The below described study will investigate the impact of nanoparticles (particles that are smaller than 100 nm) derived from orthopedic implants on the functioning of platelets – blood elements which play an important role in clotting and bleeding.

Total knee arthroplasty (TKA) and total hip arthroplasty (THA) (the types of surgery where your joint that is badly affected by arthritis is exchanged for an artificial one) are proven procedures for patients with advanced arthritis. A total of 4.5 and 6.7 million people in the US are currently living with an artificial hip or knee respectively. In England, a country with a population of about 60 million, in 2012 alone, more than 165 thousand THA and TKA procedures have been registered. This number is predicted to grow yearly in the UK to anywhere between 600 thousand to 1.4 million THA and TKA procedures performed in 2030. Those numbers show that currently approximately 2% of the population of high and medium income countries live with artificial hip or knee joints, and that this percentage will increase each year.

Venous thromboembolism (VTE) is a very serious short- and/or long-term potential complication of THA or TKA – one that we try to prevent using selected medications. A recent study found that as much as 1.3% of patients undergoing THA or TKA experience postoperative VTE, and that this risk does not change over time.

Hip or knee endoprosthesis elements can be generally divided into those composed of metal, ceramics and/or polyethylene. However, all metals are subject to corrosion over time in the human body. Shear stress and implant wear from joint articulation further cause damage to all types of implants, regardless of the material they consist of. This causes release of wear debris, nanoparticles (NPs) and ions. These particles can remain in the local tissues or disseminate into the blood stream, and accumulate in distant sites such as the liver or spleen. Patients with metal-on-metal hip implants are known to have elevated levels of several metal ions (ex. Cobalt and Chromium; even up to 200 time the norm) as well as metallic NPs in their blood. There are serious concerns over the safety of NPs released from orthopedic implants, when they reach the bloodstream. For example NPs of TiO_2 (a substance used for coating of some of the joint implants) have been shown to activate blood platelets, induce thrombus formation in mice and exert negative effects on some of the human cells.

However, though a large amount of studies has been performed on the subject of toxicity of NPs released from orthopedic implants, their impact on blood platelets has not been studied. Blood platelets are one of the key factors in blood coagulation, and whether they function correctly can be the difference between health and serious disease (for example thrombosis). The lack of studies on NP-platelet interactions might have been caused by a lack of a tool that could investigate in real time the potential platelet aggregation caused by implant-related NPs. Our group has shown that a machine called quartz crystal microbalance with dissipation is able to measure NP-induced platelet aggregation in real time at concentrations that are undetectable by other techniques. Using this technique, NP-induced platelet aggregation can be quantified in real time under flow conditions and later directly analyzed on the sensor using microscopic techniques. Thus, the planned study will explore, using innovative technologies, a completely new field, as the current literature lacks data on the interactions between platelets and NPs derived from orthopedic implants. This study will not only describe the compatibility of NPs derived from orthopedic implants towards platelets but will also investigate the mechanisms through which NPs cause platelet activation and aggregation.

The main impact the results of this study may potentially have on the society stems from the fact that we will be able to elucidate the mechanisms by which NPs derived from orthopedic implants interact with platelets and cause them to form thrombi. If we know how this happens, we will also be able to prepare appropriate treatment strategies to prevent this. This will not only help to save human lives and health but will also significantly reduce the strain on the healthcare system budget, as one VTE-related hospitalization costs between 3500 euro (Europe) and 9000 USD (USA). By limiting the number of VTE episodes we could use the money we save to battle other diseases.

The author of this study hypothesizes that NPs released from orthopedic implants may alter platelet biology increasing/decreasing their potential to adhere and aggregate, thus potentially leading to an increased risk of thrombosis/bleeding in patients with such implants. That is why the aims of this study are to (1) determine the biocompatibility of NPs released from orthopedic implants in regards to blood platelets; (2) determine the role of NPs released from orthopedic implants in NP-induced platelet aggregation; (3) determine the pathways by which chosen NPs interact with platelets; (4) in case the tested NPs induce platelet aggregation – to test whether it is possible to modulate this NP-induced platelet aggregation using selected substances.