



# Multiple Methods to Evaluate Medical Devices in Preclinical Research

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### Abstract:

The purpose of this project was to identify various techniques to utilize an individual medical device specimen to evaluate tissue response using stereoscopy, high-resolution x-ray, scanning electron microscopy (SEM), and light microscopy. In addition, utilizing the EXAKT grinding system and techniques to perform multiple stains on one slide. The results of this analysis can be used to reduce total test article numbers (thus reducing total test systems needed) and gather the most amount of data from one sample. The findings may be useful in recommending methods to evaluate medical devices for structure integrity, thrombosis, endothelialization, and healing response.

### Introduction:

Current directives, whether by the FDA or ISO guidelines, indicate specifically the types of evaluations to be performed for a test article in order to get approval for human clinical trials. Medical device companies are having to continually adhere to these regulations and tests.

This project hopes to assist device companies by outlining methods to reduce the total sample size by utilizing many different techniques on one specimen without compromising the analysis of any one area. Each method was evaluated for its contribution to the analysis and for the quality in which it could be performed in a timely manner.

### Materials and Methods:

The treated vessel was excised from surrounding tissue and photographed. The vessel was removed from the animal, photographed, and immersion fixed. The vessel was imaged via stereoscopy. The vessel was high-resolution x-rayed. From there, the vessel was cut into proximal and distal ends. The proximal end was SEM imaged. The distal end was processed and infiltrated with Spurr's resin. After embedding in Spurr's resin, the distal half of the vessel was EXAKT ground and stained with H&E and Movat's Pentachrome on the same section. A flow diagram of the steps that the vessel and device went through can be seen below.



Figure 1. Stereoscope with Light Box



Figure 2. Faxitron™ High-Resolution X-ray



Figure 3. Hitachi TM3000 Tabletop SEM



Figure 4. EXAKT Grinder System

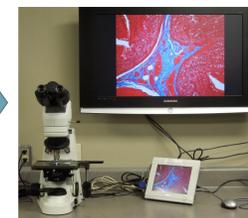


Figure 5. Microscope with Image Capture

### Results:



Figure 6. Image of device before implantation in vessel.



Figure 7. Image of device in vessel. At this point the vessel can be perfusion fixed, allowing to maintain "real life" vessel structure, or taken out and immersion fixed.



Figure 8. Image of explanted device within the vessel. Vessel was immersion fixed.



Figure 9. Stereoscope images of the device to observe any macroscopic tissue changes on the luminal surface without disrupting the tissue and device. The images from left to right show the different focusing depths of the stereoscope.

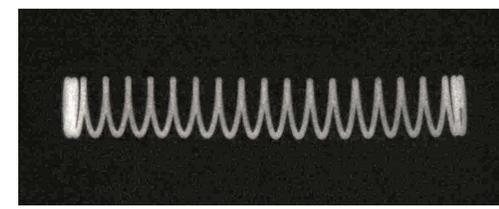


Figure 10. Faxitron™ high-resolution x-ray of device to show any possible damage.

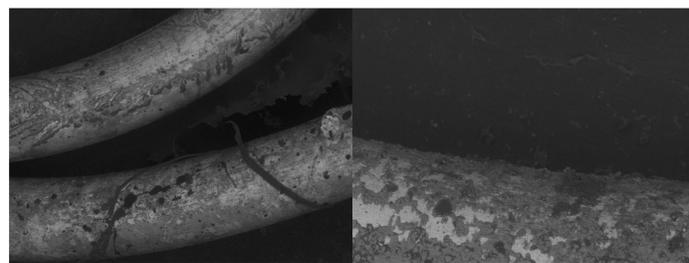


Figure 11. SEM images of the proximal vessel to show changes in the endothelium of the vessel due to implantation as well as growth on the device and imperfections in the device.

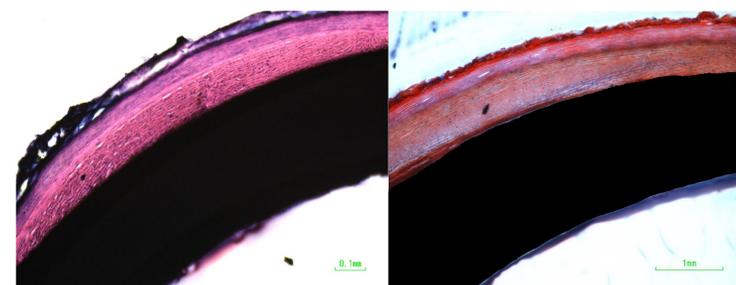


Figure 12. H&E stained (left) and Movat's Pentachrome stained (right) EXAKT ground slide. The same EXAKT ground section was used for both stains by grinding off the stained H&E tissue and re-staining with Movat's Pentachrome.

### Discussion:

The analysis of this project was performed using one medical device in one animal to fulfill the expectations of both FDA regulations and ISO guidelines and was highly successful.

The Hitachi TM3000 SEM was the key to reducing overall specimens needed for analysis due to its ability to image "wet" specimens, without having to perform the destructive steps of critical point drying and sputter-coating. This "environmental SEM" uses low vacuum and has various setting to reduce the affects of "specimen charging" by reducing the beam's intensity.

The addition of the Faxitron™ high-resolution x-ray and intra-luminal stereoscopy completes the endpoints of most evaluative studies.

Finally, being able to histologically process and embed in Spurr's resin, with subsequent EXAKT grinding and staining on the same section completes the analyses. Utilizing the same section for multiple stains on the EXAKT allows for the pathologist to evaluate tissue response for healing, endothelialization and morphologic irregularities.

Using these processes can dramatically decrease the number or test articles needed to fulfill the requirements of FDA and ISO to get clients from concept to clinic faster and more economically.

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