Atria assist device to restore transport function of fibrillating atrium ☆

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Abstract

Objective: The Maze procedure can restore sinus rhythm in patients suffering from chronic atrial fibrillation but often fails to restore the mechanical function of the atrium, the so-called atrial kick and requires long-term anticoagulation most of the time. A micro motorless pump (Atripump) based on artificial muscle technology positioned on the external surface of the atrium could compress the heart chamber, restoring atrium transport function. A bench model reproducing the mechanical function of human atrium and human environment has been developed to assess the circulatory support that such a pump can provide. **Methods:** Atripump (Nanopowers SA, Switzerland) is a dome-shape, silicone-coated nitinol actuator to be sutured on the external surface of the atrium. A pacemaker-like control unit drives the actuator and manages the external compression of the atrium. The bench model consists of an open circuit made of rubber bladder, 60 cc in volume, connected to a vertically positioned and scaled tube that is filled at different levels reproducing changes in cardiac pre-load and after-load. The pump was placed on the outer surface of the bladder and both were immersed in water having a constant temperature of 37 °C. Pressure, volume and temperature at the interface dome–bladder were recorded. **Results:** Pump ran 24 h for three consecutive months. During the experiment, no technical failure occurred and the pressure and volume values were repeatable during the experience. Nitinol fatigue was assessed measuring the wire's electric resistance that remained $400 \pm 10 \ \Omega/m$. Contraction rate was 1 Hz with power supply of 12 V, 400 m and heating time of 300 ms. Pre-load ranged from 11 to 15 mmHg. When inserted in the bath at 37 ± 0.5 °C, maximal temperature between silicone membrane and rubber bladder was 39 °C. Maximal volume pumped was 492 ml/min. **Conclusions:** This artificial muscle pump can reproduce the mechanical effect of a normal human atrium. It is compact, reliable and follows the Starling law. The surface temperature is in the physiologic range and it could represent a new tool to restore the atrial kick in persistent atrial fibrillation.
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1. Introduction

The atrium serves three major functions that affect overall cardiac performances: it is a contractile chamber that actively empties immediately before the ventricular systole and establishes ventricular end diastolic volume, it is a reservoir that stores venous return during systole and isovolumic relaxation and it is a conduit that empties its content into the ventricle down a pressure gradient after the atrioventricular valve opens and continues to passively transfer the blood during diastole. William Harvey first described the contractile activity of the atrium in 1628 and its contribution to cardiac performances [1]. This booster

pump contribution to cardiac output is even more important to preserve cardiovascular performances in patients with reduced ventricular functions. Loss of atrial contraction with the onset of atrial fibrillation (AF) is commonly associated with a reduction in cardiac output.

Chronic or persistent AF is the most frequent cardiac arrhythmia in over fifties and is associated with structural heart disease that could reduce the cardiac output up to 15% [2–5]. Moreover, it is considered a risk factor for thromboembolic events because up to 5% of patients experience one or more cerebrovascular accidents.

Therefore, AF causes a loss of quality of life (QOL) and a significant threat of stroke with the ensuing effects. The existing treatment consists primarily of palliation and is based on drugs having a negative chronotrope effect, drugs that reduce the risk of thromboembolic accidents and endovascular or surgical procedures to restore the sinus rhythm (Maze procedure). The Maze procedure was first described by Cox in the early 1990s and is based on the

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concept of isolating the regions of the right and left atrium, where the foci triggering the AF are located, using thermo or cryoablation either with percutaneous access or open surgery [6–12]. Basically, this procedure ends up with a compartmentalization of both atria creating a labyrinth with blind alleys in which the amount of atrial myocardium is insufficient to sustain multiple wavelets of re-entry.

