UNIVERSITE DE LAUSANNE

FACULTE DE BIOLOGIE ET DE MEDECINE

SERVICE DE CHIRURGIE CARDIO-VASCULAIRE

Chef de service: Professeur Ludwig K. von Segesser

CHIRURGIE VALVULAIRE PAR VOIE ENDOVASCULAIRE

THESE

Présentée à la faculté de biologie et de médecine de

L'Université de Lausanne pour l'obtention

Du grade de

DOCTEUR EN MEDECINE

par

Zhou Junqing

Médecin diplômé de l'Université de Zhejiang, Chine

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Licence, Diplôme, Doctorat décerné

Attention: *ces données servent de support à l'impression du titre.*

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Institut ou subdivision de la Faculté : *Service de chirurgie cardio-vasculaire*

☐ **Diplôme de médecin de l'Université**
☐ **Diplôme UNIL de médecin spécialiste**
☐ **Diplôme de spécialiste en pharmacologie et en toxicologie**
☒ **Doctorat en médecine**

Lieu et date : Signature du Doyen :

Lausanne, le 30 janvier 2004/sda *Prof. Patrice Mangin*

A renvoyer au Rectorat de l'Université de Lausanne, BRA Dorigny, 1015 Lausanne

Contents

Introduction

A valved stent is a combination of a biological valve and self-expandable endovascular stents — the former functions as a prosthetic valve, the latter allows fixation in an artery without suturing. Due to the specific design of this valve, it is possible to perfom valve replacement with endovascular catheter technique avoiding cardiac bypass and sternotomy. This technique is called either "endovascular transcatheter valve deployment" or "transluminal valve replacement". It is a promising treatment attractive to both the cardiac surgeons and patients.

Exciting results have been reported by pioneers over the last 40 years. In 1965, Davies H. deployed a catheter-mounted unicuspid valve above the aortic valve for the relief of aortic insufficiency [32]. In 1971, Moulpoulos S. et al designed a catheter-mounted aortic valve that consists of an umbrella shaped membrane with a controlling unit that unfolds the valve [33]. Andersen H.R. from 1989 to 1992 developed a new stent valve for transcatheter implantation in subcoronary and supracoronary porcine aorta. In his experiments, the stent valve consisted of a porcine aortic valve fixed on a steel wire stent skeleton [34,35]. In 1992, Pavcnik and colleagues placed via percutaneous transcatheter a self-expanding caged-ball valve in the aortic valve position in mongrel dogs [36]. In 1996, Moazami N. et al

constructed a trileaflet stent valve with bovine pericardium sewn on the stent[37]. In 2000, Bonhoeffer P. and Boudjemline Y. sutured a biological valve into a platinum stent and successfully performed a percutaneous pulmonary valve implantation in 5 sheep [38]. In the same year, Sochman J. et al designed a catheter-based aortic valve consisting of a stent cage and a prosthetic flexible tilting valve disc [39]. In 2002, Lutter G. et al deployed a valved stent with barbs in a porcine aorta [40].

However, all of these experiments demonstrate one or more problems. For example, the availability of various sizes of valved stents, the degree of patency and competency of the valve, the fixation of the valved stent in the artery, the paraprosthetic leakage and the uncertainty with valve function longevity. Furthermore, large sized valves are still difficult to deploy due to the large profiles and the large sized introducers required in comparison with the limited size of the peripheral access vessels. The avoiding of coronary orifice occlusion is still a difficulty with transluminal aortic valve replacement.

Hence, we attempted to develop a new valved stent to overcome these shortcomings and to explore the feasibility of deployment in the inferior vena cava (near right atrium), pulmonary valve and aortic valve position by transluminal technique without cardiac bypass.

1. History review

1.1 Valve surgery

1.1.1 Before the era of heart surgery

By the late 19th century: Much was known about cardiac anatomy, physiology, and pathology, but operating on the heart was still a taboo among surgeons.

15th and 16th century: Leonardo Da Vinci and Andreas Vesalius secretly dissected and drew the human heart. Leonardo Da Vinci described the anatomy of the mitral valve as resembling a "bishop mitre" and gave the 'Mitral Valve' its name.

1628: Experiments of William Harvey established the concept of blood circulation and marked the beginning of modern cardiology [1].

1902: Sir Lauder Brunton [2] suggested the possibility of performing a transventricular valvulotomy to treat mitral stenosis. He chose the ventricular approach on the grounds that the thicker wall of the left ventricle would be less prone to bleeding than the thinner left atrium.

1.1.2 The era of closed heart surgery

1912: Theodore Tuffier [3] successfully dilated a stenotic aortic valve of a 26 year-old patient by pushing the invaginated aortic wall through the valve with finger.

1923: Eliott Cutler and Samuel Levine [4] performed the first transventricular mitral valvulotomy at the Peter Bent Brigham Hospital on a 12 year-old girl using a special knife called a valvulotome.

1923-1928: Cutler [5] and Souttar [6] reported 10 cases of mitral stenosis surgery — only 2 patients survived these operations.

1948: Dwight Harken [7] and Charles Bailey [8] had arrived at the same surgical procedure from different backgrounds — one from Boston and World War II experiences and the other from Philadelphia and laboratory experiments. They performed their first transatrial commissurotomies to treat mitral valve stenosis only 6 days apart, Bailey on 10 June 1948 and Harken on 16 June. A breakthrough in valve surgery was made by both.

1.1.3 The era of open heart surgery

1953: John Gibbon [9] performed the first successful open-heart operation on a human patient using a heart-lung machine, initiating the era of open-heart surgery. The road to this triumph was fraught with setbacks, delays, and technical difficulties, yet Gibbon, with his perseverance, was able to pursue his dream to its end. He describes his first success as an "event that I hardly dreamed of in 1931," the year he was first inspired by the idea of extracorporeal circulation.

1954-1955: C.Walton Lillehei [10] began open-heart surgery to repair VSD and F4 with extracorporeal circulation (the cross circulation technique). He became one of the most important pioneers in this domain.

1956: Lillehei [11] On May 23, 1956, successfully performed an open mitral commissurotomy and aortic valvuloplasty in a 52-year-old man with mitral stenosis and combined aortic stenosis and incompetence. This was done with the use of a blood pump and the first bubble oxygenator.

1.1.4 The era of prosthetic cardiac valves

1.1.4.1 Ball valves

1951: Charles Hufnagel developed the first ball valve, a methacrylate ball contained in a methacrylate tube [12]. The ball sat snugly at the proximal end of the tube during diastole, and three bulbous pouches opened around the ball with its systolic position at the distal portion of the tube allowing blood to flow in one direction. In October 1952, the prosthesis was first clinically used in a patient with aortic insufficiency and was positioned into the descending thoracic aorta.

1955: In England, Judson Chesterman [13] performed the first reported mitral valve replacement. A caged ball valve designed by Clifford Lambourne of the Northern Hospital was placed into a 34-year-old man, who survived for only 14 hours.

1961: Starr and Edwards [14] reported the first four successful valve prostheses implanted in humans. Starr, a young cardiac surgeon at the University of Oregon, and Edwards, a mechanical engineer, designed the Starr-Edwards valve which consisted of an outer methacrylate cage, a Teflon-covered suturing ring, and a Silicone rubber ball (Fig1). The Starr-Edward Ball-Valve Prosthesis functioned well, and became one of the most successful and widely used prosthetic valves that continue today in clinical use.

Fig 1. Starr-Edwards Valve

1.1.4.2 Disc Valves

The physiological disadvantages of ball-valve prostheses were soon recognized. There was an inevitable low-grade but tolerable hemolysis from the serial impact of the ball on the cage. Also, the effective cross-sectional area of the valve orifice was not ideal because the poppet occupied a significant percentage of the orifice area. These considerations led to the development of disc prostheses.

The Bjork- Shiley tilting-disc prosthesis was first reported in 1969 [15]. This excellent initial prosthesis was developed by Viking Bjork at the Karolinska Institute in Stockholm, Sweden, working in conjunction with the Shiley Corporation in California. Several other disc prostheses were developed and used briefly (for example: 1963, Lillehei-Cruz-Kaster Tilting Disc Valve; 1966,Wada-Cutter Tilting Disc Heart Valve etc.), but the Bjork valve quickly became the disc valve of choice and was widely used for many years.

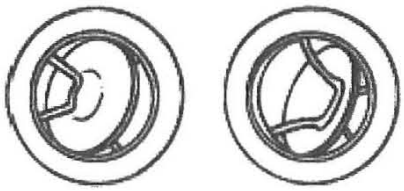

Fig 2. Bjork-Shiley tilting disc valve

In 1977, The St. Jude pyrolytic carbon disc heart valve become the first bileaflet valve to achieve major success. 20 years later, it remains one of the most popular and durable prostheses [16]. In 1976, Xinon C. (Chris) Posis, an industrial engineer, and Demetre Nicoloff, MD, a cardiovascular surgeon at the University of Minnesota, designed a floating hinge valve with the pivots near the periphery of the retaining annulas and with a central opening. It was named the St Jude valve, after being suggested by Mr Villafana who formed a company to support the research. The St Jude valve (Fig 3) was first used by Nicoloff on October 3, 1977 [17].

Similarly effective disc prostheses in current use include the Medtronic-Hall (1977), Omniscience (1978), Carbomedics (1986), ATS (1992), and others. There seems to be little physiological difference.

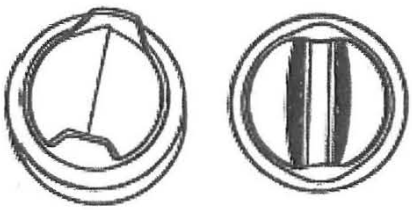

Fig3. St.Jude bileaflet disc valve

1.1.4.3 Biological valves (tissue valves)

The insolvable problem of thromboembolism with metallic prostheses quickly led to the investigation of tissue prostheses. Initially, different tissues in the human body were used, especially pericardium and fascia lata. Senning in Zurich, Switzerland, has extensive experience with aortic valves constructed with fascia lata[18]. It was quickly found that thromboembolism was much less common than with valvular prostheses.

