Transcatheter Pulmonary Valve Replacement
The Edwards Sapien Valve

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Abstract
Pulmonary valve replacement is one of the most common surgical procedures performed in older children and adults with congenital heart disease who have normally had at least one previous operation. The percutaneous alternative was first performed in man in 2000 when Dr. Bonhoeffer merged a surgically available bovine jugular vein valve (Venpro/Contegra) and a Cheatham-Platinum (CP) stent to create a percutaneous system for stenosed conduits; this valve was subsequently acquired by Medtronic and is now the Melody valve. The Edwards Sapien valve was originally designed for percutaneous aortic valve replacement (TAVI/TAVR), but its design makes it equally suitable for pulmonary implantation using a similar delivery system and it is indeed indicated for this purpose [1, 2]. The Edwards valve has evolved over recent years, increasing the range of sizes including the 29-mm Edwards XT and, more recently, the Sapien 53. The Edwards 3, incorporates a cuff/skirt outside of the frame to minimize paravalvular leaks; it was primarily designed for the aortic position where paravalvular leaks are generally more significant. Follow-up observations indicate that the performance and longevity of the Edwards percutaneous valve are comparable to surgically implanted bioprostheses which are also manufactured by Edwards Lifesciences; the catheter technique has reached a high level of sophistication to achieve successful and safe results in selected individuals. Some patients, however, would be better candidates for surgery, usually for anatomic reasons.

Transcatheter pulmonary valve implantation has some advantages over surgery, as it is less invasive, avoids repeat sternotomy and bypass, does not usually require intensive care, and results in a shorter hospital stay. Cost effectiveness is comparable, and because the Edwards valve is based on a well-established tissue valve technology, its longevity are performance are expected to be similar to that of surgery as the frame on which the valve is mounted is very robust with complete integrity maintained over at least 5 years from implantation.

Key Words: Sapien • Edwards valve • Pulmonary valve replacement • Catheter intervention

Equipment
This consists of the Edwards valve itself, a dilator kit, introducer sheaths, balloon catheter, delivery system and the Atrion inflation device. In addition, diagnostic catheters, various balloons, guide wires, snares, and stents should be available.

Edwards Equipment
The Sapien Edwards valve, which comes in the Sapien XT and Sapien 3 versions, is balloon expandable and fashioned from bovine pericardium similar to tissue that has been used for surgical tissue valves for many years. Bovine pericardium consists of densely layered collagen and has clinically proven long-term durability. The bovine pericardium is carefully inspected and chosen for uniform thickness and quality. The
Valve tissue is treated with a patented Carpentier-Edwards ThermaFix process that is designed to remove major calcium-binding sites in order to optimize valve longevity. The ThermaFix process uses (i) a heat process to remove glutaraldehyde molecules and (ii) a patented chemical process that removes 98% of phospholipids, as these are known calcium-binding sites; moreover, calcification of the valve is known to be the main reason for valve tissue degeneration but the long-term benefit of the ThermaFix still needs to be established. The pericardium is shaped into a three-leaflet valve, originally mounted on a stainless steel frame using polyethylene terephthalate fabric but the frame is now made from a Chromium-Cobalt alloy. In vitro durability testing simulating 5 years of implantation was successfully carried out for the valve components.

The pericardial leaflets are mounted on a laser-cut, biomedical grade Chromium-Cobalt frame consisting of 4 rows and 4 columns providing a high radial strength; this results in better hemodynamics by expanding into a round circle and is resistant to stress fractures. The latter was confirmed by a simulation process equivalent to 15 years of implantation. Due to the strength of the frame and for more uniform placement of the delivery system, Edwards developed a crimper to mount the valve on the delivery system. Originally, the Sapien valve came in 23- and 26-mm diameters. Edwards expanded the range, adding 20- and a 29-mm diameter options. The frame height, after implantation is 13.5 mm for the 20 mm valve, is 14.3 mm for the 23-mm valve, 17.2 mm for the 26-mm valve, and 19.1 mm for the 29-mm valve.

