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Influence of plaque calcifications on coronary stent fracture: A numerical fatigue life analysis including cardiac wall movement

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ABSTRACT

Coronary stent fracture is still an unresolved issue in the field of minimally invasive cardiovascular interventions due to its high rate of incidence and uncertain clinical consequences. Recent studies, based on clinical data, proved that there are several factors which can be identified as independently responsible of coronary stent fracture. Among these, calcifications, which increase the local stiffness and heterogeneity of atherosclerotic plaques, seem to play a major role. From a mechanical point of view, stent fracture in coronary arteries is triggered by the cyclic loading of pulsatile blood pressure combined with the movement of cardiac wall.

In this context, this study aims at simulating the stent expansion in a model of epicardial atherosclerotic coronary artery and correlating the effects of cyclic blood pressure and cardiac wall movement on the stent fatigue resistance. Two ideal cases of atherosclerotic plaques were modelled: the first one included a localised plaque calcification; the latter one did not include such calcification.

Results of stress/strain and fatigue analyses confirmed the influence of the plaque calcification on potential fracture of the devices. In addition, the effects of cardiac wall movement were quantified as more dangerous causes of the stent fatigue fracture with respect to the internal blood pressure oscillations.

In conclusion, this study demonstrates the increased risk of coronary stent fracture associated to the presence of localised plaque calcifications. This work also suggests the necessity of more realistic biomechanical models which takes into account the heterogeneity of atherosclerotic plaques in order to assess the mechanical performances of coronary stents.

1. Introduction

Coronary stent fracture (CSF) (Fig. 1A) has become an important issue in cardiovascular interventions. Preliminary reports based on follow-up angiographies quantified the incidence of CSF after drug-eluting stent implantation between 1% and 2% (Aoki et al., 2007; Shaikh et al., 2008). However, more recent studies, which were based either on autoptic analyses or on novel imaging techniques with improved spatial and temporal resolutions (Nakazawa et al., 2009; Lim et al., 2008), showed that CSF occurred in up to the 30% of the investigated cases. The type and severity of stent fracture play a fundamental role in the clinical consequences of CSF. In fact, recent clinical studies proved that the effects of CSF can be extremely variable among patients, ranging from asymptomatic cases to increased rate of target lesion revascularization, to stent thrombosis or even to sudden death (Kuramitsu et al., 2012; Adlakha et al., 2010). Consensus on routine follow-up and diagnostic methods to detect and to treat CSF has not been reached yet. In this context, CSF still remains an unresolved clinical problem.

From a mechanical point of view, failure of metallic structures like stents can be classified according to two categories: i) rupture due to static forces when these cause a stress higher than the ultimate material limit (i.e. static rupture) or ii) rupture due to cyclic loadings which are lower than the ultimate material limit (i.e. fatigue rupture). In particular, coronary stents have to operate within an environment which is extremely challenging. After being implanted and highly deformed through balloon inflation, stents undergo cyclic loading caused by both the pulsatile blood pressure and the cardiac wall movement occurring during each heartbeat. Accordingly, anatomical studies proved that coronary arteries undergo important curvature changes throughout the cardiac cycle (Liao et al., 2002). Experimental and in vivo studies showed that several factors may be identified as independently responsible for CSF. Among these, the presence of overlapping

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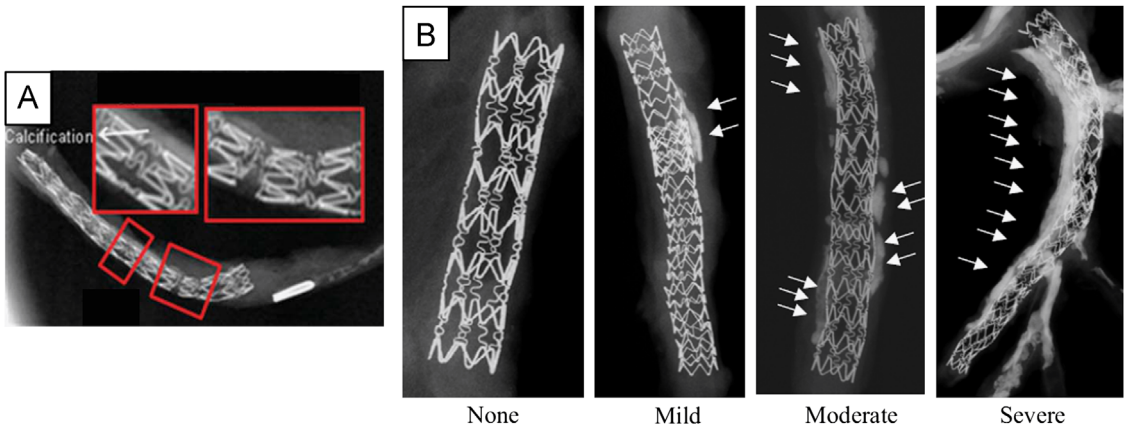