In 1967, Donald Ross [19] in London, England, reported the ingenious concept of replacing the aortic valve with the patient's pulmonary valve (autologous tissue valve), and replacing the absent pulmonary valve with a homograft pulmonary valve. With the low pressures in the pulmonary artery, the durability of the homograft valve is better than in the aortic position. With the great advantage of freedom from anticoagulation drugs and good durability for at least 10 to 15 years, the operation has become increasingly popular throughout the United States and European countries in recent years, and is now often considered the prime choice when valve replacement is required in children. The availability of cryopreserved grafts for insertion in the pulmonary position has helped significantly. The "Ross switch" is now being increasingly used in young adults.

In 1962, Aortic homograft valves were initially used by Donald Ross [20]

in London, England, and also by Barratt-Boyes in Auckland, New Zealand, in 1962[21]. In 1987, Mark O Brien [22] reported from Brisbane, Australia, long-term experiences with cryopreservation. Their remarkable data suggest that a few cells remain viable even after 10 years of preservation. Cryopreservation is now generally accepted as the best method for long periods of preservation. However, the limited availability of homograft valves in many areas of the world has restricted their widespread use.

Once the low frequency of thromboembolism with tissue valves was recognized, heterograft valves were investigated because of the limited availability of homograft valves. Experiences in the 1960s with formaldehyde preserved valves were initially encouraging, but the valves failed in 2 to 3 years. Fortunately, a few years later it was discovered that glutaraldehyde was an excellent tissue preservative. This led Carpentier [23] in Paris to explore the use of porcine aortic valves preserved with glutaraldehyde. In contrast to all other experiences with different forms of heterograft preservation, the durability of glutaraldehyde preserved prostheses was dramatically better — more than 90% functioned satisfactorily 5 years after implantation, and 75% to 85% after 10 years. Bovine (calf) pericardial valves, initially used by Ionescu and others [24], are becoming widely used as well.

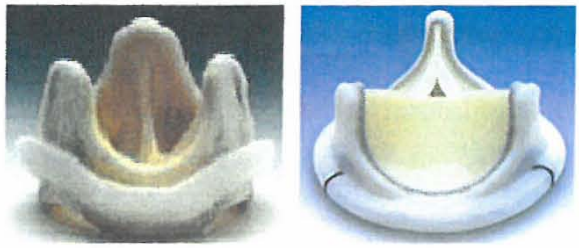

Fig.4 The porcine valve and the pericardial valve.

1.1.4.4 Mitral valve reconstruction (valvuloplasty)

All prosthetic valve have a number of problems: thromboembolism and the need for anticoagulation, the lifelong risk of endocarditis, and durability. Metallic prostheses now have excellent durability but require lifelong anticoagulation. Tissue valves often do not require anticoagulation but have limited durability, especially after the first 10 years of implantation. Both types of valves are equally vulnerable to endocarditis.

In the late 1960s and throughout the 1970s, the Carpentier team [25] in France and the Duran team [26] in Spain explored different forms of mitral valve reconstruction. Carpentier, one of the pioneers in this field, first demonstrated that thin mitral leaflet tissue could be excised and successfully sutured without dehiscence of the suture line when the heart began beating again. This was primarily accomplished with an annuloplasty, supported by a prosthetic ring, which removed tension from the suture line in the leaflets.

Over the subsequent years of clinical research [27], the impressive durability has gradually led to widespread adoption of mitral valve

reconstruction. The operation is especially attractive for young women of childbearing age. With excellent long-term durability, the operation is now performed at an early stage of significant mitral insufficiency, preferably before significant enlargement of the left atrium has developed and while the patient is still in sinus rhythm. Patients who remain in sinus rhythm after the operation remain strikingly free from thromboembolism and also have an extremely low frequency of endocarditis [27].

Fig. 5 The Carpentier-Edwards 'Physio'-annuloplasty ring

1.2 Endovascular stent graft

In 1969, Charles Dotter [28] first suggested the concept of the endovascular graft. He placed coilspring stent grafts into canine peripheral arteries, and at two years follow up, the grafts were found to be stenotic but patent.

In 1983 [29] Dotter developed the first transluminal expandable nitinol

stent graft, whilst Cragg was placing new endoprostheses in dog abdominal aortas via catheters. Short-term follow-up revealed minimal luminal narrowing and excellent vessel patency. He then used this device to treat abdominal aortic aneurysm (AAA) in dog models.

In 1986 Balko[30] et al. created artificial abdominal aortic aneurysms in dogs by enlarging aortotomies with Dacron patches. They inserted a polyurethane covered nitinol frame through a femoral artery cut-down into the canine aortas.

In 1991 Parodi[31] stitched a Dacron tube onto balloon expandable Palmaz stent and used this device to perform the first human stent graft implantation for treatment of AAA. Since then, many types of stent grafts have been developed, some balloon expandable, some self expanding, for example, Ancure Stent-Graft (EVT/Guidant, Menlo Park, CA), AneuRx Stent-Graft (Metronic, Sunnyvale, CA), Talent Stent-Graft (World Medical Inc.Sunrise, FL/Metronic, Sunnyvale, CA), Vanguard Stent-Graft (Boston Scientific Corp., Natick MA), Zenith Stent-Graft (Cook Inc., Bloomington, IN), Anaconda Stent-Graft (Sulzer Vascutech, Germany) etc. Each of these types has its advantages and disadvantages. The endovascular stent graft is now commonly used in the treatment of abdominal aortic aneurysm.

1.3 Endovascular valved stent

Many exciting results have been reported by pioneers, though there are still some distances to the summit of success.

In 1965, Davies H. reported a catheter-mounted unicuspid valve that was deployed above the aortic valve position for the relief of aortic insufficiency [32].

In 1971, Moulpoulos S. et al designed a catheter-mounted aortic valve consisting of an umbrella shaped membrane [33].

From 1989 to 1992, Andersen H.R. developped a stent valve for transcatheter implantation in subcoronary and supracoronary aorta in pigs. The stent valve consisted of a porcine aortic valve fixed on steel wire stent skeleton [34] [35].

In 1992, Pavcnik and colleagues placed a self-expanding caged-ball valve with a percutaneous transcatheter in the aortic valve position in mongrel dogs [36].

In 1996, Moazami N et al constructed a trileaflet stent valve with bovine pericardium sewn on the stent [37].

In 2000, Bonhoeffer P. and Boudjemline Y. sutured a biological valve into a platinum stent and successfully performed a percutaneous pulmonary valve implantation in 5 sheep [38]. In the same year, Sochman J et al designed a catheter-based aortic valve consisting of a stent cage and a prosthetic

flexible tilting valve disc [39].

In 2002, Lutter G. et al deployed a valved stent with barbs in the pig aorta [40]. Six of these valved stents were implanted in the descending aorta and 8 in the ascending aorta of anaesthetized pigs, 11 of which successfully implanted and demonstrated low transvalvular gradients (mean end-systolic gradient 5.4 ±3.3 mm Hg) and mild leakage. The coronary orifice, however, was problematic.

So far, approximately 7 authors have reported implanting valved stents in animals. One author reported that a valved stent was clinically implanted in a failed right ventricle to pulmonary artery conduit. Some problems still exist such as the limited open area of valved stents, fixation in the aortic position, avoidance of coronary orifice occlusion, paraprosthetic leakage and long-term valve function. In summary, the valved stent is still far from perfect and further explorations are necessary. We are therefore trying to develop a new valved stent to overcome the existing shortcomings and to explore the feasibility of deployment in the inferior vena cava, pulmonary valve and aortic valve positions.

2. In vitro evaluation of valved stents

2.1 Device construction

The following steps describe the procedure followed in constructing valved stents.

(1) A glutaraldehyde preserved bovine jugular xenograft with native valve (Venpro®) was cut 1.5cm above the valve and 1 cm below the valve, then the thick adventitia was trimmed to make the conduit much thinner. Two self-expandable Z nitinol stents were dismantled from an endovascular stent graft (Talent). The diameter of the stents were 30.25±0.15mm, the height were 15.42±0.34mm.

(2) With 7/0 prolene, two self expandable Z stents with a distance of 5-10mm were sutured outside of the trimmed conduit, ensuring that the inside native valve leaflets not be sutured or damaged, otherwise the valve would leak severely (Fig.6).

(3)Once the valved stent was prepared, its dimension was measured prior to its preservation in the glutaraldehyde solution. (Tab.1),

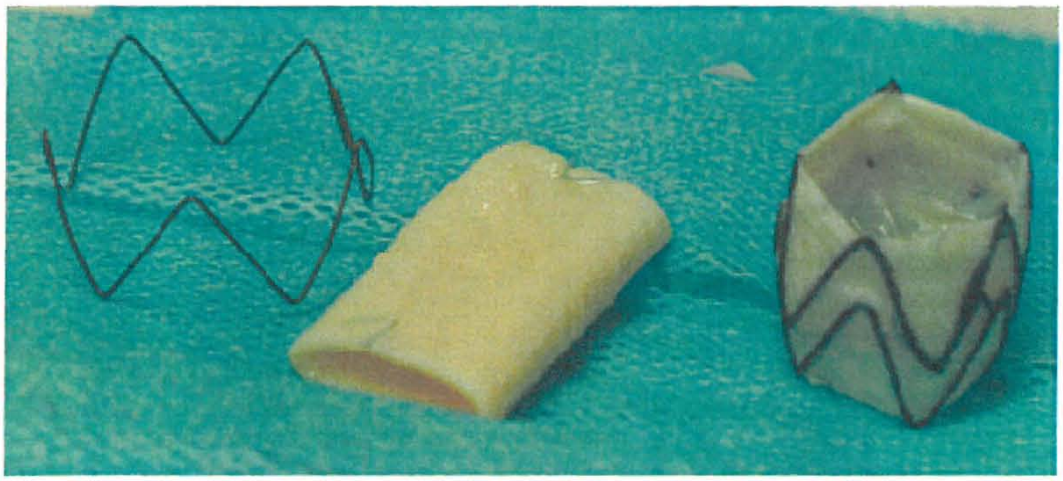

Fig. 6 The stent, xenograft and valved stent.

