Orthopaedic Infections: Pre-clinical Models, Diagnostic Tools and Novel Coatings

Valorisation

Socioeconomic impact

Healthcare-associated infections, also called nosocomial infections, are considered to be the biggest healthcare related complication worldwide. HAI annually affects hundreds of millions of patients worldwide with approximately 4.1 million patients in Europe and about 1.7 million patients in the United States The costs related to these infections are considerable and are mainly a result of prolonged hospital stay and costs related to the treatment of the patient (US: $ 10 billion/year). One of the most common nosocomial infections are surgical site infections (e.g. orthopaedic implants) with an incidence of up to 15%, mainly depending on the surgical treatment and general health of the patient. (data World Health Organisation).

In general an orthopaedic infection has a tremendous impact on the patient's daily life. These infections require multiple major revision surgeries in combination with aggressive antibiotic treatment regimens. If an antibiotic treatment is not successful (due to the severity of the infection or the presence antibiotic resistant bacteria), such infections can lead to severe disabilities, loss of limb, bacterial sepsis and in some cases even death. In most cases orthopaedic infections are the result of the use of foreign material within the patient's body.

Treatment of these infections with antimicrobial substances is a challenging task, mainly due to the high incidence of resistant bacterial strains. Together with the potential risk of systemic toxicity of some broad-spectrum antibiotics, local antibiotic delivery and thus local treatment is the key to success. Currently, infection treatment consists of retraction of the implant and systemic antibiotics in combination with local delivery of antibiotics by antibiotic release from acrylic beads or spacers.

Prevention of orthopaedic infections is achieved by the incorporation of antibiotics in the bone cement used for the fixation of cemented prosthesis. However, there is no local prophylactic measure in case of an uncemented prosthesis, an osteoconductive antimicrobial coating is the proposed solution to this problem.

This thesis describes both experimental models and diagnostic tools for the evaluation of novel biomaterials and orthopaedic implant coatings and also brings these evaluation methods to practise by the assessment of a novel osteoconductive antimicrobial coating.

Collaborations

The majority of the work described within this thesis was funded by the BioMedical Materials program (BMM) which in turn was co-funded by the Dutch Ministry of Economic Affairs. BMM is a Dutch initiative initiated in 2007 to establish a nationwide consortium to promote collaboration in scientific research between academic and industry partners. In general this consortium comprises 18 research projects with a total budget of € 90+ million and holds research positions for over 400 researchers divided over 50 public or private partners.

Close collaboration with other Dutch research consortia like TiPharma (60 projects, 72 partners, € 260 million), CTMM (22 projects, 119 partners, € 300 million) and TeRM (6 projects, 13 partners, € 25 million) enables open communication and discussion resulting in innovation in medical science all originating from Dutch soil.

BMM comprises multiple projects and the herein described research was part of the BMM NANTICO project (Nonadhesive ANTImicrobial COatings for biomedical implants). This project was a collaboration between 4 academic partners (University Medical Centre Groningen, Amsterdam Medical Centre, Utrecht University and Maastricht University Medical Centre) and 2 industrial partners (DSM and Dolphys Medical), with the general focus on antimicrobial coating development and coating evaluation for biomedical implants (e.g. urinary catheters, vascular catheters and metal prosthesis).

This thesis mainly focusses on the implementation and evaluation of antimicrobial coatings for orthopaedic implants, which was mainly a joined effort of DSM Biomedical (coating development and the application to titanium implants) and the department of Orthopaedic Surgery of the Maastricht University Medical Centre (experimental model development and coating evaluation).