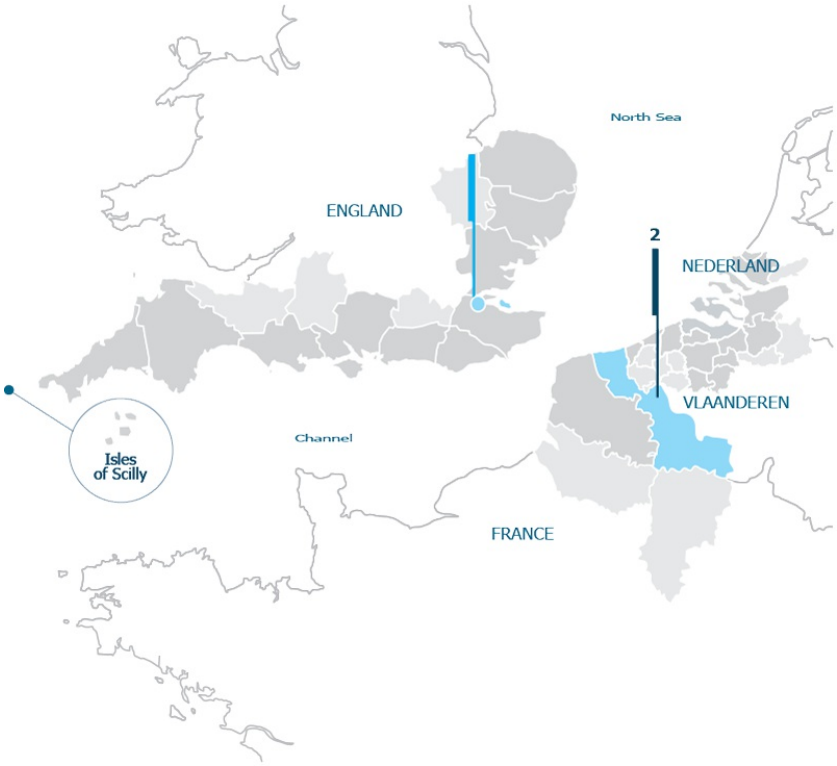
MultiDES

Development of a multifunctional drug eluting stent (DES)

■ Project summary



The main aim of MultiDES is to develop a new vascular stent. It will have a coating which allows the absorption of one or more active substances released for several months in order to reduce the post-operative risk related to stent implantation (restenosis, thrombosis, inflammation or infections). The coated CD polymers serve as a versatile drug delivery carrier where the loading of more than one active substance will be possible and the surgeon can select the type of bioactive molecule that responds to the patient needs before implantation. This new Drug Eluting Stent (DES) is expected to improve patient care by lowering the risk of clot related complications. The highly complementary expertise and knowledge of the two respective Universities will be called upon to pass a technological bolt in the development of a new DES and medical devices. Universities have an excellent infrastructure and it will be beneficial to utilize the full capacity on offer. MultiDES will also encourage the mobility of English and French students as well as cooperation between Universities and hospitals of the crossborder area since many clinicians will also be informed of the project and invited to take part in the clinical evaluation planned as a follow-up study to this project.

■ Activities

What was the project trying to achieve?

The main aim of the MultiDES project is to develop a new vascular stent with a coating, which allows the adsorption of one, or more active substances and subsequent release for several months in order to reduce the post-operative risk related to stent implantation (restenosis, thrombosis, inflammation or infections). The new stent will improve the treatment of cardiovascular diseases. The objectives for the development of multifunctional biocompatible DES are the following: a) Apply uniform coating by using two novel techniques named layer-by-layer (grafting or cross linking) and ink-jetting coating b) Incorporate two active substances on

the stent strut will control release at different time periods c) To evaluate the cyto-compatibility, hemo-compatibility, safety and effectiveness of the produced coated stent d) Conduct full physicochemical characterization studies (e.g. in vitro release) that will help to optimize the DES properties e) Conduct pre-clinical evaluation of the DES therapeutic effect by using the “rat model” f) To contribute to the cross-border area by increasing competitiveness through innovation, research and development. g) Improve patient’s life and wellbeing in the cross-border area h) Increase public awareness and attract interest of medical companies, healthcare providers and hospitals. i) Disseminate and communicate project’s results through a strategic plan of well organized activities

What were the activities implemented?

The project preparation and design prior the project submission involved the following: - Three meetings were held at Lille 2 University in June 2009, November 2009 and June 2010 to discuss and finalize the research proposal. In these meetings the administration, financial, experimental plan roles and responsibilities of each partner were also discussed. -Literature and patent review. A literature study carried out by each partner to identify the advantages of the proposed stent compared to the existing commercial products. -Contacts with cardiovascular experts from the National Health System (NHS) in UK. Further discussions involved the vascular surgeons of CHRU (France) partners to further develop the design of a multifunctional stent. -Group meetings to finalize the project proposal prior to the submission - Initial experimentation at Greenwich and Lille Universities with the preparation and evaluation of the first sample while waiting the approval of the proposal.

■ Results

What were the key results of the project?