Tab.1 The measured sizes of the valved stents

No.	*Length (mm)*	*Inner diameter (mm)*	*Outer diameter (mm)*
1	21.6	21.0	26.4
2	23.7	21.5	27.6
3	23.1	20.5	26.0
4	23.2	22.1	26.1
5	23.2	22.2	26.1
6	23.7	22.5	26.8
7	23.4	21.8	25.2
Mean	23.1±0.7	21.6±0.7	26.3±0.7

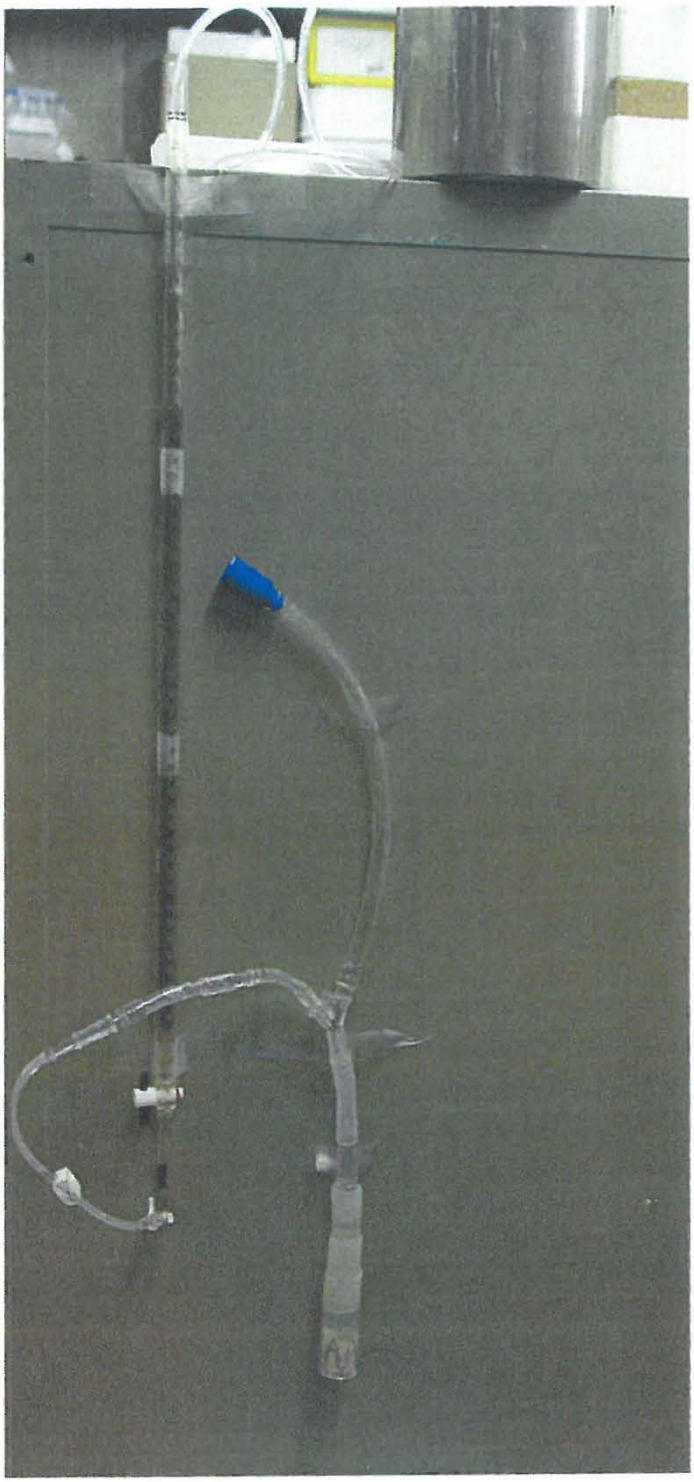

Fig. 7 Static leakage test

2.2 Device leakage test

2.2.1 Objective:

To test for valve regurgitation under static water pressure.

2.2.2 Materials:

- A water reservoir
- Calibrated glass tube,
- One silicone tube with an inner diameter of 20mm,
- A three-way stopcock,
- A measuring cylinder,
- 7 Glutaraldehyde preserved valved stents.

2.2.3 Method:

The valved stented was tested for leakage by subjecting it under a pressure of 61cm of water (or 45mmHg). This was achieved by connecting silicone tube to the water column (refer to fig 7). The valved stent was compressed and deployed the inside of the silicone tube by hand. Leakage from the valved stent was confirmed by measuring the rate of water leak below it. The silicone tube was used in order to recreate the compliance characteristic of the vessel.

2.2.4 Results:

In vitro static performance testing of the 7 valved stents showed a mean leakage rate of 32.5±12.4 ml/min when subjected to a simulated afterload of 45mmHg, (See Tab.2). The valved stent was fixed well in the silicone tube without migration.

Tab. 2. The leakage test under 45mm Hg water column pressure

Valved stent	1	2	3	4	5	6	7	Mean
Leaking rate (ml/min)	35.3	47.6	18.1	28.9	50.1	23.8	23.6	32.5±12.4

2.2.5 Conclusion:

The new valved stent has little regurgitation and no migration under a static pressure of 45mmHg,

2.3 Mock loop simulation test

2.3.1 Objective:

To test the valved stent in a simulated dynamic circulation in vitro.

2.3.2 Materials and methods:

2.3.2.1 Materials and setup of the Mock loop

Mock loop was set up according to Fig 8 so as to form a closed circulation. The picture of this experiment was showed in Fig 9. Materials were described as following.

- A pulsatile pump (Bi-ventricular Support system 5000, Oberdorfstrasse11-13, CH-6342, Baar ZG).
- Several connecting tubes Ø1/2
- A silicone tube with an inner diameter of 18mm
- Two 5F Millar pressure transducer catheters (mpc-500, Houston, Texas, USA.)
- Data recording system
- Intravascular ultrasound (Clearview, Boston Scientific Corporation, Sunnyvale, California)

- 7 Valved stents
- A 24 French stent introducing catheter with a piston inside (self-made).
- A reservoir
- Two gloves were regarded as the compliance chamber that simulated the elastic resistance of a blood vessel.

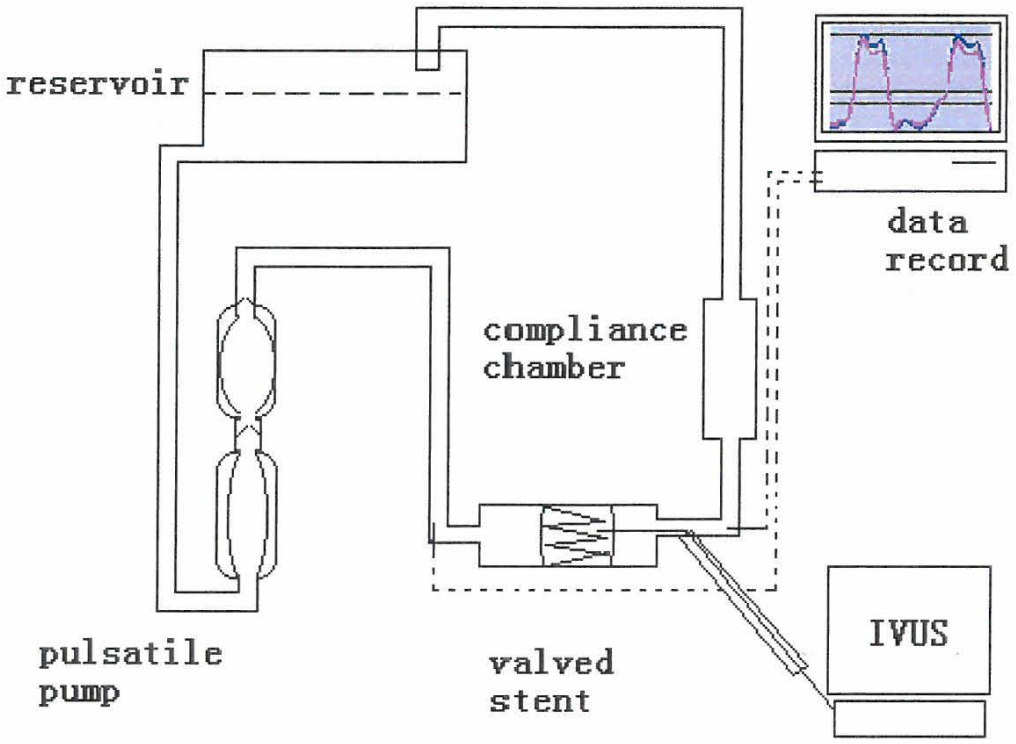

Fig 8. Schematic mock loop

Fig 9. Mock loop device and the dynamic test of the valve

2.3.2.2 Circulation of the mock loop

The pump ran at a flow rate from 2 to 5 litres/min, with a systolic pressure between 87 and 144 mmHg.

2.3.2.3 Deployment of the valve

The valved stent was deployed into the silicone tube (diameter = 18mm) in the following fashion.

- One plastic tube was first connected to the silicone tube by a "Y" connector.
- The valved stent was loaded into the 24 F introducing catheter by hand cramping.
- The introducing catheter now containing the valved stent was inserted into the silicone tube via the plastic tube. Once the introducer was in position, the valved stent was released by withdrawing the outside catheter while holding the inside piston in place. After deployment, the introducing system was withdrawn. The distal end of the plastic tube was connected to a hemostatic valve permitting the IVUS catheter to go in from here.

2.3.2.4 Measurement

The Millar catheter was used to measure the pressure on both sides of the valve for estimation of valve gradient.

The Intravascular ultrasound (IVUS) catheter was inserted from the

hemostatic valve to the valved stent to measure valvular function.

2.3.3 Results

2.3.3.1 Peak systolic gradient across the valve

The peak systolic gradient was 6.42 ± 2.75 mmHg at a mean flow rate of 4.32 ± 0.97 L/Min. In Fig 10, the gradient is the difference between the two curves.