The Maze procedure has been reported as effective in restoring sinus rhythm (95% of patients at 3 years follow-up are free from AF), but the rate of restoring atrial contraction varies from 21 to 75% [11]. The percentage of patients with restored atrial contraction seems to differ with the etiology of AF: more than 90% of the patients with isolated AF or an atrial septal defect have restored atrial contraction, whereas only between 21% and 90% of patients with mitral valve disease have restored atrial contraction after the Maze procedure [11,12]. Therefore, even if sinus rhythm is restored, atria have definitively lost their capability to coordinate their contraction in order to produce an efficient transport function, thus the hemodynamic gain is negligible. Patients continue to require anticoagulation therapy for their lifetime and are exposed to the risk of hemorrhagic complications as high as 1% per year.

An atrial assist device represents a new concept to treat AF. It could restore the transport function of the atrium and avoid the need of chronic anticoagulation therapy. Nano-technology enables the construction of micro-actuators where the movement, and therefore the work, is generated by changing the molecular structure of the so-called smart materials when a low voltage is applied to them or when they are heated or cooled. A micro motorless pump based on artificial muscle technology positioned on the external surface of the atrium could compress the heart chamber restoring the pump function of the atrium. The artificial muscle technology could avoid the limitations of current cardiac assist devices such as tubes piercing the skin, heavy power supplies and the need of lifetime anticoagulation therapy.

Because this is a totally new concept, the primary aim of this study is to assess the hemodynamic performances of the atrial assist device in a bench model.

2. Methods

2.1. Device description

Atripump (Nanopowers SA, Lausanne, Switzerland) is a dome-shape, silicone-coated nitinol actuator 5–10 mm high, mounted on a plastic ring having a diameter ranging from 45 to 55 mm (Fig. 1). Nitinol is a shape memory alloy (SMA). This material undergoes changes in shape and hardness when heated or cooled, and does so with great force. SMAs belong to a class of metal alloys displaying a property called shape memory effect. The source of the shape memory effect is a diffusionless phase transformation as a solid, in which atoms move cooperatively, often by shear-like mechanisms. SMAs have a uniform crystal structure that radically changes to a different structure at a specific temperature. When the memory alloy is below this transition temperature (marten-
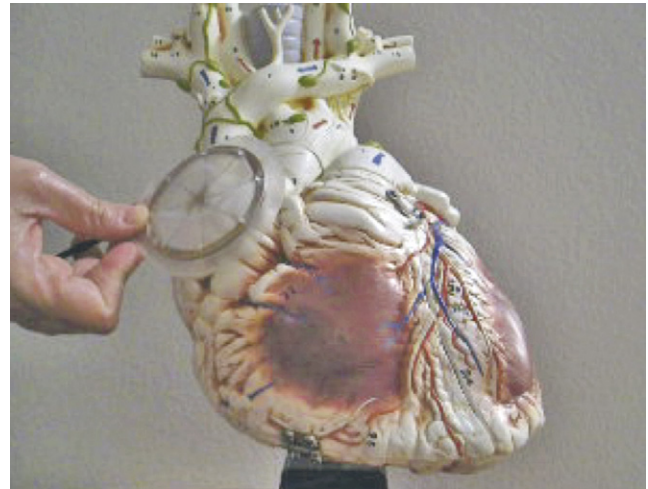

Fig. 1. The dome is made of nitinol fibers connected to a plastic ring and covered with a double layer of silicone (hand hold). This dome is placed on the external surface of the right atrium and restores the atrial kick.

sitic state) it can be stretched and deformed without permanent damage. After the alloy has been stretched, if it is heated above its transition temperature (austenite state), the alloy recovers to the un-stretched shape and completely reverses the previous deformation [13].

When the nitinol wires are electrically heated they reduce their length and pull down the apex of the dome therefore causing a reduction of the dome concavity. This is the hemodynamic equivalent of a systole. When the current is cut off, the nitinol wires get back to their rest temperature and elongate to their rest length. Therefore, the dome recovers the initial concavity. This is the hemodynamic equivalent of a diastole. The changes in dome concavity result in volume displacement. This cycle is controlled by a pacemaker-like unit that senses ventricular activity and gives current to the wires following a dedicate algorithm. The dome should be sutured onto the atrium's epicardium in order to provide the mechanical support to the blood circulation.