The original Sapien valve was mounted on a balloon that was part of the delivery system. Initially, this was known as the Retroflex and was upgraded to the RetroFlex 3 System, until recently. All the current models, except for the Edwards 3, can be delivered through the NovaFlex system; the Edwards 3 is delivered through a Commander delivery system. The change in design to the NovaFlex delivery system has made it possible to go through a smaller sheath by mounting the Edwards valve on the shaft proximal to the balloon for easy of entry into the patient and it is then placed across the balloon within the inferior vena cava. The NovaFlex ranges from 18 to 21 Fr in size and consists of a long catheter with a short, soft tapered tip for easy transition and to protect the Edwards valve during delivery. Proximal to the tapered tip is the balloon, over which the valve is placed for deployment. The balloon is volume and not pressure driven; the recommended volume of dilute contrast is placed in the Atrion QL inflation device to achieve the desired diameter for the size of valve being deployed.

The Edwards valve is crimped on to the shaft of the NovaFlex at the time of the procedure proximal to the balloon and using the Edwards crimper of the appro-
appropriate size for the valve that is being used. Proximal to where the valve is mounted on the shaft, there is a flared sheath which is part of the delivery system and designed to place the valve over the balloon when the system is inside the patient. Precise and fine placement of the valve on to the center of the balloon is achieved by a rotating knob on the delivery handle. To inflate the balloon to a predetermined diameter, the Edwards Atrion inflation device is used with nominal volumes for the various size valves.

Edwards LifeSciences also manufacture a set of precisely tapered hydrophilic dilators as well as 35-cm hydrophilic introducer sheaths with a tri-seal valve in various diameters to accommodate the NovaFlex delivery system; however, nowadays, the expandable 16 Fr eSheath is preferred and uniformly suitable.

Edwards also provide the short Ascendra/Certitude sheath and delivery system designed for minimally invasive surgical implantation using a hybrid approach.

Additional Equipment

Diagnostic Catheters

A selection of catheters may be required to obtain angiography of the right ventricle, the right ventricular outflow tract (RVOT), and the pulmonary arteries, and to assess the degree of pulmonary and tricuspid regurgitation. Common types of catheters include the pigtail, multipurpose A2, the Gensini/MPB3, multi-track, balloon wedge/floatation, and pre-shaped coronary catheters for angiography during balloon interrogation of the RVOT.

Wires

Apart from the standard guide wires, it is important to have a hydrophilic wire and a selection of stiff exchange length wires, such as, the Amplatz stiff wires (Extra Stiff, Super Stiff, and Ultra Stiff by William Cook), the Lunderquist wire (William Cook) and the Back-up Meier wire (Boston Scientific).

Balloons

These are required for interrogating the RVOT, not only to assess the anatomy of the outflow tract but also to look at the impact on coronary artery patency, compression, and flow. Although compliant sizing balloons, such as the ones from St Jude Medical or NuMed, can be used, semi-compliant ones may be more appropriate; examples of these balloons include the Cristal (Balt) and BiB (NuMed) balloons. These balloons are also used for pre-stenting the RVOT when required. High pressure noncompliant balloons, such as the Z-Med and Mullins (NuMed) and the Atlas (Bard) are required to abolish resistant stenosis of the RVOT and these are usually used after stent placement and before valve implantation.

Stents

In many instances, pre-stenting is usual in order to cover areas of stenosis longer than the Edwards valve frame both in the context of a previous tissue homograft/xenograft conduit but also when there has been a trans-annular patch placed at the time of surgical repair. Pre-stenting not only helps to scaffold the RVOT, but it prepares the landing zone for the valve. Although pre-stenting is essential for the
Melody valve because of the fracture rate, this is not essential for the Edwards TM valve as the frame is very robust with no fractures recorded on bench testing or in clinical trials. The stent material does not seem to matter with respect to metal to metal interaction that may cause corrosion or valve dysfunction although there are Chromium-Cobalt stents, such as the Andrastent XXL which are both robust and material compatible. The stents used must be able to dilate to large diameters with predetermined shortening to allow for accurate placement and to cover the length of any narrowing. Although most of the time bare metal stents are used, it is essential to have covered CP stents (NuMed) either for primary use if there is the possibility of conduit rupture or for a bailout situation. If a longer covered stent is required above those available, these can be obtained from the manufacturer as a special order up to 55mm in length. Stents that are commonly used for the RVOT include:

- a) Andrastent (Andramed)
- b) CP bare metal and covered (NuMed)
- c) Maxi LD (Ev3)
- d) Palmaz (J & J)

These stents are often mounted on BiB, Cristal, or Z-Med balloons for deployment and delivered after RVOT interrogation to make sure that the stent or calcified material will not compress the coronary arteries.