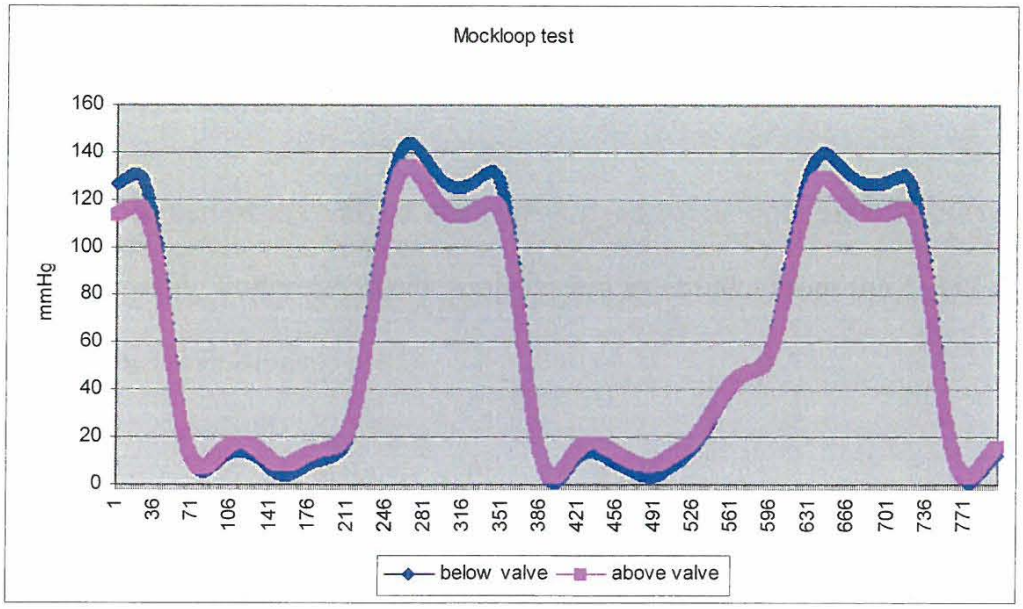

Fig. 10 The pressure curves recorded by the computer.

2.3.3.2 The open and closed area of the valve.

The open area of the valved stent is 204.8±10.5mm^2 and the closed area is 0 mm^2 (see Fig 11). From the IVUS images, the two leaflets of the valve are seen to open and close completely. The valve was well fixed in the silicone tube without any migration.

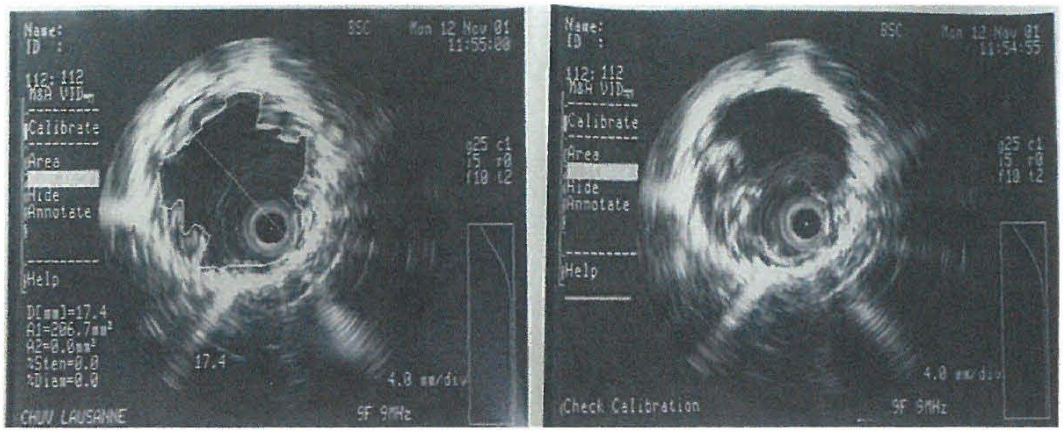

Fig 11. IVUS views of the valve in open (left) and close (right) state.

2.3.4 Conclusion:

The competence of the valved stent (as judged by its opening and closure) tested favorably under our mock loop system as evident from the IVUS and Miller catheter findings.

3. In vivo evaluation of valved stents

3.1 Inferior vena cava

3.1.1 Background:

Despite the successful introduction of the extracardiac total cavo-pulmonary connection [41] [42] in order to improve the surgical results in "functionally" univentricular hearts [43], the conversion of a failing conventional total cavo-pulmonary connection (modified Fontan procedure) can still be necessary, because of different anatomical as well as functional reasons, all of them leading to systemic venous hypertension [44] [45] [46].

One of the main reasons for the failure is the elevated venous pressure in the right atrium and coronary sinus, with the subsequent development of supra-ventricular arrhythmias and myocardial failure. Gomez-Jorge J. [47] has percutaneously deployed a valved bovine jugular vein (which was mounted to a self-expanding nitinol stent) in the inferior vena cava of swine for the treatment of systemic venous valve insufficiency. Hence, we speculated that the insertion of a valve in the inferior vena cava, by creating a pressure gradient across the valve, could also reduce the right systemic venous hypertension and congestion due to the incompetent tricuspid valve or

failing total cavo-pulmonary connection, and therefore might become an alternative option in case of failing total cavo-pulmonary connection or regurgitation of the tricuspid valve.

This experiment study has been designed to evaluate the feasibility of the off-bypass (transluminal) implantation of a self-expandable valved stent in inferior vena cava.

3.1.2 Materials:

Materials used were as follows:

- 5 Bovine jugular xenograft containing native valves.
- 10 Rings of nitinol Z stents, 7-0 Prolenes.
- 2.5% Isoflurane for general anaesthesia.
- Heparin.
- Self-made stent delivery system.
- X-ray machine (Telam C comet)
- IVUS (Clearview, Boston Scientific Corporation, Sunnyvale, California).
- Machine for anaesthesia (Drager sulla 909v).
- Oximeter (Ohmeda4700).
- ECG and Pressure recording system (HEWLETT PACKARD Model 88s).

3.1.3 Methods:

3.1.3.1 Valved stents preparation

The valved stents were constructed as described in Chapter **2.1**, after the tests of leakage and mock loop, they were sterilized and stored in glutaraldehyde solution.

3.1.3.2 Mounting the valved stent to the stent delivery system

The delivery system consists of one guide wire, an interior piston and an exterior Teflon sheath (27 F), as shown in Fig. 12. The valved stent was hand crimped into a small profile and mounted inside the Teflon sheath making sure that the valve open direction was toward the introducer tip (After being deployed in the inferior vena cava, the valve should open toward the heart).

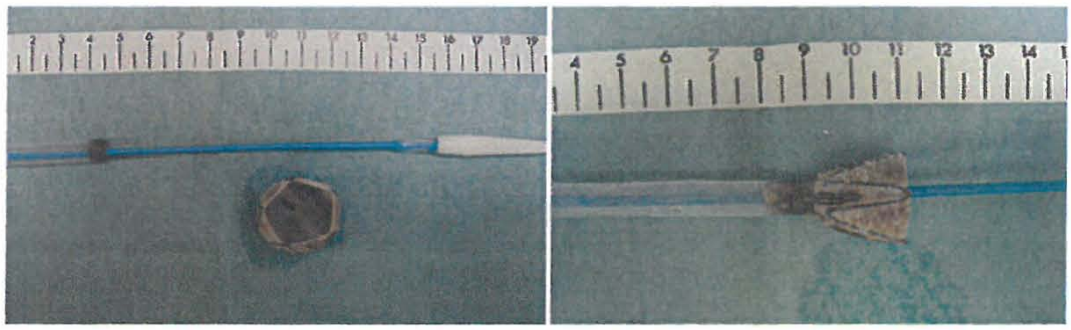

Fig. 12 The loading of the valved stent into the delivery system

3.1.3.3 Valved stent deployment in the inferior vena cava

5 pigs weighing 80.5± 5.0kg, received care in compliance with the

Principles of Laboratory Animals" formulated by the National Society of Medical Research and «the Guide for the Care and Use of Laboratory Animals» prepared by the Institute of Laboratory Animal Resources and published by the National Institute of Health (NIH publication 85-23, revised 1985). The protocol was approved by the Institutional Committee on Animal Research. All the data were expressed as mean± standard deviation.

After general anaesthesia with tracheal intubation and mechanical ventilation (ketamine 22mg/kg and atropine 0.8mg/kg intramuscularly, Thiopental 15mg/kg intravenously for induction, Isoflurane 2.5% for maintenance anesthesia), under the continuous monitoring of electrocardiogram, arterial pressure and oxygen saturation, we made an oblique incision in the lower left quarter of abdomen, reached the inferior vena cava by retroperitoneal approach, a purse string sutured with 6-0 prolene, a needle punctured, a guide wire inserted, a short 9-F sheath was introduced.

Heparin (100IU/kg) was administered intravenously. The intravascular ultrasound (IVUS) Catheter (6F, 12.5MHZ transducer) was inserted, the length and the diameter of the inferior vena cava segment between liver and right atrium were measured.

At the inferior vena cava 2 cm below the right atrium, we marked this site with a needle on the body surface under the guidance of fluoroscopy regarding it as the prosthesis implantation site. Then a superstiff guide wire

was introduced and the 27F delivery introducer loaded with the valved stent was advanced along the guide wire, until the stent was located at the desired site, with the sheath pulled back while the piston held in place, the valved stent was correctly deployed. Blood pressure, ECG, and satO2 were monitored.

3.1.3.4 Measurement

A high fidelity tip mounted Millar pressure transducer system was used to measure the pressure proximal and distal to the valve, and IVUS was used to assess the valve function. The animals were electively sacrificed to check the adequate position of the stent mounted valve, as well as its deployment and anchorage.

3.1.4 Results:

(1) During the experiment, the vital signs were stable, all pigs survived the manipulation. Intra-vascular ultrasound showed a mean length of the inferior vena cava between heart and liver was 7.9 ± 0.3 cm (range 7.5 to 8.4 cm) and the internal diameter was 20.4 ± 1.6 mm (range 18.21 to 22.56mm).

(2) The mean pressure gradient across the self-expanded stent mounted valve was 1.0 ±0.5 mmHg (range 0-2mmHg).