2.2. Bench model

The bench model reproducing the hemodynamic characteristics of the atrium of a healthy man consists of an open circuit made of latex bladder 60 mm in diameter filled with water at room temperature. The bladder is connected to a vertically positioned graduate tube that is filled at different levels (from 10 to 30 cm with respect to the dome level) reproducing changes in cardiac pre-load. The Atripump is placed on the outer surface of the bladder and activated at a fix rate of 60/min. A temperature probe is placed in between the inner silicone membrane and the latex bladder, right in the middle of the dome where eight nitinol fibers cross each other. The dome and the bladder are then immersed in a water bath kept at 37 °C to reproduce the physiologic environment (Fig. 2). The height of the water column with the dome in the off position corresponds to the pre-load. The height of the same column at the end of the dome's contraction corresponds to the after-load. Pressures are
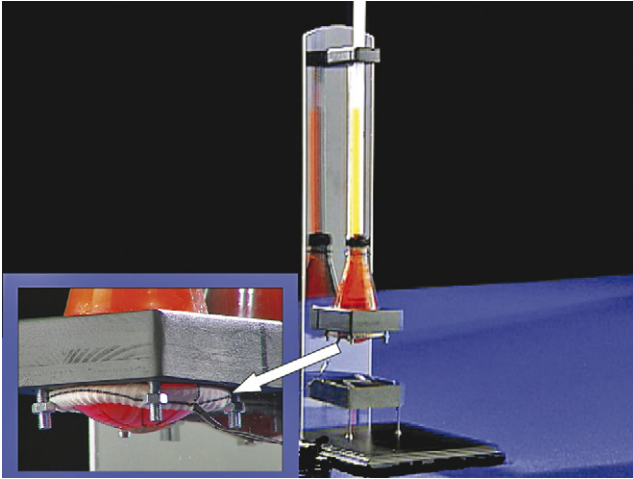
Fig. 2. The bench model. The dome (detail in the left low corner) is placed on the outer surface of the rubber bladder that is connected to vertical and graduate column water. A control unit activates the dome 60 times per minute causing the water column to go up and down. Volume ejected per single contraction is measured directly on the scaled column: 10 mm corresponds to 2 ml.
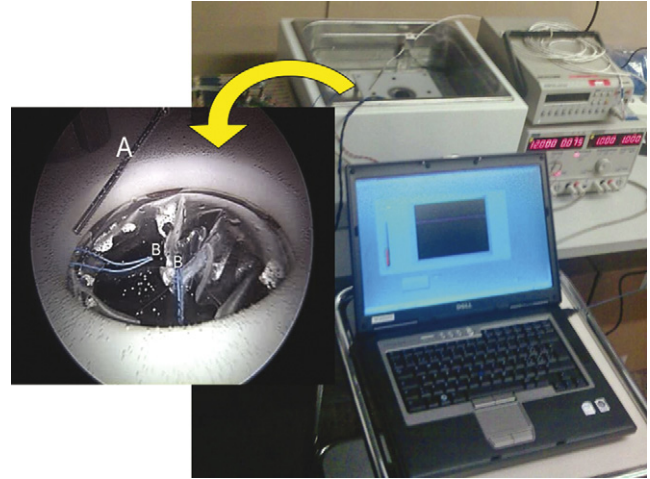

Fig. 3. The dome is placed underwater and bath temperature is kept at 37 °C to mimic in vivo environment. Rubber bladder has been removed to show the details. Water temperature is monitored by the probe A. Probe B monitors the temperature between the dome and the rubber bladder. This temperature corresponds to the temperature the cardiac cells are exposed to. All data are gathered using a dedicate software and stored in the laptop.

expressed in cmH_2O. Volume ejected per single contraction (VJ) is measured directly on the scaled column: 10 mm corresponds to 2 ml. Because the contraction rate is 1 Hz, we calculate the pump output per minute with the following formula: pump output = VJ × 60 ml/min. A temperature probe is placed between the outer surface of the dome and the bladder in order to measure the hypothetical temperature on the atrium surface (Fig. 3). Data are expressed as mean and standard deviation.

