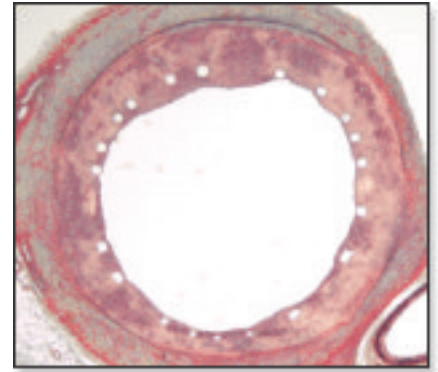


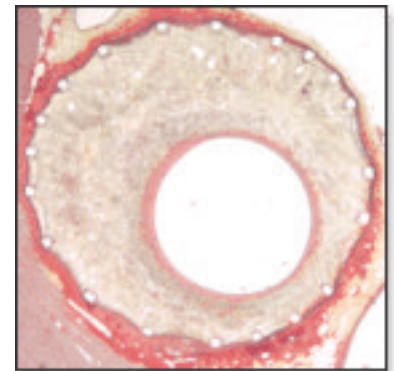
PRE-CLINICAL STUDIES

DISA Vascular has shown that with even a tenth of the drug load compared to certain high dose Paclitaxel Eluting Stents, the tissue response can be highly toxic if the drug is released too quickly. While this toxic effect at the standard endpoint of 28-days in the pig model looks angiographically good - with a widely patent lumen - the histology shows that this patency has been achieved through considerable necrosis of the media, leading to a loss of tone, subsequent lumen dilatation, stent malapposition and then an accumulation of immature, amorphous, thrombus-like tissue between the stent and the media. We found that at 3 months this unstable environment resolves via a profound late-catch-up phenomenon, leading to excessive neointimal hyperplasia. Typical examples of these results are shown on the right:

DISA Vascular have subsequently developed a coating formulation with a proven safe erodible polymer that provides controlled and gradual release of a low total dose of Paclitaxel (10µg on an 11mm stent) without an initial burst. Sustained neointimal inhibition in the porcine model has been demonstrated with this formulation even at the 3 month mark. However the stent does allow for a small margin of late loss, which we believe is necessary for endothelialisation and safety. A small amount of stent coverage does not compromise efficacy.



28 Days



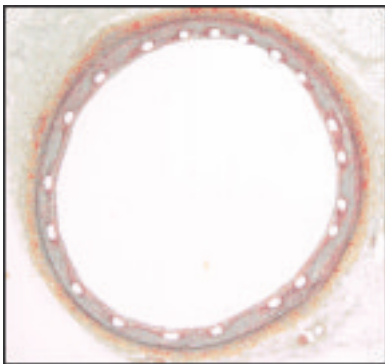
3 Months

Histology results from DISA Vascular porcine study - showing severe toxicity, late malapposition and late catch-up for rapid release Paclitaxel (Journal of Invasive Cardiology, Vol 18, No 8 2006)

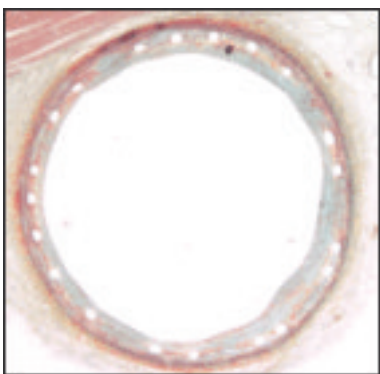
A series of 28-day and 90-day porcine coronary implant studies was conducted by the American Cardiovascular Research Institute (Atlanta, USA).

A total of 15 pigs were used in these studies and 45 implants were analysed. These included a subset of drug-free implants, higher and lower dosing variations and variations in dose-rate to investigate the window of safety of the platform/drug delivery device.

There were no premature deaths in these studies and all animals were sacrificed at the protocol prescribed end-point. At time of explant all stented arteries were widely patent. Histological examination by an independent expert vascular histopathologist confirmed consistent safety of the drug formulation across a narrow range of total dose and elution rates in the porcine coronary model through grading of various healing markers such as inflammation, fibrin, necrosis and endothelial coverage. Results also demonstrated significant neointimal suppression compared to historical bare metal controls, suggesting a level of efficacy. Based on these favourable results, DISA Vascular is currently finalizing its First in Man Clinical Trial to determine the clinical safety of the Stellium DES.



28 Days



3 Months

Histology results from Stellium porcine study - slow release, total elution, stable, progressive healing