Venous closure
Venous access closure devices are not essential but some operators prefer to use these; however, simple manual compression or the use of a FemStop is an acceptable, alternative option. Devices that are commonly used include the Perclose/Proglide or the ProStar both from Abbott Vascular. An alternative is to form a figure-eight suture at the site of skin entry using thick silk on a large curved cutting needle; this invaginates the skin applying pressure to the femoral vein entry point and achieves hemostasis. The suture can be removed after six hours.

Patient Selection and Preparation

Patients are selected for pulmonary valve replacement, according to accepted guidelines that include symptoms as well as supportive evidence of significant stenosis, regurgitation, or a combination of these; in other words, these patients would be equally candidates for surgery. Although some patients are suitable for either surgery or percutaneous pulmonary valve replacement some may carry a higher risk or are considered not to be surgical candidates either because of cardiac or non-cardiac conditions (e.g. Scoliosis, respiratory insufficiency, motor and/or developmental delay, psychological imbablance, amongst others). Some patients are asymptomatic but have objective evidence of significantly hemodynamic compromise. Those with symptoms often fall into NYHA class II or III.

Anatomic Situations
These include:
- a) Truly native RVOT (usually stenosis due to dysplastic pulmonary valve or regurgitation following previous balloon valvuloplasty)
- b) Trans-annular patch repair of native RVOT
- c) Ventricle to pulmonary artery conduit (homograft or xenograft)

Physiologic Factors
- a) Severe RVOT obstruction with a peak gradient of greater than 50 mm Hg
- b) Severe pulmonary regurgitation with right ventricular volume over load, a right ventricular end diastolic volume of greater than 150 ml/m² on MRI, a regurgitant fraction of greater than 35% and a right ventricular ejection fraction of less than 40%
- c) A combination of RVOT obstruction and regurgitation
- d) Some patients may not have the above criteria but are nevertheless symptomatic with impaired CPEX. Sometimes restrictive right ventricular physiology contributes to this clinical presentation.

Clinical Scenarios
- a) Repaired Fallot’s tetralogy or pulmonary atresia with VSD
- b) Repaired persistent arterial trunk
c) Post-Ross procedure (pulmonary autograft)
   a) Post arterial switch/Rastelli in transposition of the great arteries
   b) Post left ventricle to pulmonary artery conduit in congenitally corrected transposition
   c) Any dysfunctional conduit/tissue valve between ventricle and pulmonary artery

General Criteria

There are no strict rules with respect to patient’s age and weight, but as a guide, patients should be older than six years and weigh more than 25 kg as the delivery systems are still bulky.

It is essential for the entry veins to be of adequate size, that is, around 6 mm or more. Ultrasound evaluation of these is usually sufficient. Arterial access from the femoral or radial arteries is required to assess the coronary arteries during balloon interrogation of the RVOT.

There are some situations where percutaneous pulmonary valve implantation should not be considered:
   a) If the coronary arteries are compromised or within 5 mm of the interrogating balloon
   b) If the landing zone is too large for the available valve sizes; for non-stenosed outflow tracts, the valve size should be 10–15% larger to ensure anchorage and stability
   c) Infection within the previous 6 months which includes systemic infection or endocarditis

Specific Observations/Investigations

Evaluation consists of clinical assessment as well as supportive investigations.

The ECG may show a broad, complex, right bundle branch block; if the QRS is wider than 180 msec, this usually implies significant right ventricular volume overload with arrhythmogenic tendencies although in many the QRS width is closer to 160 msec when other indications already exist. Holter monitoring is part of the work-up and the presence of ventricular tachycardia may be an indication for intervention although there are several mechanisms apart from mechanical right ventricular dysfunction. In general, however, the mechanical component is addressed first followed by electrophysiology if ventricular tachycardia persists following haemodynamic optimization.

A cardio-pulmonary exercise test (CPEX) provides quantitative workload capacity and is useful to demonstrate any progression over a period of observation and this helps to optimize the timing for intervention as well as to observe any benefits following intervention.