3. Results

Pump ran 24 h for three consecutive months. During the experiment, no technical failure occurred and the pressure and volume values were repeatable during all the experience. Nitinol fatigue was assessed measuring the wire's electric resistance that remained $400 \pm 10 \, \Omega/m$. The contraction rate was 1 Hz with power supply of 12 V, 400 mA for 300 ms. Wire recovery time was 700 ms. Pre-load ranged from 15 to 21 cmH_2O. Volume ejected per single contraction (per s) ranged from 2 ± 0.5 ml (pre-load 15 cmH_2O) to 8 ± 0.5 ml (pre-load 21 cmH_2O). Fig. 4 represents detailed results. Maximal silicone membrane temperature was 55 ± 2 °C when the dome was activated in air at room temperature. When inserted in the bath at 37 ± 0.5 °C, the maximal temperature between silicone membrane and rubber bladder temperature was 39 ± 0.5 °C. The pump produced a maximal work of 16×10^{-3} J. Maximal volume pumped was 492 ml/min. Mean volume pumped was 120 ± 10 ml/min with a pre-load of 15 cmH_2O and maximal after-load of 16.5 ± 0.5 cmH_2O; 210 ± 10 ml/min with a pre-load of 17 cmH_2O and maximal after-load of 20.5 ± 0.5 cmH_2O; 362 ± 15 ml/min with a pre-load of 19 cmH_2O and maximal after-load of 25 ± 0.5 cmH_2O and 489 ± 10 ml/min with a pre-load of 21 cmH_2O and maximal after-load of 27 ± 0.5 cmH_2O.

4. Discussion

Atripump is a laboratory prototype of atrial assist device based on smart materials technology for the surgical treatment of chronic AF. An implantable battery, to be charged transcutaneously, will power the system. Intraoperatively, Atripump will be wrapped over the right and left atrium and connected to the battery and a control unit, which can be set transcutaneously, according to the patient's need.

The concept of an atrial assist device is completely new probably not because anyone has thought of it but because it was not worth it to implant a conventional pump to just restore the atrial kick. Standard cardiocirculatory pumps, either pneumatic or magnetically suspended, are very expensive, require major surgical procedures to be implanted and require anticoagulation therapy as well.

The proposed technology is based on artificial muscle concepts using shape memory alloy technology. The major advantage of this technology is that the material itself is the engine, exactly as it happens in real life with the skeletal muscle, with a tremendous simplification of the engineering process of any cardiac assist device. The advantages of nitinol wire are well known since the early 1970s when the first ventricular assist devices and artificial hearts were designed [14]. However, at that time, contraction cycle, material fatigue, heating and energy supply were the major limitations to face and this project never went further.

More recently, Yambe and co-workers [15,16] have developed a nitinol-based artificial muscle to be used as VAD that can be activated at a frequency of 40 times per minute, which represents an important improvement with respect to first experimental data. Today's nitinol alloys provide a billion working cycles in bench models and that should correspond to more than 10 years lifetime. These data make us confident that the described device should last for a few years before a break of nitinol fibers occurs.

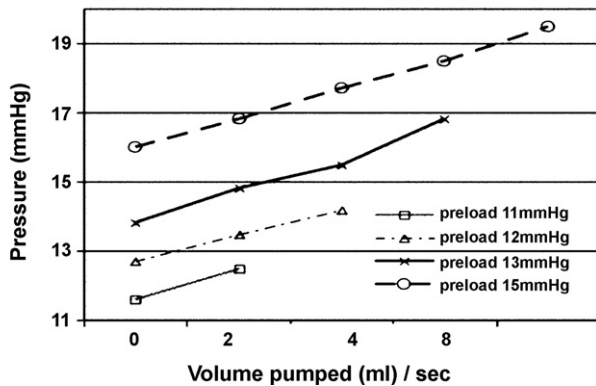**Volume ejected per single contraction with different preloads**

Fig. 4. Changing in pressures generated and volumes displaced in different pre-load conditions are plotted. Each cycle is over 1 s. The pump seems to follow the Starling law because the volume ejected increases when the pre-load increases.