The MultiDES project results are summarized below: a. A new DES stent can be developed by applying drug/polymer (e.g. PLGA) coatings on the stent strut. The coatings are highly reproducible, accurate without any defects (bridges) b. The ink-jetting can control the coated drug/polymer ratios, deposited amounts, release profile and combine two drugs on the same stent c. DES can be also produced by applying biocompatible molecules (e.g cyclodextrins) on the metal surface by using a layer-by-layer approach. The polymers are cross-linked on the stent using a chemical reaction while the drug is loaded in a later stage d. The polymers were proved to be biocompatible, hemo-compatible, non-toxic and sage for use in humans e. In vitro drug release could efficiently controlled for 1-3 months depending on the drug/polymer ratios and polymer grades f. A new anti-proliferative drug (station) was used to prevent stent restenosis and it was proved to differentiate between endothelial and smooth muscle cells rendering it a advantageous compared to marketed drugs. g. Preliminary clinical trials showed excellent results when applied to rats. The Intra Stent Restenosis (ISR) values where similar and in some case even better when compared to commercial stents (controls). h. By combining both coating technologies stents with different polymer coatings (e.g. one polymer or combinations of two) could be easily applied on the stent surface i. There was no animal mortality during the stent implantation and also after one month the animals remained healthy. j. These results suggest that MultiDES are safe, non toxic and can be used for cardiovascular diseases. However, further evaluation is required before the stents are implanted to humans.

Did all partners and territories benefit from the results?

The beneficiaries of the project are initially the partners involved and the scientific community within the cross-border area but also worldwide. The partners provided new insights in the development of DES and treatment of coronary artery diseases (CAD). New scientists were trained and improved their skills by participating in the project. Medical companies especially within the cross-border area will benefit from a possible commercialization of the developed stent. The clinical findings attracted already the interest of various companies but also NHS in UK. The general public and patients benefited as they were informed about the symptoms, treatment, risks, surgery, medications, follow-up visits, diet and lifestyle of those suffering from CADs. Public awareness was increased as they were informed about the group's research and development for the past two years. In long term the patients will benefit, as the new MultiDES will improve the treatment of CADs due to its supreme performance, which subsequently will improve patient's life quality and wellbeing. In addition, the consumers will benefit due to the reduced manufacturing cost (fully automated process) of the new stents. This will also reduce the spending on health by various agencies such as NHS.

What were the effects / outcomes for the territories involved?

The MultiDES project improved the conditions for innovation research and development by strengthening scientific research (publications) and fostering of international collaborations. It improved academic competency by providing training and education (research days) to higher education graduates. More importantly the project promoted the cross-border collaboration between three Universities from UK and France. The long-term outcomes include the promotion of patient's access to adequate health (increase life span and wellbeing). In addition, the project is expected to increase the support of industrial R&D especially for SMEs leading to their growth in the case they introduce a new DES in the market.

■ Distinctiveness

What was the real added-value of doing this cross-border project?

The real added value of the project is the combined multidisciplinary expertise of the partners. Without this expertise it would be impossible to build up the MultiDES concept and generate the impressive results. For example the University of Greenwich is the only one in UK working in the development of DES – Lille 2 University has unique clinical expertise in medical implants and Lille 1 University is one of the few in Europe with strong experience in the development of implants with LbL process. The project brought together a unique group of leading researchers in the relevant areas with the support of the 2seas program.

Have any synergies been developed with other projects or networks?

The MultiDES project developed synergies with IDEA project which is also supported by the INTERREF IV A 2seas call. Both projects aim to create a Cluster named Advanced Materials and Pharmaceutical Technologies (AMPTEC) with the participation of partners from UK, France and Belgium including SMEs. The Clusters scope is to establish a Centre of Excellence in the area of pharmaceutical and medical research. The partners under the lead of Lille 1 University applied already to the new INTERREG Cluster initiative but they also plan to continue Cluster

sustainability by applying to the coming INTERREG and Horizon 2020 calls.

What are the key messages , key lessons learned you would like to share?

Our group realized the importance of the communication and dissemination strategy to the successful delivery of the project. These actions increase the interactions with stakeholders and can be proved beneficial. For example the exchange of ideas between scientists can provide a concrete idea of the market's needs, growth and trends. The meetings with patients can also provide a very good understanding of their needs and difficulties before and after implantation of stent. This can affect the stent design (e.g. use of two drugs) in order to improve patients' life. The communication strategy can boost the awareness of the target groups and open new horizons for the project continuation. The 2seas support helped the MultiDES project to enhance the value, quality and productivity of scientific research The cross-border collaboration of three academic institutions resulted in significant clinical findings that can improve the patients' life and wellbeing. The project increased the public awareness about cardiovascular diseases including the developments of the MultiDES activities The project informed the public about the key role and contribution of the 2 seas program in the cross-border area.

Project Information

Title	Development of a multifunctional drug eluting stent (DES)
Total project budget	€ 869 449
ERDF	€ 432 805
Priority & objective	Priority 1 c. Support innovation, research and cooperation between universities, knowledge institutes and businesses
Timeframe	2009-06-01 - 2013-03-31
Lead partner	University of Greenwich
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