(3) IVUS showed partial closure of the valve during expiration (reduction of the mean valve effective orifice from 148.5±56.7 mm2 to 81.5±55.3 mm2 (Fig.13). Almost complete valve closure occurred only during deep breaths (Fig.14) (video in CD-rom).

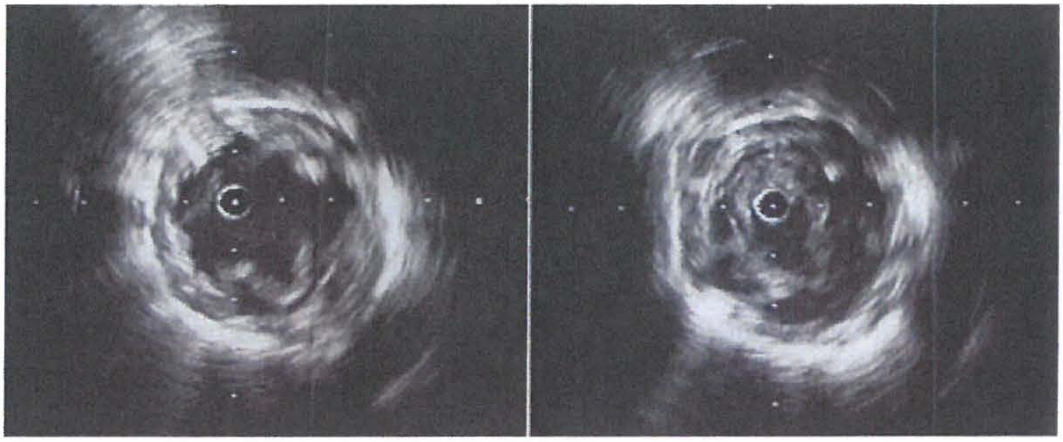

Fig. 13. IVUS showed the valve well opened (right) but closed partially (left)

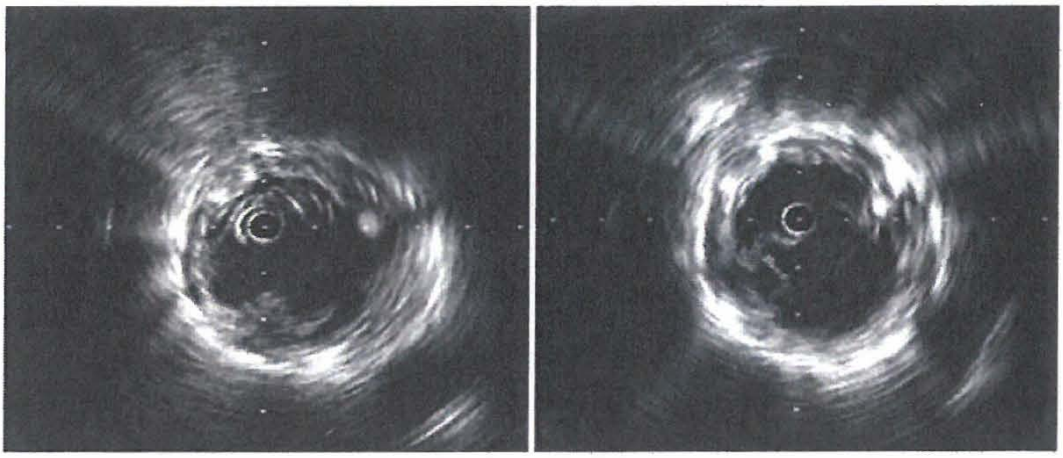

Fig 14. IUVS showed the valve closed completely only during deep breaths (right in an open state, left in a closed state).

(4) Macroscopic view: In all animals autopsy confirmed the adequate position of the valved stent at about 2cm proximal to the right atrial junction and the supple valve leaflets without any damage, in 2 of 5 cases we found small thrombus on the leaflets.

3.1.5 Discussion

The idea of an off-bypass or percutaneous approach to the treatment of cardiac valve problems has been proposed by several authors. The reported experimental studies demonstrated the feasibility of implantation of a valved stent in the pulmonary valve position [38] and deployment of a catheter-based valve in the descending aorta or aortic valve position [35,36,37,39,40], while another experimental study tested the deployment of a stented valved bovine jugular vein in the inferior vena cava or in the external iliac vein as a potential treatment of venous insufficiency [47].

The first goal of our study was to evaluate the feasibility of mounting a biological valve on a self-expandable stent: In our in vitro test, both the static leakage test and the dynamic pulsatile mock loop test, demonstrated excellent competency, effective open orifice and integrity of the valved stent. In the in vivo acute study, though there was not enough reflux in the vena cava of a healthy swine heart, we were still able to view the opening and

partial closure of the stent valve with complete closure being observed during deep breaths. This device might represent an advantage over the currently available biological valves mounted on platinum stents that are balloon-expanded but not self-expanding [38] [48].

The second goal of our study was to demonstrate the feasibility of the off-bypass implantation of the self-expandable valved stent between inferior vena cava and right atrium. Our study showed that the internal diameter and the length of the inferior vena cava were 20.4±1.6mm and 7.9±0.2cm(body weight 80.5± 5.0kg), which are suitable for implantation of the valved stent whose outer diameter and length are 26.3±0.7mm and 2.3±0.1cm. Our measurements of inferior vena cava, performed with the intra-vascular ultrasound, provided results in agreement with the values reported with CT scans on human beings of 2 and 19 year-old groups, where the mean diameter of the inferior vena cava varied from 13.8mm(range 6.1 to 21.6mm) at an age of 2 years old to 28.4 mm (range 20.5 to 36.4mm) at an age of 19 years old [49].

Our acute experimental observations confirmed that the retro-peritoneal approach allowed for an easy introduction of the valved stent via the inferior vena cava or the iliac vein, as well as its deployment in the inferior vena cava between the right atrium and the liver. This approach has almost no limitation for the sizes of all kinds of vessel stents and delivery introducers, therefore has advantages over the percutaneous approach that is limited by

the calibre of the femoral vessels, which will consequentially limit the sizes of stents and introducers available.

We also have the advantages of allowing for a much larger biological valve to be implanted – up to 22mm of internal diameter. This size has been demonstrated in our clinical practice to be adequate not only for the entire systemic venous return but also for the pulmonary blood flow, even in patients up to a body weight of 91kg [50].

The last goal of our experiment, to evaluate the potential application of the stent-valve for patients with failure of a total cavo-pulmonary connection, was feasible, but has not been completed. We demonstrated the complete opening of the valve but only a partial closure, which became complete only during deep breaths with small hemodynamic pressure gradients across the valve. Therefore, our speculation regarding the potential clinical application remains open, requiring additional experimental chronic studies in animals with artificially induced right heart failure (for example, through damage to the tricuspid valve).

The last advantage proved by our experimental study was the possibility of performing both the implantation and the evaluation of the self-expanding valved stent with intra-vascular ultrasound as a diagnostic tool. As already shown for the endovascular treatment of the aortic aneurysm [51], the off-bypass implantation of valved stent does not require angiography or the utilization of any contrast medium.

The shortcomings of this study were that the experimental animals were healthy without any reflux from tricuspid regurgitation or right ventricle-pulmonary conduit insufficiency, this model doesn't completely represent the diseased state, as follow-up, we will design a model with high right atrial pressure induced by tricuspid damage to test the valved stent.

3.1.6 Conclusion:

a) The in vitro and in vivo experiments confirmed the feasibility of potential application of the self-expanding valved stent implanted off-bypass (transluminal) in the inferior vena cava for late conversion of failing total cavo-pulmonary connection.

b) The functioning of the valved stent is limited in the inferior vena cava position by the absence of right heart failure.

c) Intravascular ultrasound allows for adequate implantation and evaluation.

3.2 The pulmonary valve position

3.2.1 Background

Endovascular transcatheter valve deployment may provide a good alternative to cardiac surgery. A number of these techniques for replacing heart valves have been experimentally developed over the last 40 years. In 1965, Davies H. reported a catheter-mounted unicuspid valve to be deployed above the aortic valve position for the relief of aortic insufficiency [32]. In 1971, Moulpoulos S et al designed a catheter-mounted aortic valve consisting of an umbrella shaped membrane with a controlling unit of unfolding valve [33]. Andersen H.R. from 1989 to 1992 developed a new stent valve for transcatheter implantation in subcoronary and supracoronary aorta in pigs, the stent valve consisted of a porcine aortic valve fixed on steel wire stent skeleton [34,35]. In 1992, Pavcnik and colleagues placed a self-expanding caged-ball valve by percutaneous transcatheter in the aortic valve position in mongrel dogs [36]. In 1996, Moazami N et al constructed a trileaflet stent valve with bovine pericardium sewn on the stent [37]. In 2000, Bonhoeffer P and Boudjemline Y. sutured a biological valve into a platinum stent and successfully performed a percutaneous pulmonary valve implantation in 5 sheep [38]. In the same year, Sochman J et al designed a catheter-based aortic valve consisting of a stent cage and a prosthetic

flexible tilting valve disc [39]. In 2002, Lutter G et al deployed a valved stent with barbs in porcine aorta [40].

All the experiments still have problems. For example, the various sizes of valved stent, the patency and competency of the valve, the introducer size is limited to the size of the peripheral access vessels, the avoiding of coronary orifice occlusion is still difficult, the paraprosthetic leakage and long term valve function is not clear.

In patients with congenital cardiac malformations (such as tetralogy of Fallot, pulmonary atresia etc) who had surgical pulmonary valvectomy or transannular pulmonary patches or right ventricle-pulmonary conduit, long lasting pulmonary insufficiency can result in right ventricular dilatation and severe right ventricular failure, even the development of arrhythmias or sudden death [52] [53] [54] [55]. It will be a good alternative to replace the old valve with a new prosthetic valve that can be easily deployed without cardiac bypass, avoiding the risk of reoperation.

In this report, we designed a valved stent for testing its feasibility in pulmonary position, which could be deployed by transcatheter via right ventricular approach without bypass.

3.2.2 Materials

- 6 Pigs weighing 55.6± 6.0 kg.