Atripump working cycle corresponds to healthy adult heart rate in rest condition. This is possible because the nitinol fiber takes only 300 ms to reach its transitional temperature when electrically heated and has 700 ms to cool down. We believe that in the next prototype's generation, the maximal activation rate will go up to 80 cycle/min.

Ventricular activity triggers the contraction of the pump; an electrode placed on the epicardium senses the electrical activity of the right ventricle and informs the control unit: 100–200 ms after the QRS an electric signal from the control unit activates the dome.

The Atripump is able to pump the same volume, if not more, as a normal atrium in physiologic conditions. The work of normal human atrium is 0.19 Nm that corresponds to 0.19 J. This is easily calculated assuming the minimal atrial pressure is 8 mmHg, maximal 36 mmHg, volume ejected per systole 80 ml, with the following formula: $W = \Delta P \times \Delta V$. The work the Atripump provides is one order of magnitude bigger than necessary and the contraction of the dome is very smooth. With a maximum output of about half a liter per minute it clearly satisfies the hemodynamic needs. More interestingly, it seems to follow the Starling law revealing a response to pre-load increasing similarly to natural cardiac muscles: in the experimental set-up, pre-load was increased from 15 to 21 cmH$_2$O producing the right shift of the pressure/volume curb plotted in Fig. 4. This way of behaving gets the nitinol wire closer to natural muscle than ever.

The heating issue has always been one of the major limitations for human applications of nitinol actuators because the transitional temperature used to be above 100 °C. Local and systemic effects of heat dissipation associated to thermally powered LVAS implantation are well known [17]. In an elegant study published in 1988, Emoto and co-workers reported the effects on surrounding tissue [17]. Systemic (lungs, kidneys, blood tissue, coagulation process) and local effects of 20 W heat dissipation were analyzed in five calves. Conclusions were that heat promoted neointima proliferation at the interface pump–blood flow and angiogenesis was observed in the tissue capsula adjacent to the heat-dissipating surface. However, no deleterious systemic or local effects of 20 W heat dissipation were reported. The

transitional temperature of the nitinol wire used in this application is 70 °C. However, the amount of thermal energy transferred to surrounding structures is very low as has been demonstrated by the increase of the temperature between the membrane and the bladder in wet environment. The heat dissipates so quickly in a wet environment that the temperature does not go over 39 °C. Moreover, in real life, the atrium and the blood circulating in it will work as a heat exchange keeping the membrane temperature in a range compatible with human implantation. However, only long-term animal studies will confirm the safeness of this device with respect to the thermal injury of surrounding tissues.

Another concern is pressure-induced lesions on the surface of the atrium. The pressure imposed by the dome structure may result in functional obstruction of the ramifications of the coronary vessels causing diffuse hypoxia of the myocardium. In addition one may expect compression-related cell degeneration or necrosis in the myocardium. Once again, only long-term animal study will give an appropriate answer to this question.

The pump's design presented in this paper has been developed for the right atrium and is not suitable for the complex geometry of the left atrium. Oval and/or figure-of-eight configurations should better match left atrium anatomy without impairing the flow in pulmonary veins.

We are conscious that there are still several critical issues deserving further experimental studies to be addressed, but Atripump represents a new and superior strategy in fully restoring the transport function while maintaining the natural biological lining of blood exposed surfaces. Its realization requires leading edge technological innovation. However, upon realization, this may in future avoid the need for drug therapy and complications due to anticoagulation treatment and monitoring. With sufficient longevity of the device this technology has the potential to significantly reduce the treatment cost for atrial fibrillation and opens new hopes to the treatment of end-stage cardiac failure.

References

[1] Keynes G. The anatomical exercises of Dr William Harvey. De motu cordis 1628; De circulatione sanguinis 1649: the first English text of 1653. London Nonesuch; 1928. p. 202.

