were 31%. They fell to 5% in AF and rose to 20% in aaAF. Detailed results are presented in figure 5:

Figure 5
Results.



	Baseline	AF	aaAF
Mean heart rate (bpm)	67±12	89±29	85±21
Mean art. press. (mm Hg)	75±22	70±13	69±22
Mean pulm. Press. (mm Hg)	16±2	15±2	17±3
Central venous press. (cmH_2O)	8±2	15±6	12±5
RA diastolic surface (cm^2)	6.8±0.3	6.5±0.1	6.4±0.2
RA systolic surface (cm^2)	5.2±0.3	6.2±0.1	5.4±0.3
RA ejection fraction (%)	31	5	20

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Discussion

We propose a new surgical concept for the management of chronic AF. Atripump is a laboratory-made prototype based on smart material technology and intended to restore the mechanical function of fibrillating atria. An implantable battery, to be charged by the transcutaneous electromagnetic energy transfer (TEET) will power the system. Intraoperatively, the device is sewn over the diseased atrium and connected to the battery as well as to a control unit, which can be set according to the patient's needs.

The idea of using nitinol actuators to help a deficient heart is not new and potential advantages were investigated, mainly in ventricular as-

sistance, from the early 70's [21]. At that time, contraction speed, material fatigue, heating and energy supply were the major limitations.

Today's alloys are different and our approach is totally novel. In a previous assay atripump successfully reproduced haemodynamic performance in a bench model [20]. Data made us confident that the device in question should last for several years before fibre-fracture occurs. The device even seemed to follow the Franck-Starling law, responding to increasing preload, thus behaving in a similar fashion to natural muscle. This animal study unmasks some relevant "in vivo" and clinical outcomes.

All the devices ran without any technical failure. Mean heart rate increased, as soon as AF was induced, because of the conduction properties of the AV node controlling ventricular rate. Atrial assistance does not influence this haemodynamic value, which can better be dealt with by the PVI procedure or antiarrythmic pharmacotherapy. The temperature probe placed on the atrial surface, revealed a mean value of 39 ± 1 ºC, demonstrating that the amount of caloric energy transferred by the device onto surrounding structures is very low. In this case, blood circulation and the wet environment may have performed together as a heat exchanger, keeping the organ temperature in a range, compatible with human implantation.

Considering the haemodynamic results illustrate atripump's real purpose. First, during our experiment, in two animals, after 20 min of AF, a small thrombus appeared in the right atrial appendix (ICUS assessed) and was washed out once the pump was turned on. Virchow's triad encompasses three broad conditions, thought to contribute to thrombosis. Hypercoagulability is not an issue here. Our experiment had no direct effect on the surfaces exposed to blood (no endothelial injury). However, alteration of blood flow is prevented (stasis).

Additionally to thromboembolism, AF can also lead to clinical consequences including an upstream congestion and a fall in backward blood pressure, both of which contribute to heart failure [22, 23]. Although we based our research on the right-sided heart, analogous effects occur in left cardiac function.

Central venous pressure seemed to reproduce the congestive corollary during AF. Fibrillation also gave rise to a significant RA systolic surface extension (close to 1 cm²), while diastolic observations went on stand by. Up to this point one might hesitate in concluding that intraoperative haemodynamic support, or a real consequence of AF provoked these changes. What may reinforce the AF hypothesis and therefore suggest a lack of atrial draining activity, is the immediate and substantial redress of these values after atripump was switched on. Central venous pressure slightly refined when RA systolic surface was corrected. More relevantly, loss of the atrial work was demonstrated by its EF, which fell from a 30% (baseline) to about 5%. With atrial assistance running, it climbed to 20%. Successfully finding or defining a cut-off value for a left atrial EF able to prevent thrombosis would be interesting.

Many studies have shown how influential atrial mechanical activity is. Schimpf et al. brought left atrial "kick" recovery forward, as an element for improvement in respiratory function and contribution to normalisation of pulmonary arterial pressure [24]. In the early 80's, Linderer et al. elegantly demonstrated that atrial systole enhances LV performance by means of the Franck-Starling principle, increasing preload (end-diastolic fibre's length). In addition during induced withdrawal of atrial function they remained relatively full, accounting for increased pericardial pressure. As a result, LV stroke-volumes were reduced with a resultant reduction in function [25]. Restoration of left atrial EF could have a positive influence, still to be determined, in chronic HF.

A further area of concern requires analysis to establish whether the pressure imposed by the dome structure on the atrial surface results in functional obstruction of the coronary ramification. We are mindful that the pump depicted in this paper has been elaborated for the right atrium and does not match the complex left atrial field. A figure-of-eight or oval configuration would better fit this anatomy. However, only long-term animal studies will confirm applicability and safety of our device.

Conclusion

Atripump represents a new strategy in restoring the atrial blood transport. One key advantage of this proposed technology is the tremendous simplification in engineering since the material itself is the motor. Our experiment showed a retrieval of the atrial "kick" and a possible beneficial effect on thrombembolic events. Were a plausible model to be realised, it could eliminate the need for anticoagulation drug therapy. Also, it opens new avenues in the management of end-stage HF.

Correspondence:
Etienne Abdelnour-Berchtold
rue des pressoirs 32
1180 Tartegnin
E-Mail: etienne.abdelnour@unil.ch

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