- 6 Bovine jugular xenograft containing native valves.
- 12 Rings of nitinol Z stents.
- 2.5% Isoflurane for general anaesthesia.
- Self-made stent delivery systems.
- X-ray machine (Telam C comet).
- IVUS (Clearview, Boston Scientific Corporation, Sunnyvale, California).
- Machine for anaesthesia and ventilation(Drager sulla 909v).
- Oximeter (Ohmeda4700).
- ECG and Pressure recording system (HEWLETT PACKARD Model 88s).
- IVUS (SEQUOIA 512, Acuson corporation, CA94039-7393, USA).
- Swan-Ganz Oximetry Catheter (Baxter Edwards).

3.2.3 Methods

3.2.3.1 Valved stents preparation

The valved stents were constructed as described in Chapter **2.1**, only those passed the tests of leakage and mockloop were sterilized and stored in glutaraldehyde solution.

3.2.3.2 Valved stent mounted to the stent delivery system

The delivery introducer system is the same as used in the inferior vena cava (See Fig12), the valved stent was rinsed in saline solution three times, each time for 5 minutes, then hand crimped into a small profile and mounted inside the Teflon sheath (24F), to ensure that the valve open direction is also toward the introducer tip (because after it is deployed in the pulmonary trunk position, the valve should open toward the bifurcation).

3.2.3.3 Valved stent deployment in the pulmonary position

6 pigs weighing 55.6 ± 6.0 kg, who received care in compliance with the "Principles of Laboratory Animals" formulated by the National Society of Medical Research and the Guide.

The swine were supine, the superficial vein of the left ear was cannulated to build a line for the transfusion of Ringer's solution. With tracheal intubation and mechanical ventilation, general anaesthesia was induced by ketamine 22mg/kg, atropine 0.8mg/kg intramuscularly, Thiopental 15mg/kg intravenously, maintained by Isoflurane 2.5%. Continuous monitoring of electrocardiogram, arterial pressure (from a catheter in the right carotid artery), central venous pressure and oxygen saturation was performed.

First, a midline vertical incision (6-8cm) was made in the neck, the right carotid artery and the vein were found, then catheterized – one for arterial

pressure measurement and the other for the Swan-Ganz catheter and the measurement of the central venous pressure. A midline sternotomy was made (16-18cm), the pericardium was opened and suspended, two purse-string sutures on the right ventricle with 6-0 prolene, then heparized (100U/kg intravenously). Via a needle puncture, a guide wire was inserted and a short 9-F sheath was introduced and fixed (see next page Fig. 15).

Second, a stiff guide wire was introduced into the pulmonary artery, the catheter transducer (6F, 12.5MHZ) of the intravascular ultrasound (IVUS) was inserted over it, the original pulmonary valve identified, the diameter of the pulmonary trunk and the length were measured. Under the intravascular ultrasound and the fluoroscopy, the valve position and the upper and lower end of the trunk were marked by three needles on the body surface to assist the precise deployment.

Third, the catheter of the IVUS was taken out, the stent delivery introducer was advanced over the guide wire up to the original pulmonary valve position. The valved stent was slowly released and deployed at the position of pulmonary valve by pulling the sheath back while holding the piston in place, then the delivery system was taken out, the duration of this manipulation was 3-4 minutes. The original valve was thus compressed against the vessel wall and lost function while the implanted valve began functioning.

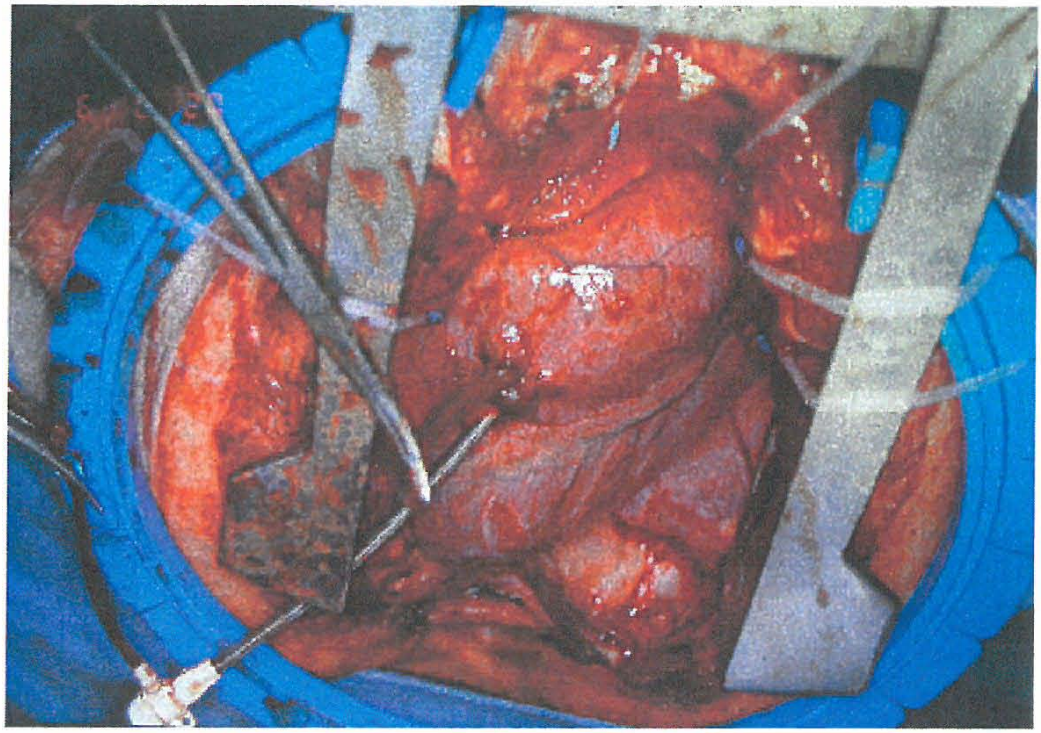

Fig 15 a short 9-F sheath was introduced in the right ventricle.

3.2.3.4 Measurements

First, the 6F transducer of the IVUS (Clearview, Boston Scientific) was reintroduced to the valve position to observe valvular opening and closure, recorded on videotape.

Second, an 8F transducer of the other IVUS with Doppler (Acuson Corporation) was placed onto the anterior surface of the pulmonary artery where the valved stent could be felt, to observe the blood flow across the valve as well as regurgitation or any paravalvular leakage.

Third, a 5F catheter (Cook Inc) was introduced over the guide wire

untill below the valve, then above the valve. Systolic and diastolic pressures across the valve were measured. Via the right carotid vein, a 7.5F Swan-Ganz catheter was advanced into the pulmonary artery and cardiac output was measured.

The animals were electively sacrificed to assess the adequate positioning of the stent mounted valve, as well as its deployment and anchorage.

All the data were expressed in Mean±SD. A paired Student T test was used for statistics, $P<0.05$ was regarded as a significant difference.

3.2.4 Results

3.2.4.1 General state

All the six cases survived the implantation of the valved stents without complication, the mean carotid arterial pressure, the saturation of oxygen and the central venous pressure before and after the implantation have no differences statistically ($P_1=0.45$, $P_2=0.57$, $P_3=0.64$), during the procedure 2 cases had temporal superaventricular tachycardia.

3.2.4.2 The diameter and length of the pulmonary trunk

Measured by the IVUS, the diameter of the pulmonary artery at the

valve level, was 21.7±1.6 mm, the length was 4.5±0.6mm.

3.2.4.3 The transvalvular gradient and the cardiac output

The Swan-Ganz catheter and the Cook catheter demonstrated the transvalvular peak systolic pressure gradient was 4.5±3.1 mmHg (range 0 to 7 mmHg) at a mean cardiac output of 3.03±0.05L/Min.

3.2.4.4 The function of the valved stent under ultrasound evaluation

The IVUS demonstrated the complete opening and closure of the valve with a large effective open area. The mean valve orifice area was reduced from 315.08±54.13 mm^2 in the open state to 0 mm^2 in the closed state (see Fig.16 and video in CD-rom).

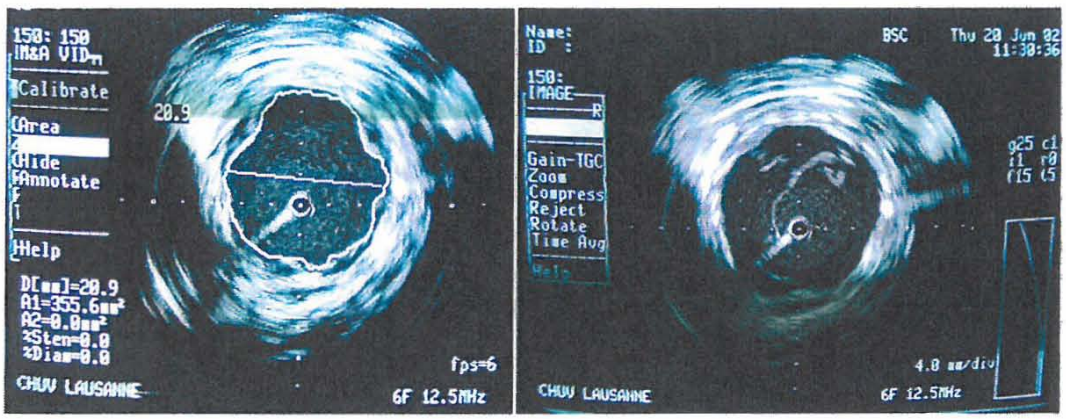

Fig.16 The completely opened (right) and closed (left) state in pulmonary artery, the effective open area was 355.6 mm^2.

3.2.4.5 Regurgitation and paravalvular leakage

The inoperative Color Doppler ultrasonograghy by the IVUS showed no regurgitation and no paravalvular leakage in 6 of 6 cases (see Fig17).