[2] Shemin RJ, Cox JL, Gillinov AM, Blackstone EH, Bridges CR. Guidelines for reporting data and outcomes for the surgical treatment of atrial fibrillation. Ann Thorac Surg 2007;83(3):1225–30.

[3] Therkelsen SK, Groenning BA, Svendsen JH, Jensen GB. Atrial and ventricular volume and function evaluated by magnetic resonance imaging in patients with persistent atrial fibrillation before and after cardioversion. Am J Cardiol 2006;15;97(8):1213–9.

[4] Fuster V, Ryden LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzy JL, Kay GN, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann S. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task force on Practice Guidelines and the European Society of Cardiology Committee for practice guidelines. J Am Coll Cardiol 2006;48:e149–246.

[5] Clark DM, Plumb VJ, Epstein AE, Kay GN. Hemodynamic effects of an irregular sequence of ventricular cycle lengths during atrial fibrillation. J Am Coll Cardiol 1997;30:1039–45.

[6] Cox JL, Boineau JP, Schuessler RB, Kater KM, Lappas DG. Five year experience with the Maze procedure for atrial fibrillation. Ann Thorac Surg 1993;56(4):814–23 [discussion 823–4].

[7] Melo J. How to establish normal biatrial contraction and sinus rhythm without drug therapy. Heart Surg Forum Rew 2002;1(1):5—6.

[8] Falk RH. Atrial fibrillation. N Engl J Med 2001;344:1067—78.

[9] Levy S, Breithard G, Campbell RWF. Atrial fibrillation: current knowledge and recommendations for management. Eur Heart J 1998;19:1292—320.

[10] Ferguson TB, Cox JL. Surgery for atrial fibrillation. In: Zipes DP, Jalife J, editors. Cardiac electrophysiology: form cell to bedside. 2nd ed. 1995. p. 1563—76.

[11] Cox JL, Schuessler RB, D'Agostino Jr HJ, Stone CM, Chang BC, Caine ME. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure. J Thorac Cardiovasc Surg 1991;101:569—83.

[12] Kamata J, Kawazoe K, Izumoto H, Kitahara H, Shiina Y, Sato Y. Predictors of sinus rhythm restoration after Cox Maze procedure concomitant with other cardiac operations. Ann Thorac Surg 1997;64:394—8.

[13] Gennes PG, Okumura KO, Shahinpoor M, Kim KJ. Mechanoelectric effects of ionic gels. Europhys Lett 2000;50(4):518—1518.

[14] Sawyer PN, Page M, Baseliust L, Mc Cool C, Lester E, Stanczewsky B, Srinivasan S, Ramasami N. Further studies of nitinol wire as contractile artificial muscle for an artificial heart. Cardiovasc Dis Bull Texas Heart Inst 1976;3(1):65—78.

[15] Yambe T, Shiraishi Y, Yoshizawa M, Tanaka A, Abe K, Sato F, Matsuki H, Esashi M, Haga Y, Maruyama S, TaKagi T, Luo Y, Okamoto E, Kubo Y, Osaka M, Nanka S, Saijo Y, Mibiki Y, Yamaguchi T, Shibata M, Nitta S. Artificial myocardium with an artificial baroreflex system using nano technology. Biomed Pharmacother 2003;57(1):122—5.

[16] Shiraishi Y, Yambe T, Sekine K, Saijo Y, Wang Q, Liu H, Nitta S. Development of an artificial myocardium using a covalent shape-memory alloy fiber and its cardiovascular diagnostic response. Conf Proc IEEE Eng Med Biol Soc 2005;1(1):406—8.

[17] Hemoto H, Harasaki H, Fujimoto LK, Navarro R, White M, Whalen R, Kiraly RJ, Nose Y. Systemic and local effects of heat dissipation in the thermally powered LVAS. ASAIO Trans 1988;34(3):361—6.

