ABSTRACT

The first part of this thesis provides an update on thrombolytic treatment of peripheral arterial occlusions. In chapter 2 we provide an extensive overview of thrombolysis throughout the years: a systematic review of literature provides an update of all reported patient cohorts with peripheral arterial occlusions treated with catheter-directed thrombolysis since its introduction. In chapter 3 the results of a contemporary high-dose thrombolysis protocol performed on an intensive care unit are discussed with the specific aim to assess risk factors of bleeding complications and predictors of successful lysis. In chapter 4 the results of a low-dose thrombolysis protocol performed on a general ward are evaluated: it illustrates whether it equals the efficacy of a high-dose protocol and its impact on patient safety with regard to adverse events. In chapter 5, the results of a contemporary protocol in an Asian population are described, since peripheral arterial occlusions pose a globally increasing problem but are expected to increase exponentially especially in Asian populations.

In the second part of this thesis we describe novel treatments of thrombolytic therapy of peripheral arterial occlusions. We focus on the use of contrast-enhanced ultrasound, in an ultimate effort to improve thrombolytic therapy and eventually reduce the patient burden. In chapter 6 we describe an experimental pilot study using contrast-enhanced ultrasound to accelerate conventional thrombolysis in a porcine model of peripheral arterial occlusion. Chapter 7 illustrates the translation of this experimental technique from bench to bedside and will discuss the protocol of a phase-II clinical trial to investigate the safety and feasibility of this technique in patients with acute limb ischemia due to peripheral arterial occlusion. In chapter 8 we discuss an experimental setup which investigates the feasibility of combining microbubbles and an ultrasound catheter to treat peripheral arterial occlusions.

As a final novel treatment, local thrombolysis without catheter could be reality since chemical engineering allows to incorporate therapeutic agents into the microbubbles by different mechanisms. This provides the opportunity for targeted drug delivery since the compound can be unloaded at the site of interest by only local external application of ultrasound. In chapter 9 we investigate this new technique for feasibility and lytic efficacy in our porcine model of peripheral arterial occlusion.