The echocardiogram/Doppler is the commonest investigation carried out to evaluate the RVOT obstruction as well as the effect of obstruction and regurgitation on the right ventricle. It provides information about the proximal pulmonary arteries, the velocity across the RVOT, the degree of pulmonary regurgitation, as well as the velocity and regurgitation of the tricuspid valve to estimate the right ventricular pressure and observe the degree of regurgitation. Transesophageal echocardiography is sometimes used during pulmonary valve implantation and may help with identifying the landing zone, but the valve leaflets are not easily seen due to scatter from the frame and if there is a suspicion of valve dysfunction, intra-cardiac echocardiography (ICE) is superior.

More specific and objective information is obtained on MRI/CT. These provide details of the RVOT including the diameter and length, spatial orientation of pulmonary an coronary arteries, quantitative RVOT obstruction and regurgitation, right ventricular function, and the right ventricular end diastolic volume correlated to body surface area. A right ventricular end diastolic volume of greater than 150 cc/m² is considered significant, as are an end systolic volume of more than 90 cc/m², a regurgitant fraction of more than 35% and an RV ejection fraction of less than 40%. MRI is superior particularly for quantitative observations and these are important to assess progression but some patients with implantable devices, such as pacemaker/defibrillators are only suitable for CT.

Angiography and direct hemodynamic assessment can be done during the pulmonary valve implantation but increasingly this is carried out in advance during which balloon interrogation of the RVOT is carried out for more accurate measurement and to assess whether the coronary arteries could be compromised with stenting and/or valve implantation. If the balloon interrogation proves safe, the RVOT can be stented at the same time and for the pulmonary valve to be implanted a few months later. A gap between these pro-
Procedure

Pulmonary valve implantation can be carried out under sedation although most are carried out under general anesthesia. A biplane system is preferable and the room must have adequate levels of sterility and air change to minimize risk of infection. The operators must adhere to strict sterile protocols throughout. Antibiotics are generally given to cover the procedure mainly to cover staphylococcal infections but this is not a substitute to good operator and patient preparation. The procedure is covered with heparin in therapeutic doses based on ACT measurement.

The femoral vein is accessed percutaneously high up to enter the external iliac vein. If the femoral veins are occluded or tiny or if there is absence of the IVC with azygos replacement, a right internal jugular approach is required. The jugular approach may also be preferred in patients with TGA or cctGA.

A 5–6 mm skin incision is made at the entry site and if a closing device is planned this should be inserted at this stage. It is customary to place a 16–18 Fr short sheath to allow for angiography, balloon interrogation, or stenting of the RVOT if required. Right sided pressures are recorded and a right ventriculogram carried out to show the RVOT anatomy and pulmonary arteries, as this helps to determine which pulmonary artery to use the exchange wire in order to optimize the catheter course. In general, the left pulmonary artery is preferred when approaching from the femoral and the right pulmonary when approaching from the jugular but there are no hard and fast rules as this depends on the anatomy, approach, and operator preference. Arterial access with a 4–6 Fr sheath is obtained.

Once the RVOT is prepared with stenting, the PPVI procedure can proceed. Having a stiff exchange-length guide wire in a peripheral pulmonary artery is essential and this is placed through a MP catheter; a Lunderquist 0.035” wire is commonly used. Over the wire, an appropriate Edwards introducer sheath, often nowadays this is the eSheath, is inserted having pre-dilated the track with the Edwards dilator kit. The Edwards XT or Sapien 3 valve is loaded and crimped on to the NovaFlex/Commander delivery system proximal to the balloon and making sure that it is orientated for pulmonary implantation—at least two people must see and confirm this. Choose the correct crimper for the valve size. The delivery system is then passed through the introducer sheath until the valve is well out of the delivery sheath in the upper part of the IVC. The valve is pushed forward on the proximal part of the balloon by releasing two catches on the delivery handle and pushing the flared sheath forward monitoring this on fluoroscopy - during this maneuver, it is essential to keep an eye on the wire position to avoid inadvertent withdrawal. Fine tuning of the valve position on the center of the balloon as judged by the radio-opaque markers, is achieved by the rotating knob on the delivery handle. It is best for this maneuver to be done in the IVC and not the RVOT. Once the valve is optimally placed on the balloon, the whole assembly is pushed over the wire towards the procedures allows the stent to embed and to get a better idea of diameter in the event of recoil. If the latter is dynamic or significant (arbitrarily, a gradient of greater than 20 mm Hg), a second stent may be required. Right ventricular outflow tract preparation must be done prior to valve implantation and do not rely on post dilatation after the valve is implanted.

