29.1 Introduction

Atherosclerosis is considered a paradigmatic age-associated disease, since it progresses slowly and manifests clinically significant symptoms primarily in the elderly segment of the population. However, more recent evidence suggests that the atherosclerotic process begins at a much earlier age and thus may be accessible to early diagnostic imaging approaches and imaging guided targeted therapeutic interventions [1–4]. Since atherogenesis begins early, the prolonged course of disease provides a “window of opportunity” for in vivo diagnosis prior to clinical manifestations, as well as the opportunity for early, specifically targeted, therapy.

Novel “molecular” technological developments in the last decade have advanced beyond “non-molecular” or “classical” radiological techniques to allow imaging of cardiovascular anatomy and physiology on a macroscopic scale, making it possible to image atherogenesis in vivo on the cellular and sometimes even molecular level [5–14]. Non-invasive in vivo imaging is a fast emerging specialty in experimental Radiology aiming at developing imaging modalities and appropriate imaging agents to visualize the molecular basis and pathophysiological processes of many pathological conditions, including cardiovascular diseases (CVD). Several serological markers of atherosclerosis, including pro-inflammatory cytokines and vascular stress proteins are known predictors for, and/or diagnostic biomarkers of, CVD, and are accepted for both routine and experimental use to monitor patients at risk or after manifestation of cardiovascular symptoms [15, 16]. Numerous serological factors are known to be involved in the pathophysiology of atherosclerosis, but not all proved useful targets for molecular imaging techniques.
29.2 Imaging Targets in Atherogenesis

The list of potentially useful factors in the cascade of events occurring in atherosclerosis has been narrowed down to some very promising endothelial targets.

Atherosclerosis has historically been considered a lipid storage disease. However, not all patients who develop CVD present with a history of hypercholesterolemia [17]. Thus, in the pathogenesis of atherosclerosis a fundamental role for inflammation in all stages of this disease must be considered – from its molecular initiation, through progression, and also during “non-molecular” thromboembolic complications of fully developed plaques [18, 19]. Therefore, atherosclerosis does not result simply from a subintimal accumulation of lipids in large arteries [20]. An atherosclerotic lesion can represent different stages of an inflammatory process in the artery that may be visualized with molecular imaging techniques (Fig. 29.1); if excessive, this process will eventually result in a complicated lesion with plaque rupture and thrombosis.

During many of these stages, the endothelial expression of certain pro- and anti-atherogenic molecules and proteins might be assessable for specifically targeted, non-invasive molecular imaging techniques. This consideration has several consequences in prevention, risk stratification, diagnosis, and therapy.

When stressed, endothelial cells, which under normal circumstances prevent adhesion of leukocytes and platelets, are initiated to express surface proteins, e.g. heat-shock proteins (HSPs) together with cellular adhesion molecules, such as

![Fig. 29.1 Schematic overview of atherogenesis and the expression of pro- and anti-atherogenic molecules that might be assessable for targeted non-invasive molecular imaging techniques](image)