Appendix A. Conference discussion

Dr C. Schlensak (*Freiberg, Germany*): It's an innovative design. I wonder how it will be able to be put into clinical practice. As I understood, you put that device on top of the right atrial appendage. However, if you support the contraction of the right atrial free wall, it will not increase the output of the right atrium.

Secondly, what do you do about fibrillation? With the Maze procedure we want to convert patients to a sinus rhythm in order to prevent thromboembolic complications. What do you do about that?

Dr Tozzi: First of all, I'm sorry to disagree with you. I don't know why you say that we can put it just on the appendix. We can put this dome all around the right atrium. For the left atrium we are developing a figure-of-8 shape, another shape in order to squeeze the atrium. It's a very soft structure. You can adapt the structure to what meets your needs. So I disagree with you. It's not just the right appendix.

For the second question, this device doesn't contraindicate the Maze procedure. You can do the Maze procedure to restore sinus rhythm, to have a nice ECG, but basically, because of the Maze procedure, you are creating a labyrinth in the right and left atrium. You just lose the contractile function. If you are able to restore the pump, you can get rid of anticoagulation, because

the reason why you keep the patient on anticoagulation after the Maze procedure is because there is a recirculation of blood in the atria. If you use this device, you don't need any more anticoagulation because it's outside the heart and it moves both chambers, atrial chambers, so basically you do not have the recirculation.

Dr Schlensak: I'm very curious to see that in clinical practice.

Dr Tozzi: Me too.

Dr J. Horisberger (*Lausanne, Switzerland*): I understand that the nitinol needs a high temperature in order to contract. Is this going to be a problem when it's implanted? You talk about 37° in the bath here.

Dr Tozzi: It's a very tricky question, because one other point with this fiber is that in order to get movement, in order to have the actuator effect, you have to heat the fiber up to 70 °C. 70° is not compatible with humans. I mean you cannot put a device such as this in the body, because otherwise you risk cooking the heart. This is the reason why we isolated the fibers with silicone, and we tested them in the bath at 37°, so in physiologic conditions. On top of this, we should remember that the heart is a wonderful heat exchanger. It's able to cool down everything, of course everything that has a temperature above 37°. So preliminary results in the setup I showed you showed that the temperature on the top of the dome is just 39°, so 2° more than physiologic conditions, which is absolutely compatible with animal implantation. We just started the chronic animal study this month, and I will love to show you the results of this chronic animal study next year.

Dr J. Mueller (*Berlin, Germany*): I would like to talk about the temperature problem. You mentioned that the rate you can create with this material is 60 bpm. If you go up to a higher rate, the power consumption goes up too. Will this create more problems with the heat, with the temperature of the device? I calculated the device would have power consumption of more than 5 W. That is a lot for this little device, so it will heat up dramatically. Do you think the device will be able to pump with rates of 70 or 80 bpm or even higher rates?

Dr Tozzi: Thank you for your two questions. The first one, we can go up to 80. We already have done this. But it's not a matter of temperature, because the working temperature is always 70° for these fibers, so no matter the frequency, it keeps at 70°. But I definitely agree with you that if you go up with frequency, you need more energy. If you run your car at 180 km/h, you need more fuel. Of course the battery that will drive this device is not as small as the battery for pacemakers, because the amount of energy, as you just said, is two orders of magnitude bigger than a pacemaker battery. But we already identified special batteries that can run for at least 24 h, and they can be recharged transcutaneously with the TET system. I don't know if you remember the LionHeart. A few years ago we implanted the LionHeart with a TET system. Basically it's the same concept.

Dr Mueller: You end up finally with a TET system. You will not be able to implant a device the size of a pacemaker. This is impossible.

Dr Tozzi: You mean the volume of the battery?

Dr Mueller: Yes, because of the volume of the battery you need.

Dr Tozzi: The volume will be something around 250 cc, so a quarter of a liter.

Dr Mueller: For how long?

Dr Tozzi: For 24, 36 h. And the TET system today is 2 by 2 cm. They are not able to do this all over the world. We identified one company that is able to do this, a small one. I would love to give you all the technical details on this.