Figure 3: Animation of pulmonary valve implantation with the Edwards valve.
landing zone. This may require perseverance and usually requires steady forward push but avoid rotation. It is essential to maintain the wire position in the pulmonary artery, although sometimes gentle traction is needed to straighten the course. Occasionally, it may be necessary to push the delivery system to create a loop in the right atrium in order to reach the landing zone, but this should be used only when necessary, as it may kink the wire or damage the delivery system and may cause damage to the heart. Once the valve is in an optimal position, the balloon is gently inflated to the predetermined volume for the valve size using the Atrion inflation device. The balloon is inflated gradually to give the operator chance to fine tune the valve position either by pushing the delivery system forward or pushing the wire to retract the system proximally. For large RVOT where there is marked movement during the cardiac cycle, fast ventricular pacing may be used to achieve stability; this can be assessed during balloon interrogation of the RVOT. If the procedure is being carried out under anesthesia, the operator can request apnea to minimize movement during valve deployment. It is important to inflate the balloon fully with the pre-determined volume. Occasionally, one may anticipate that a larger volume than the nominal may be required in which case the Atrion syringe may be filled with an additional 1–3 cc but only to give additional volume if it appears that

Figure 7: Valve-in-valve device with pre-stenting of RVOT. Courtesy of Dr. Eric Horlick.
the valve may not be totally stable so it is important to deflate the balloon slowly and observe the valve carefully. It is common for the blood pressure and heart rate to fall during valve deployment but these recover quickly. Once the balloon is fully deflated, the delivery system is withdrawn under fluoroscopy making sure that there is no resistance against the Edwards valve. It may be necessary to adjust the wire to keep the balloon in the center of the valve during withdrawal. The gradient can be measured using a multi-track catheter over the wire and a pulmonary angiogram is performed to make sure the valve is competent. Mild regurgitation is acceptable especially when there is still a catheter across the valve, but if the leak is more than mild, it is important to establish if this is due to a paravalvular leak or leaflet dysfunction. A paravalvular leak, if significant, may be addressed by inflating the balloon to a larger diameter adding between 1–3 cc to the nominal volume. If the leak is due to valve dysfunction, ICE may be required to establish the reason. If this is due to a stuck leaflet, this may be mobilized using a pigtail catheter, but if the valve leaflet is damaged, a valve-in-valve device should be considered. With the NovaFlex/Commander system, the valve is pushed over the balloon against the leaflets and theoretically, damage can occur but in vitro testing has shown that this is not a problem.

If the hemodynamics are satisfactory and the valve is stable, the wire can be withdrawn and the procedure terminated. It is advisable for the dilator to be placed within the eSheath during withdrawal in order to avoid inadvertent pinching of the IVC wall as this may cause vessel tear with uncontrollable internal bleeding. It is customary to prescribe an antiplatelet agent for 6 months; many administer antibiotic prophylaxis for invasive procedures for the first 6 to 12 months, although this depends on local and national practice (Figures 4, 5 and 6).

If there is an existing failing bioprosthetic valve in the pulmonary position, an Edwards TM valve can be placed within the surgical valve; in this situation, pre-stenting is not usually required and coronary compression is not an issue. Pre-stenting may be needed if the obstruction extends beyond the bioprosthetic valve. What is essential is to find out exactly what type and size of bioprosthetic valve had been implanted and to know the exact characteristics of the valve, including the height, internal diameter and the leaflet design as this will determine the precise position of the Edwards valve within the bioprosthesis. In general, only one row or part of this of the Sapien is deployed proximal to the surgical valve ring and the majority of the implanted valve is distal to the surgical ring in order to open up the degenerated leaflets of the surgical valve.

**Tips to reach RVOT**

The delivery system is stiff and unwieldy and the course to reach the RVOT can be tortuous and in different planes, this making it difficult to deliver the mounted valve to the RVOT. A very stiff wire helps to rail road the valve but this can sometimes also proved a handicap particularly when the RVOT has been presented and the wire abuts against the stent preventing free movement of the valve in the RVOT. When difficulties are experienced delivering the Sapien from the IVC to the RVOT, there are several tips that can be considered:

- **a)** Make the delivery system less stiff by withdrawing the catheter on the delivery system proximally. A variable degree of withdrawal can be checked to get the best of stiffness and softness for smooth movement of the valve. If the valve is in the right ventricle but cannot reach it’s target in the RVOT, the catheter may only need to be withdrawn to the level of the tricuspid valve.