Fig. 1. (A) Example of coronary stent fractures on a Cypher vein graft stent in correspondence of a heavily calcified plaque. In the right inset is clearly visible how the stents split in two distinct parts. Image modified with permission from Halwani et al. (2012). (B) Different plaque calcifications in coronary arteries: the rightmost image shows a highly asymmetric calcified plaque. Arrows identify the location of mild, moderate or severe plaque calcifications. Image modified with permission from Nakazawa et al. (2009).

stents, plaque calcifications, high curvature of the vessel, length and design of the stent seem to play a role in CSF (Nakazawa et al., 2009; Halwani et al., 2012; Aoki et al., 2007; Shaikh et al., 2008). In particular, plaque calcifications are currently considered as an active disease process similar to embryonic bone formation (Hjortnaes et al., 2013). Their initiating mechanisms are not fully understood yet, but they appear as a consequence of tightly regulated processes culminating in organized extra-cellular matrix deposition by osteoblast-like cells (Johnson et al., 2006). Eventually, the calcification process results in highly stiff bone-like structures, locally increase the heterogeneity of atherosclerotic plaques and their radial stiffness.

Computational models have been widely used for their ability to replicate the biomechanical response of medical devices under physiological conditions. Also, regulatory bodies have begun to consider computational modelling as a valid tool to evaluate intravascular stents through both pure stress/strain analyses and fatigue analyses (FDA, 2010). For this purpose, both static structural numerical models (Martin and Boyle, 2011; Morlacchi and Migliavacca, 2013) and fatigue life studies (Marrey et al., 2006; Hsiao et al., 2012; Schievano et al., 2010; Li et al., 2010) have been developed to provide new insights and, eventually improve both the clinical procedures and the stent design.

In this study, structural finite element models were implemented to simulate the stent expansion in a simplified model of epicardial atherosclerotic coronary artery and to investigate the effects of cyclic blood pressure and cardiac wall movement on the fatigue resistance of the stent. Two different cases were compared to quantify the response due to the presence of a localised calcification in the atherosclerotic plaques. The aim of this work was to provide a mechanical explanation of the increased risks of stent fracture when associated with the presence of plaque calcifications (Fig. 1B) (Halwani et al., 2012). Furthermore, since the current state-of-the-art mostly focuses on the effects generated by the blood pressure, the effects of either cardiac wall movement or blood pressure were explored to investigate their relative importance during fatigue analysis of coronary stents.

2. Material and methods

2.1. Finite element model of stent expansion

A finite element model of a simplified epicardial atherosclerotic coronary artery (Fig. 2A) was created using Rhinoceros 4.0 Evaluation CAD software (McNeel and Associates, Indianapolis, IN, USA). The model of the coronary artery was embedded into the myocardium and characterized by a curvature radius of 20 mm (Ding and Friedman, 2000) and a total length of 31 mm. Lumen radius and arterial wall thickness were equal to 1.35 mm and 0.9 mm, respectively. The artery was surrounded by the cardiac wall for half of its circumference; the wall was assumed to be 7 mm thick, which is within the physiological range of adult human left ventricular walls (Grossman et al., 1975). The geometry was discretized with a total of 245,856 linear reduced integration hexahedral elements. In particular, 146,016 and 99,840 elements were used for the cardiac wall and the artery, respectively. A grid sensitivity analysis was performed to guarantee the independence of the solution from the spatial discretization. The material of the arterial wall was described as an incompressible isotropic and homogeneous material fitting the experimental data in the circumferential direction as obtained by Holzapfel et al. (2005) for the *tunica media*. In particular, the following reduced polynomial strain energy density function of the sixth order was implemented:

$$U = C_{10}(\bar{I}_1 - 3) + C_{20}(\bar{I}_1 - 3)^2 + C_{30}(\bar{I}_1 - 3)^3 + C_{40}(\bar{I}_1 - 3)^4 + C_{50}(\bar{I}_1 - 3)^5 + C_{60}(\bar{I}_1 - 3)^6$$

where C_{10}–C_{60} are the material parameters (Table 1) and $\bar{I}_1$ is the first deviatoric strain invariant. Experimental data were modified removing the first portion of the stress–strain curve up to 0.15 of strain. This assumption can be justified by the fact that the model of the artery was designed in a pressurized condition (radius = 1.35 mm, diastolic blood pressure) while experimental tests were performed on fully unloaded tissues. The presence of the cardiac wall in the model is a convenient way to simulate the heart movement and transfer its cyclic kinematic displacements to the stented region, avoiding the presence of concentrated external boundary conditions close to the region of interest. An elastic material model was adopted for the cardiac wall with Young modulus and Poisson ratio equal to 20 MPa and 0.3, respectively. Simulations with Young moduli ranging between 2 and 40 MPa were also carried out to investigate the sensitivity of the model to this modelling assumption.

An asymmetric atherosclerotic plaque (Fig. 2B) was included in the model, taking into account the typical cross-sectional plaque distribution which is larger at the myocardial side of coronary arteries (Iwami et al., 1998). The maximum grade of stenosis value was equal to 60% of the arterial lumen and localised at the central section of the model. Two different models of atherosclerotic plaques were used, differing in the presence of a localised calcification within a homogeneous