Background
Thrombogenicity testing is required by ISO 10993-4 for blood contacting medical devices. This process can be difficult when devices are complex in design and not simple catheters suitable for intravenous deployment. There is also a need to assess thrombogenicity endpoints in models that simulate their clinical use. We designed and performed an anticoagulated in vivo thrombogenicity study for a dual lumen aortic cannula, the CardioGard Emboli Protection Cannula Gen2. The device is specifically designed for use in cardiopulmonary bypass (CPB).

Study Design

Each animal was subjected to a thoracotomy and then placed on cardiopulmonary bypass (CPB) using the Test Article as the arterial supply cannula. Once implanted, the heart was arrested and the device was allowed to dwell for ~6 hours. For the duration of the dwell period the heart was maintained at arrest and the animal was on CPB with a normal flow rate of 5 L/min output and 1 L/min inlet through the cannula. Heparin was administered prior to implantation and throughout the dwell time to maintain an ACT level between approximately 400 and 600 seconds (consistent with clinical targets for patients on CPB). Blood samples were collected for ACT, complete blood counts (to obtain platelet counts), and coagulation pathway assessment prior to heparin administration (at baseline), post-implant, post-arrest, and at term.

At the end of the procedure additional heparin was administered to prevent post-mortem clotting. Blood samples for ACT and CBC were collected both pre- and ~5 minutes post-administration of the terminal heparin dose. The animals were then euthanized. Necropsy was then performed for gross pathological evaluation of selected end organs (brain, kidney, and liver). Semi-quantitative thrombus assessment was also performed wherever any surface on the Test Article and the surrounding ascending aorta lumen was evaluated for thrombus formation using a pre-defined scale. Representative images were obtained of the device and the filter.

Implant

The device was implanted into the ascending aorta as the aortic return cannula. Each animal had an aorta with a diameter of approximately ~2.5 cm. The ascending aorta of the animals were sufficiently long to place the Test Article cannula, the cross clamp, and the cardioplegia cannula.

Specific Endpoints

- ACT Management
- Systemic Thromboembolism
- Peripheral Tissue Assessment
- Local Thrombogenicity
- Visualization of Thrombus on Device
- Platelet Modulation

Anticoagulation Management (Heparin)

Heparin administration was continued peri-operatively and throughout the study period.

Test Article

The test device was implanted into the ascending aorta as the aortic return cannula. Each animal had an aorta with a diameter of approximately ~2.5 cm. The ascending aorta of the animals were sufficiently long to place the Test Article cannula, the cross clamp, and the cardioplegia cannula.

Thrombogenicity Scoring

Scoring for thrombogenicity: Visual assessments after termination of the main tube, the suction tube, the tip fixture and the tip fixture in situ in the artery wall. All scores were "0".

Summary

- All relevant blood coagulation parameters and platelet counts were normal.
- All scored device surfaces had no formed thrombus and scored 0 on the pre-defined scale.
- All clinical relevant end organs assessed for thromboembolism had no grossly visible signs of thromboembolism.

Overall this study demonstrated the capability of a complex surgical procedure to safely evaluate the potential thrombogenicity of an extracorporeal blood contacting device in a manner consistent with ISO 10993-4 and sufficient for regulatory review and approval. There is growing interest within the regulatory community to assess biocompatibility endpoints in models wherein medical devices are deployed or implanted under conditions that closely parallel the proposed clinical use.