- **b)** Balloon assisted wire anchoring. This is achieved by inserting a separate wire in the pulmonary artery where the stiff wire has been parked and a balloon is inflated in the pulmonary artery adjacent to the deployment wire in order to anchor this and achieve counter traction to help deliver the Sapien in the RVOT. The wire and balloon must be withdrawn before valve deployment.

- **c)** Partial inflation of the balloon on the delivery system. This only requires 1 -2 cc of dilute contrast delivered through the Atrion and observed on fluoroscopy in order to create a smoother tip particularly if the RVOT is heavily calcified or if it has been presented.

- **d)** Replace wire with a less stiff alternative. A very stiff wire may be more of an obstacle when the
valve is trying to reach the RVOT and it can be replaced with a less stiff valve so long as the distal tip of the delivery system is already in one of the pulmonary arteries. Consider doing any of the above one at a time. A constant but gentle push on the delivery system with controlled counter traction on the wire are much more likely to be successful in reaching the RVOT than aggressive pushing and struggling.

**Complications**

The procedure is generally safe but the following complications may occur:
- a) Vascular injury that may require surgery
- b) Stent or valve displacement
- c) Conduit rupture
- d) Tricuspid valve damage
- e) Arrhythmias which include heart block or ventricular tachycardia/fibrillation
- f) Valve malfunction – may require a valve-in-valve device
- g) Coronary occlusion
- h) Infection
- i) Death

**Current Limitations**

- a) Anatomical features. As many as 70% of patients with Fallot’s Tetralogy will require a trans-annular patch and this can become large and aneurysmal over the years. Although a 29 mm valve in the pulmonary position is adequate for haemodynamic purposes, some RVOTs can be much larger. For this reason, several options are being considered by manufacturers including the concept of a reducer designed to narrow the RVOT to allow placement of a 29 mm Sapien or to have a combined reducer with an integral valve to accommodate within the very dilated RVOT. There are several designs being evaluated at the moment, most of which using self expanding Nitinol technology.
- b) Technical issues. The current loading design with the valve mounted on the shaft and eventually placed on the balloon within the patient has allowed for smaller introducer sheaths.

This design works well for the aortic implantations and for the majority of pulmonary ones too. There are, however, 2 theoretical concerns when the Sapien is pushed over the balloon when orientated for placement in the RVOT:
- c) The valve is pushed over the balloon against the valve leaflets whereas for aortic implantation the leaflets are in-line and less likely to be damaged by the balloon. This is more theoretical although there are anecdotal reports of valve leaflet damage but the precise cause was not established.
- d) The uncovered distal valve frame is pushed against the balloon and the sharp tips of the cells may potentially create pinhole punctures in the balloon which may impede full balloon inflation. It is always wise to have a Luer lock syringe with dilute contrast available in case balloon perforation has occurred and rapid injection is required to inflate the balloon and deploy the valve avoiding displacement from the target zone.

If operators are concerned about the above potential problems, an option is to mount the Sapien directly on the balloon outside the patient (instead of placing the valve on the catheter shaft) but this will mandate using a larger sheath; however, this is not usually an issue for pulmonary valves as the veins are large and stretchable and do not have the stenotic calcified lesions seen in the iliac arteries when the Sapien is used for TAVR.

**Conclusion**

The Edwards XT and Edwards 3 valves are very suitable for implantation in the pulmonary position. Their size range from 20 to 29 mm and this allows for broader indications; the XT valves are all delivered through a NovaFlex delivery system whereas the Sapien 3 uses the Commander delivery system [3-7]. The technique is well established. Pre-stenting is often performed except for some types of valve-in-valve implantation. Longevity is expected to be similar to surgical bioprosthetic valves and is likely to take over most cases for pulmonary valve replacement, although a few may still require surgery. The Compas-
sion and Premiere studies should give valuable data on the procedure as well as longevity and follow up.

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References


Conflict of Interest

The author has no conflict of interest relevant to this publication.