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Graphene based coating on bare metal stents improves human coronary artery endothelial cell growth

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Introduction
Revascularisation strategies for coronary artery disease include stent implantation. The first stents used clinically were bare metal stents that were associated with a 20-30% restenosis risk. To address this risk, drug eluting stents were developed, which then introduced late in-stent thrombosis with the requirement for adjunct anti-platelet therapy.

Purpose
The aims of this study are to improve the complication incidence from currently available coronary artery stents by introducing a novel graphene-based coronary stent coating. Graphene is a single layer of hexagonal carbon atoms. The unique properties of graphene make it an ideal material to use as an implantable device coating: It has a high surface to volume ratio; offers an impermeable membrane; is atomically smooth and has been shown to exhibit bio-compatible properties.

Methods
Liquid phase exfoliated graphene based dispersions were manufactured and used to coat coronary stents. Two graphene based dispersions were used, Graphene based 1 and graphene based 2. Different coating methods to achieve thin and uniform coating of the graphene based material on the bare metal stents were also investigated.

In order to study human coronary artery endothelial cell (HCAEC) adhesion, viability and growth, cells were cultured on coated and uncoated stainless steel coronary stents at day 0, and fixed at day 1 and day8. Subsequently, fixed cells were nuclei and actin stained using Hoechst and Phalloidin stains, followed by image acquisition using fluorescence microscopy to count number of adherent cells. One-Way ANOVA with multiple comparison was performed to determine significance.

Results
Raman spectroscopy demonstrated that spray coating achieved the optimal uniform and thin coating when compared to other coating methods. Moreover, cell culture experiments demonstrated significantly increased HCAEC growth (P<0.05) on the Graphene based 1 coating when compared to both Control and Graphene based 2 coating.

Conclusions
Spray coating results in a thin, uniform coating of graphene onto bare metal stents and graphene based coating 1 improves HCAEC number. These data demonstrate initial feasibility of the use of graphene based materials as a
novel stent coating. Further work is aimed at investigating the effect of graphene based coating on neointimal formation in a porcine model of stenting.

**Difference in HCAEC count per mm² stent area at day 8 and day 1.** Significantly better growth is observed on the Graphene based (1) coating when compared to control (*) and graphene based (2) coating (**), P<0.05.