

Physical Characterization of XIENCE™ V Drug Eluting Stent Coating
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Statement of Purpose: Coating integrity, coating uniformity, micro-phase imaging, micro-phase composition, and thermal properties are a few of the key attributes determined by the coating design of a drug eluting stent (DES). Characterization of these coating properties provides important information in understanding and interpreting the device performance, drug release mechanism, and biological response in the vascular environment. These characterization results facilitate formulation and process design to obtain the desired drug/polymer coating mechanical properties, consistent drug release profile, and optimum biocompatibility.

The XIENCE™ V stent consists of a primer layer coating of poly(butyl methacrylate) (PBMA) on which is placed a drug reservoir coating of everolimus blended with poly(vinylidene fluoride-co-hexafluoropropylene) (PVDF-HFP).

CAUTION: XIENCE™ V is an investigational device. Limited by Federal (U.S.) law to investigational use only.

Methods: Physical characterization tools such as Scanning Electronic Microscopy (SEM), Focal Planar Imaging FTIR, Atomic Force Microscopy (AFM), Laser Con-focal Raman (LCR), and Differential Scanning Calorimetry (DSC) are powerful techniques for characterization of materials and DES coatings. These tools are used for (1) coating morphology, (2) drug distribution and coating thickness measurement, (3) surface (swelling) analysis, (4) microstructure and phase dispersion analysis, and (5) thermal transition analysis, of DES coatings.

Results: SEM image of an expanded XIENCE™ V stent after the stent has undergone accelerated aging for 2 years was taken. The coating is conformal with no changes after aging.

The drug distribution imaging and interference patterns for coating thickness uniformity evaluation were taken using focal planar imaging FTIR. XIENCE™ V The relative drug concentration at each location is equivalent to the optical absorbance at drug peak and can be used to quantify the relative drug distribution as a function of positions. An imaging FTIR scan also generates constructive interference patterns when operated under reflectance mode. Coating thickness is calculated from the interference patterns.

The coating thickness and drug density (in IR absorbance unit), respectively, as a function stent locations, were

measured. The results demonstrate a uniform coating across the stent surface.

AFM topographical imaging of a gelatin sample prepared by partially immersing into cold water for a short period of time was first investigated. Results show the swollen region is clearly identified as a high area and the non-immersed as a low area. Same method is used to characterize the swelling behaviour of a drug eluting stent using polymeric materials as drug carrier. Data demonstrate there is no polymer swelling on the XIENCE™ V DES coating.

AFM and Raman images for the analysis of polymer and drug, respectively, on a cross sectional surface of a DES coating were taken and evaluated. The results demonstrate a homogeneous distribution of the drug in the polymer matrix at a sub-micron scale. There is no evidence of phase separation between the drug and the polymer.

Thermal analysis was performed on XIENCE™ V stent coatings by DSC. The thermograms show a melting endotherm indicating the semi-crystalline nature of the PVDF-HFP. A summary of this data and that from stent coatings with no drug is given in Table 1.

| ΔH_f Percent of Polymer Only (n=6) | Melting Point Percent of Polymer Only (n=6) |
|--|---|
| 104 ± 8.9 | 99.0 ± 0.90 |

Table 1: Thermal Properties of the PVDF-HFP/Everolimus/PBMA Coatings Relative to PVDF-HFP/PBMA Coatings with No Drug

The presence of the drug in the polymer does not appreciably alter the PVDF-HFP degree of crystallinity or melting point. This indicates that coating properties which depend on polymer crystallinity, such as ultimate tensile strength, are maintained.

Conclusions: A broad range of DES coating characteristics have been evaluated including coating uniformity, surface morphology, microstructure, and thermal properties,. These results demonstrate that the XIENCE™ V coating design has excellent coating integrity, uniform coating thickness on the OD or ID surfaces, and uniform drug distribution longitudinally. The coating is homogeneous without marked drug-polymer phase separation. These characteristics contribute to good mechanical properties and a permeation controlled, reproducible drug release profile for the XIENCE™ V stent resulting in excellent clinical performance.