

THE ON-X[®] PROSTHETIC HEART VALVE— WHY CHOOSE ANY OTHER MECHANICAL VALVE?

*Clinical Update
Number Twenty-three*



The potential exists for a reduced level of anticoagulant medication with the On-X valve depending upon the outcome of the FDA approved PROACT (Prospective Randomized On-X Anticoagulation Trial) study.

The study results could mean a better quality of life for patients due to lowered anticoagulation medication, a resulting reduction of related complications and longterm durability—a potential that does not presently exist with any other mechanical valve.

In January of 2006, the FDA approved the first and only IDE (Investigational Device Exemption) lowered anticoagulation trial for a mechanical valve to be conducted in the United States for the On-X valve, the Prospective Randomized On-X[®] Valve Anticoagulation Clinical Trial (PROACT).¹ It did not take long to recruit 20 centers for participation in this groundbreaking randomized trial. Patients contact Medical Carbon Research Institute regularly to inquire about study participation. The advantages of a valve that will last a lifetime and lower anticoagulant-related complications are clearly apparent to surgeons and patients alike.

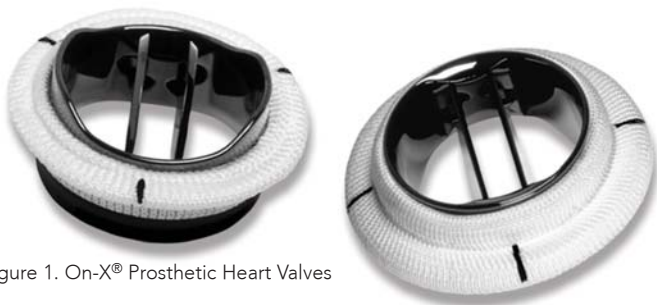


Figure 1. On-X[®] Prosthetic Heart Valves

PROACT Update

The first implant occurred on June 7, 2006, in Atlanta, Georgia, at Emory University/Crawford Long Hospital.² Sixteen of twenty centers have received Institutional Review Board (IRB) approval to date and there have been a total of 42 implants. Randomization occurs at three postoperative months according to the Clinical Trial Investigation Plan.³ Of 42 patients implanted, 17 have been randomized to one of six study groups (3 test groups, 3 control groups).³ Enrollment of a total of 1200 patients is expected to be complete by mid-2008 with a first look at statistics annually by the PROACT Data and Safety Monitoring Committee, which is led by Sidney Levitsky MD of Harvard University.

The three study groups are high risk aortic, low risk aortic and mitral valve implants. Each group has a control group. These groups are defined in Table 1.

Test Group I (high risk AVR)

First 3-months postoperation, Coumadin at an INR target of 2.0 to 3.0 with 81 mg/day aspirin will be used. After 3-months, Coumadin dose will be reduced to an INR target of 1.5 to 2.0 with 81 mg/day of aspirin continued.

Test Group II (low risk AVR)

First 3-months postoperation, Coumadin at an INR target of 2.0 to 3.0 with 81 mg/day aspirin will be used. After 3-months, Coumadin dose will be removed and clopidogrel will be added using a loading dose of 300 mg followed by 75 mg/day with aspirin at 81 mg/day continued.

Test Group III (MVR regardless of risk)

First 3-months postoperation, Coumadin at an INR target of 2.5 to 3.5 with 81 mg/day aspirin will be used. After 3-months, Coumadin dose will be reduced to an INR target of 2.0 to 2.5 with 81 mg/day of aspirin continued.

Control Groups

Postoperatively Coumadin with an INR target of 2.0 to 3.0 with 81 mg/day aspirin throughout the study for aortic implants and an INR target of 2.5 to 3.5 with 81 mg/day aspirin throughout the study for mitral implants. A separate control group will be used for each test group above.

Table 1. PROACT test groups³

Exclusion criteria from the low risk group of aortic patients who will receive non-warfarin treatment after three months postoperatively are seen in Table 2.

- Chronic atrial fibrillation
- Left ventricular ejection fraction < 30 %
- Enlarged left atrium > 50mm diameter
- Spontaneous echo contrasts in the left atrium
- Vascular pathology
- Neurological events
- Hypercoagulability
- Left or right ventricular aneurysm
- Lack of platelet response to aspirin or clopidogrel
- Women receiving estrogen replacement therapy

Table 2. Exclusion criteria from low risk aortic valve patient group³

Non-warfarin treatment consists of aspirin 81 mg every day along with clopidogrel (300 mg loading dose followed by 75 mg every day).³

Until the completion and analysis of study data, MCRI continues to recommend standard anticoagulation therapy as presently prescribed by various professional societies for the On-X valve.

