

## Publication

### In vitro study of dual drug-eluting stents with locally focused sirolimus and atorvastatin release

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Within the context of novel stent designs we developed a dual drug-eluting stent (DDES) with an abuminally focussed release of the potent anti-proliferative drug sirolimus and a lumenally focussed release of atorvastatin with stabilizing effect on atherosclerotic deposits and stimulating impact on endothelial function, both from biodegradable poly(L-lactide)-based stent coatings. With this concept we aim at simultaneous inhibition of in-stent restenosis as a result of disproportionally increased smooth muscle cell proliferation and migration as well as thrombosis due to failed or incomplete endothelialisation. The especially adapted spray-coating processes allowed the formation of smooth form-fit polymer coatings at the abluminal and luminal side with 70 % respectively 90 % of the drug/polymer solution being deposited at the intended stent surface. The impacts of tempering, sterilization, and layer composition on drug release are thoroughly discussed making use of a semi-empirical model. While tempering at 80 °C seems to be necessary for the achievement of adequate and sustained drug release, the coating sequence for DDES should be rather abluminal-luminal than luminal-abluminally, as reduction of the amount of sirolimus eluted lumenally could then potentially minimize the provocation of endothelial dysfunction. In vitro proliferation and viability assays with smooth muscle and endothelial cells underline the high potential of the developed DDES.

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