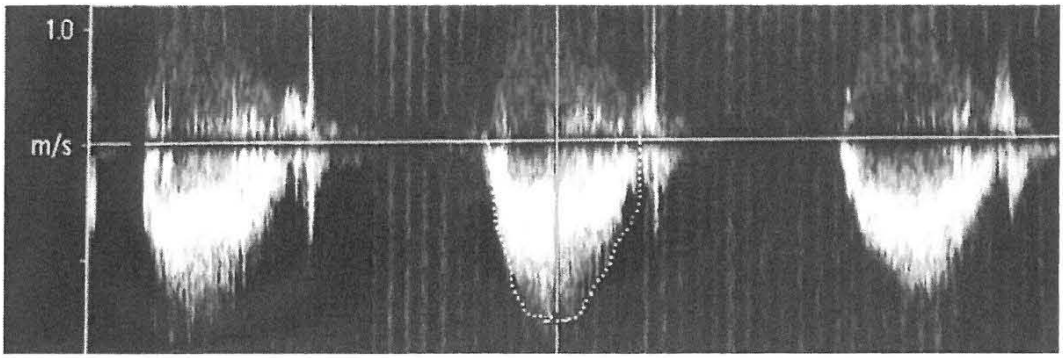

Fig 17 Doppler ultrasound showed no regurgitation or paravalvular leakage in diastole

3.2.4.6 Macroscopic analysis

Autopsy confirmed in 4 cases that the valved stents situated adequately in the original pulmonary valve position. In one case the valved stent was found between the original valve and the bifurcation. In another case the valved stent was found in the left pulmonary artery. Neither thrombus nor valve leaflet damage were found in these cases (see Fig18 and Fig 19).

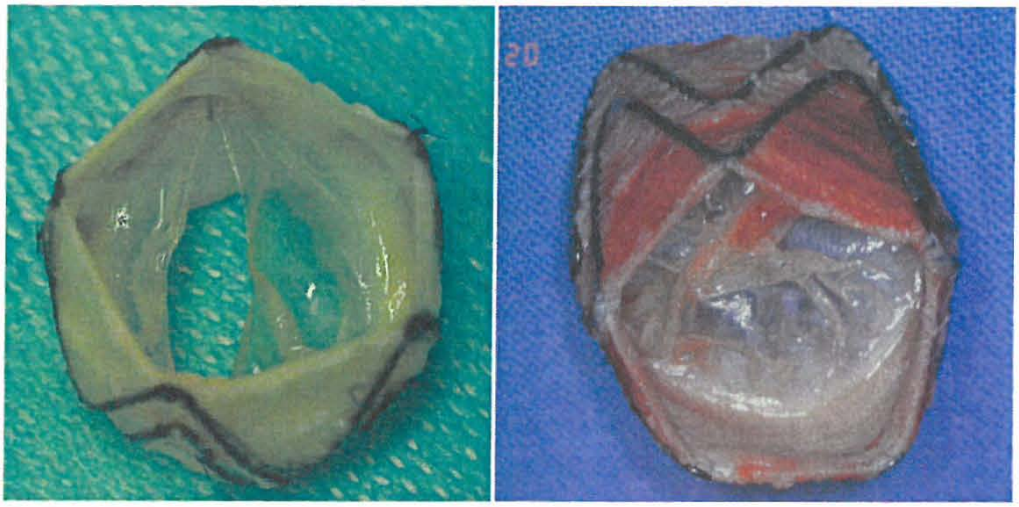

Fig 18 Showed the valved stent had little change before implant (right) and after explant (left).

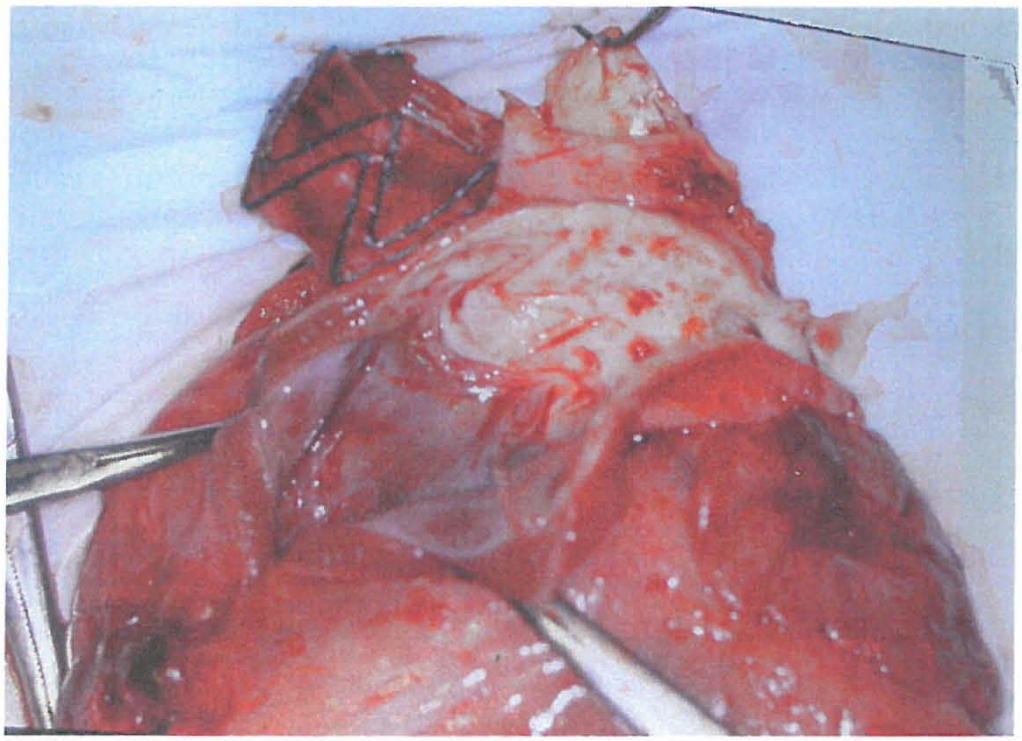

Fig. 19 The autopsy demonstrated the accurate implantation and the imprint of the Z stent against the pulmonary artery wall.

3.2.5 Discussion

Clinical value

In many congenital cardiac malformations (such as tetralogy of Fallot, pulmonary atresia etc.) that have had surgical pulmonary valvectomy, transannular pulmonary patches or right ventricle-pulmonary conduit, pulmonary insufficiencіy occurrs commonly. This can result in right ventricular dilatation and severe right ventricular failure after several years, necessitating reoperation [54] [64]. The use of extracardiac conduit between the right ventricle and the pulmonary artery has allowed for the correction of many complex cardiac lesions [56]. However, because of calcification and degeneration, progressive obstruction and regurgitation become the most frequent reasons for surgical reintervention [57]. Conduit stenting can palliatively relieve conduit stenosis and postpone surgical conduit replacement [58] [59] but this technique leads to more severe pulmonary insufficiency [60]. Our study demonstrates that the new design of valved stent could solve this problem by correcting the obstruction as well as the insufficiency. It can also be used in patients with simple pulmonary regurgitation caused by previous interventions. This has also been confirmed by a previous report [61].

Advantages and disadvantage of the right ventricular approach

(1), there are few limitations for the size of the delivery introducer

system, even a 45F introducer can be inserted easily. Our 26mm (inner diameter 22mm) valved stent has a profile of 8mm after hand crimping, and can be easily delivered by a 24F introducer. Therefore this approach leaves room free for even larger valved stents to be implanted without difficulty.

(2), the valved stent can be more easily deployed with direct hand guiding outside the heart and the pulmonary artery, especially practical for patients who have anatomical changes caused by previous operations.

(3), the Doppler ultrasound evaluation is much easier and clearer, because the transducer can be placed directly upon the pulmonary arterial wall where the valved stent is located.

The shortcoming of this procedure is that it is more invasive than the percutaneous femoral approach, which should be considered in humans since their femoral vessels (7-11mm diameter) are wider.

Advantages of the valved stent

Patency - This valved stent boasts a large inner diameter (20.5-22.5 mm). Its systolic open valve area is 315.08±54.13 mm^2, that is high patent for any human adults, and has advantages over the 18mm pulmonary valved stent available [62]. The peak systolic gradient across the valve is 4.5±3.1 mm Hg at a mean cardiac output of 3.03±0.05L/Min, this reveals that there is no stenosis of the valve. This result is in agreement with the gradient reported by Lutter G. [40] 5.4±3.3 mm Hg across a valved stent in the descending aorta

position).

Competency - In the diastolic state, the valve closed completely without regurgitation showing the competency of this valved stent.

Approximation- No paravalvular leakage was found in this study, which demonstrates good wall contact of the valved stent with the outer vessel.

Fixation- Because of its outer diameter of 26.3±0.7 mm and the enough extension force of the Z stents, when implanted in the 21mm pulmonary artery it was well fixed without any migration.

Design pitfall

During the deployment, there were two valved stents not placed in the exact original pulmonary valve position, one was between the original valve and the bifurcation, the other was in the left pulmonary artery, that was because of the short and sharply curved pulmonary trunk (4 cm) which limited the free movement of the delivery introducer, also because of the tendency to jump of the expandable Z stents when released. This can be controlled by traction on the suture line, which was previously attached to the Z stent [63], or by increasing the numbers of Z stents so as to prolong the valved stent.

IVUS utility

The intravascular ultrasound was practical in both implantation and evaluation of the self-expanding valved stent in the pulmonary position. We

did not need angiography nor the utilization of any contrast medium.

Shortcomings of this experiment and future research direction

This is an acute experimental study, many important questions remains to be answered about the valved stent: long-term durability of the valve, risks of neo-intimalization, thrombogenicity, calcification and dislogement. Another possibility will be the implantation of this valved stent in the aortic valve position, so in our next step, we will test the valved stent in a chronic experiment in the pulmonary position and test it in acute experiment in the aortic valve position.

3.2.6 Conclusions

a) The experiment confirmed the feasibility of off-bypass implantation of the new self-expandable valved stent in the pulmonary valve position.

b) The off-bypass surgical approach allows for valved stent implantation of large size valved stents.

c) The functioning of the valved stent is adequate in pulmonary position.

d) IVUS allows for adequate implantation and evaluation without need for contrast medium or more invasive diagnostic procedures.

