Valorization addendum

Relevance for society

Cardiovascular disease is the leading cause of morbidity and mortality in the modern society\(^1\). Patients with clinical manifestation of atherosclerosis are regularly subjected to revascularization procedures such as balloon angioplasty with or without stent implantation or endarterectomy. Post-procedure, patients receive long term dual antiplatelet therapy to ensure thrombosis prophylaxis until full endothelial recovery. Meanwhile, secondary interventional procedures with high risk of bleeding, such as dental extractions or surgical interventions in multimorbid patients are denied. It is of high clinical relevance to develop a screening protocol to monitor early endothelial recovery which could help in personalization of medication and deciding the cessation of otherwise unnecessarily prolonged medication.

Additionally, cardiovascular patients with subclinical atherosclerosis usually have accompanying pathologies such as oscillatory arterial blood pressure. Our results suggest that molecular ultrasound imaging of acute endothelial activation may be suitable to assess the risk of patients with oscillatory arterial blood pressure to develop biologically-active atherosclerotic lesions and thrombosis.

Target groups

Target groups of the research studies included in this dissertation are 1) patients with symptomatic atherosclerotic carotid arteries, which are subjected to revascularization procedures; 2) cardiologists; 3) the community of scientists in basic research; and 4) pharmaceutical and medical industry.

The advances in knowledge presented within this thesis may be beneficial for the development of new imaging protocols and contrast agents for patients subjected to carotid artery revascularization procedures or patients with oscillatory arterial
blood pressure and hypercholesterolemia. These new imaging approaches could be easily performed by cardiologists with general US imaging competences. Moreover, advancing low cost diagnostic methods, which could partially replace expensive diagnostic imaging approaches, such as PET, CT, and MRI, would have both health and socio-economic impact, as it decreases the financial burden on the healthcare system and simultaneously increases US’s potential as a routine medical prevention modality. Additionally, this thesis reports findings and results for scientists, as well as pharmaceutical and medical industry, that may further use these innovative methods and principles as basis for future research and to develop new diagnostic and therapeutic agents.

**Activity/Products**

Several new findings have been developed and described in this dissertation. An *ex vivo* TPLSM protocol for imaging explanted murine carotid arteries has been described and implemented in Chapter 2. Moreover, TPLSM was combined with molecular US imaging and the combination is presented as a multiscale diagnostic approach.

Finally, different targeted MB have been generated that can be used to monitor endothelial regeneration (Chapter 2 and Chapter 4) or to evaluate transient endothelial activation under acute blood flow variations (Chapter 5).

**Innovation**

The studies included in this thesis are innovative thanks to several reasons. Multiscale molecular vascular imaging with TPLSM and US using targeted MB was successfully applied as new approach to examine endothelial dysfunction. Moreover, dual TPLSM/US molecular imaging of carotid arteries, subjected to high shear stress, can be described as novel and innovative. Additionally, the idea to use molecular US to evaluate vascular damage and repair after
revascularization procedures, or to assess early vascular dysfunction triggered by oscillatory arterial blood pressure is as well original.

**Implementation**

The research results of this thesis have been implemented and shared in numerous presentations on national and international conferences, receiving international recognition and a best poster award at the 81st Congress of the European Atherosclerosis Society, Lyon 2-5 June, 2013, France.

Moreover, the research results have been published in international peer-reviewed journals with high impact factor.

**References**