Risks Associated with Older Valve Designs

Older design mechanical valves with “lower” profiles are known to permit pannus overgrowth.⁴⁻⁹ Cumulative valve related complication rates for these valves at 20 years are most often greater than 50%.¹⁰⁻¹² For tissue valves, reoperation rates are high at 15 years and as many as 50% of these patients end up on warfarin therapy in spite of the touted advantage of tissue implantation not requiring warfarin therapy.¹³⁻¹⁸

The On-X valve is the only valve with an optimal profile for reduced turbulence and lowered blood damage (Figure 2).¹⁹⁻²¹ This advantage has led to consistently low morbid event rates from study to study with varying anticoagulation regimes and no anticoagulation with warfarin.²²⁻²⁷ Pannus overgrowth of an On-X

valve has not been reported to Medical Carbon Research Institute in its 10-year history of implantation.²⁸

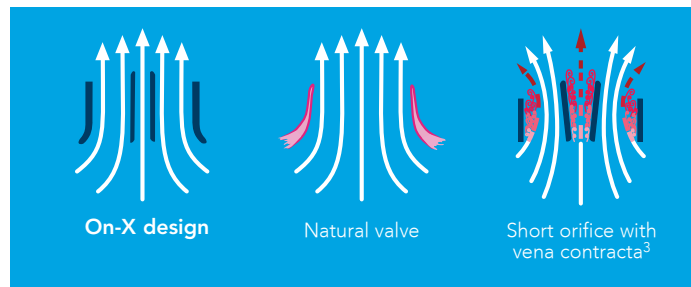


Figure 2. Theoretical comparison of valve designs

Patients deserve the optimal conditions for a long life with the possibility of reduced or no warfarin anticoagulation—the On-X[®] Prosthetic Heart Valve!

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On-X aortic and mitral valves are FDA approved.

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. **INDICATIONS FOR USE:** The On-X[®] Prosthetic Heart Valve is indicated for the replacement of diseased, damaged, or malfunctioning native or prosthetic heart valves in the aortic and mitral positions. **CONTRAINDICATIONS:** The On-X Prosthetic Heart Valve is contraindicated for patients unable to tolerate anticoagulation therapy. **WARNINGS AND PRECAUTIONS:** 1. FOR SINGLE USE ONLY. 2. DO NOT use the On-X Prosthetic Heart Valve if: the prosthesis has been dropped, damaged, or mishandled in any way; the tamper evident seal is broken; the serial number tag does not match the container label; or the expiration date has elapsed. 3. DO NOT re-sterilize any On-X Prosthetic Heart Valve once it is removed from its plastic container. 4. DO NOT re-sterilize more than 3 times. 5. DO NOT re-sterilize with any method other than steam sterilization, with the identified re-sterilization parameters. **Note:** Gamma radiation is known to damage the sewing ring. 6. DO NOT pass a catheter, surgical instrument, or transvenous pacing lead through the prosthesis as this may cause valvular insufficiency, leaflet damage, leaflet dislodgment, and/or catheter/instrument/lead entrapment. 7. Handle the prosthesis with only MCRI[®] On-X Prosthetic Heart Valve Instruments. Only MCRI On-X Prosthetic Heart Valve Sizers should be used during the selection of the valve size; other sizers may result in improper valve selection. 8. Avoid damaging the prosthesis through the application of excessive force to the valve orifice or leaflets. 9. Avoid contacting the carbon surfaces of the valve with gloved fingers or any metallic or abrasive instruments as they may cause damage to the valve surface not seen with the unaided eye that may lead to accelerated valve structural dysfunction, leaflet escape, or serve as a nidus for thrombus formation. **POTENTIAL ADVERSE EVENTS:** Adverse events potentially associated with the use of prosthetic heart valves (in alphabetical order) include, but are not limited to: angina, cardiac arrhythmia, endocarditis, heart failure, hemolysis, hemolytic anemia, hemorrhage, myocardial infarction, prosthesis leaflet entrapment (impingement), prosthesis non-structural dysfunction, prosthesis pannus, prosthesis perivalvular leak, prosthesis regurgitation, prosthesis structural dysfunction, prosthesis thrombosis, thromboembolism and stroke. It is possible that these complications could lead to: reoperation, explantation, permanent disability and death.

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