Conclusions

From the above several experiments, our conclusions are as follows:

1. In vitro and in vivo experiments confirm the satisfactory patency, competency, and durability of the home made self-expandable valved stent.
2. In vivo experiments confirm the feasibility of potential application of the self-expandable valved stents implanted off-bypass in the inferior vena cava for late conversion of failing total cavo-pulmonary connection.
3. In vivo experiments confirm the feasibility of the valved stents implanted off-bypass in the pulmonary position as an alternative treatment for pulmonary valve insufficiency or insufficiency of the valved conduit between the right ventricle and the pulmonary artery.
4. Intravascular ultrasound allows for the adequate implantation and evaluation of the valved stent both in the inferior vena cava and the pulmonary position.

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Résumé

Objectif:

Evaluer un nouveau stent valvé auto-extensible, monté sur cathéter, qui permet d'être implanté par voie transventriculaire en position pulmonaire ou par voie endovasculaire dans la veine cave inférieure, sans circulation extracorporelle.

Méthodes:

Une xénogreffe d'une veine jugulaire bovine de 22mm de diamètre intérieur, est traitée à la glutaraldéhyde et ensuite adaptée et montée sur deux stent de type Z en nitinol.

Dans un premier temps des tests statiques in vitro sont réalisés par l'intermédiaire d'une colonne d'eau développant une pression de 45mmHg sur les feuillets de la valve. L'essai dynamique in vitro du stent valvé a été réalisé sur un circuit hydrodynamique pulsatile sous contrôle sonographique intravasculaire (IVUS).

Des évaluations in vivo ont été exécutées dans cinq modèles porcins aigus (poids corporel moyen 80.5±5.0 kilogramme, allant de 74-85kg). Le diamètre interne et la longueur de la veine cave inférieure ont été mesurés avec l'IVUS. Le stent valvé auto-extensible est alors monté sur un système

de libération avec une gaine en teflon (diamètre 9.0 millimètre = 27 F, Fig. 2), introduit dans la veine cave inférieure par une approche rétropéritonéale et ensuite placé et déchargé au niveau de la cible, 2 centimètres au-dessous de l'oreillette droite dans la veine cave inférieure. Un cathéter à capteur de pression de type Millar est utilisé pour mesurer la pression proximale et distale de la valve. L'évaluation de la fonction valvulaire c'est fait par l'IVUS. Les animaux ont été sacrifiés pour vérifier la position correcte du stent valvé, ainsi que son déploiement et son ancrage.

Une autre évaluation aiguë in vivo a été réalisée dans 6 cochons adultes (poids moyen 55.6±6.0 kilogramme, de 53 à 67 kilogrammes). Le stent valvé a alors été implanté en l'absence de CEC (off-pump) par un système de libération non-commercialisé, de 22 à 24F, en position pulmonaire par une approche trans-ventriculaire droite. Un cathéter 5 F de type Cook a été utilisé pour mesurer le gradient en amont et en aval de la valve. Un contrôle par IVUS a permit d'évaluer le fonctionnement de la valve en position ouverte et fermée ainsi que le degré de régurgitation (grade de régurgitation: 0 pas, 1 légère, 2 modéré; 3, importante).

Résultats:

La longueur moyenne des stents valvés était de 23.1±0.7 millimètres, le diamètre interne de 21.6±0.7 millimètres, le diamètre externe de 26.3±0.7 millimètres. Les tests statiques in-vitro ont mis en évidence une fuite

moyenne transvalvulaire de 32.5±12.3 ml/min (allant de 18.1 à 47.6ml/min). L'évaluation dynamique a mis en évidence un gradient systolique transvalvulaire maximal de 6.42±2.75 mmHg sous un débit de 4.32±0.97 L/min.

La longueur moyenne de la veine cave inférieure entre le cœur et le foie était de 7.9 ±0.2 centimètres (allant de 7.5 à 8.4 centimètres) et le diamètre interne mesuré 20.4 ±1.6 millimètres (allant de 18.71 à 22.56 mm). Le gradient moyen de pression à travers la valve implantée était de 1.0 ±0.5 mmHg (allant de 0 à 2 mmHg). L'IVUS a mis en évidence une fermeture seulement partielle de la valve pendant l'expiration (réduction moyenne de la surface d'ouverture de la valve de 148.5 mm2 à 81.5 mm2). La fermeture quasi complète de la valve s'est produite seulement pendant des cycles respiratoires profonds chez ces animaux sains, sans insuffisance ventriculaire droite. Chez tous les animaux l'autopsie a confirmé la position correcte du stent valvé à environ 2cm proximal de la jonction auriculaire droite.

En position pulmonaire le gradient transvalvulaire systolique maximal était de 4.5±3.1 mmHg (range 0 à 7 mmHg) en moyenne sous un débit cardiaque moyen de 3.03±0.05L/Min. La pression artérielle moyenne carotidienne, la saturation d'oxygène et la pression veineuse centrale pré et post implantation n'ont pas changer de manière significative (P1=0.45, P2=0.57, P3=0.64). L'ouverture et la fermeture complète de la valve est

démontrée par une réduction moyenne de la surface d'ouverture de 315.08±54.13 mm2 à 0 mm2. L'autopsie a confirmé chez 4 de ces animaux un placement correct du stent valvé alors que chez les deux animaux restant on constate un largage trop distal, soit entre la valve pulmonaire et la bifurcation de l'artère pulmonaire soit dans l'artère pulmonaire gauche.

Conclusions:

Les expériences in vitro et in vivo ont confirmé la faisabilité de l'implantation d'un nouveau stent valvé auto-extensible soit en position pulmonaire, soit dans la veine cave inférieure sans nécessité d'une circulation extracorporelle.

L'approche transventriculaire permet de mettre en place des stents à valve de grande taille.

Le fonctionnement du stent valvé est bon en position pulmonaire. Par contre il est limité dans la veine cave inférieure en raison de la fermeture partielle des feuillets valvulaire en l'absence d'une insuffisance ventriculaire droite qui normalement entraînerait une augmentation de la pression veineuse.

L'IVUS permet d'identifier le site de libération du stent valvé et d'évaluer la fonction valvulaire sans utiliser de produit de contraste ou de procédures diagnostic plus invasives.

Appendices

Tab 3. The data of Mock loop test

	Systolic peak pressure (mmHg)		Pressure gradient (mmHg)	Flow rate (L/min)
	Above valve	Below valve		
Valved stent1	87.326	92.486	5.160	4.425
	88.447	93.313	4.866	4.688
	87.639	92.627	4.988	4.903
	89.305	93.648	4.343	5.023
	90.185	94.624	4.439	5.076
	89.96	94.326	4.366	5.068
	89.814	94.222	4.408	4.874
Valved stent2	92.752	103.217	10.465	2.771
	99.092	109.652	10.560	2.615
	117.521	121.571	4.050	2.806
	134.597	144.092	9.495	4.74
	130.089	139.974	9.885	4.833
Mean	99.727±17.383	106.146±18.945	6.419±2.749	4.319±0.975

Tab 4 The data in pulmonary position

N.	Weight(kg)	P trunk diameter(mm)	Cvp(mmHg)	Hb(g/dl)	SatO2%	EKG	HR	Heparine(IU)
16	53	24.5	5		96	NSR	94	6000
17	54	22.5	11	12.4	98	NSR	109	8000
18	47	20.7	7		97	NSR	77	6000
19	55	19.9	4	15.1	94	NSR	108	6000
20	57	22.5	3		96	NSR	76	10000
21	56	20.3	9	11.2	95	NSR	115	6000
22	67	21.3	3		99	NSR	69	10000
M	55.6	21.7	6.0	12.9	96.4		92.6	7428.6
SD	6.0	1.6	3.1	2.0	1.7		18.6	1902.4

NS: Normal sinus rhythm, P trunk: Pulmonary trunk.

Tab 5 The Sat O_2 before and after implantation in pulmonary artery

N.	Before	After	T value
17	98	99	
19	94	93	
21	95	96	
22	99	95	
M	96.5±2.38	95.75±2.5	0.57

Tab 6 ACT (seconds) before and after the valve implant in PA

N.	Pre-operation	Post-operation
17	130	520
18	120	495
19	120	435
20	115	600
21	135	415
22	110	500
M	121.67±9.31	494.17±65.83

PA: Pulmonary artery.

N.	Gradient(mmHg)	Pulmonary trunk (above valve)		RV (below valve)	
		sys	dia	sys	dia
17	5	25	15	30	7
19	7	10	3	17	0
21	6	40	23	46	3
22	0	45	29	45	16
M	4.5	30	17.5	34.5	6.5
SD	3.1	15.8	11.2	13.8	7.0

Tab 7 the gradient across the pulmonary valved stent measured by a catheter of Cook type

N.	CVP and blood pressure after implantation				CVP and blood pressure before implantation			
	sys	dia	*mean*	cvp	sys	dia	*mean*	cvp
17	78	54	61	11	82	57	67	10
19	96	65	78	2	74	45	56	3
21	94	73	80	9	80	53	63	9
22	67	36	44	2	70	42	51	1
M	83.75	57	65.8	6.0	76.5	49.3	59.3	5.8
SD	13.8	16.0	16.8	4.7	5.5	6.9	7.1	4.4

Tab 8 the blood pressure and CVP compare (valve in PA)

Tab 9 Acuson Color Doppler ultrasound catheter

N.	Velocity(m/s)	Gradient(mmHg)	Regurgitation rank (0,1,2,3)
19	1.55	9.6	0
21	0.95	4.5	0
22	1.11	4.9	0
M	1.20	6.33	0
SD	0.31	2.84	0

N.	Debit du cœur (L/min)
19	2.99
22	3.06
M	3.03
SD	0.05

Tab 10 the cardiac output after implant in PA

Measured by Swan-Ganz

No.of pigs	Weight(Kg)	inferior vena cava		valved stent	
		Diameter(mm)	length	open area(mm^2)	closed area
1	84	19.9	7.9	114.5	23.8
2	77.5	18.21	8.36	158.2	54.6
3	74.5	20.2	7.5	91.6	65.8
4	85.5	22.56	8.1	239.4	169.9
5	81	21.1	7.8	138.7	93.2
M	80.5	20.4	7.9	148.5	81.5
SD	4.5	1.6	0.3	56.7	55.3

Tab 11 the length and inner diameter of inferior vena cava

And the open and closed area of valved stent in IVC