



## *In vivo* porcine left atrial wall stress: Effect of ventricular tachypacing on spatial and temporal stress distribution

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### ABSTRACT

Animal models of ventricular tachypacing (VTP) have been successfully used to reproduce the relevant features observed in patients with atrial fibrillation, such as increased atrial pressure and volume, ion-channel alterations and fibrosis. After performing VTP on a healthy Yorkshire pig, we measured an increase in volume of 60%, a two-fold rise in pressure, and a complex pattern of local mechanical, histological and biochemical changes, including a generalized stiffening of the wall. A protocol recently developed was employed to generate computational models of the porcine left atrium mechanics in healthy conditions and after VTP. Comparison of the stress distribution in the healthy vs. VTP case provided a map of how pressure overload affects and modifies left atrium mechanics. Overall, a positive increase in stress was computed after the VTP treatment. Regions of large increase in the stresses post-VTP were the appendage boundaries, the area around the lower pulmonary vein and the area in the front of the atrium towards the appendage. Due to the elevated stress, the back of the atrium mainly modified its mechanical response, while the appendage remodeled both its shape and its mechanical properties. Large changes in the shape of the mitral valve annulus could be observed as a consequence of the remodeling in the front of the atrium. The relation between local mechanical stress and remodeling that emerges from the results is in agreement with our hypothesis that the structural changes in the atrium are a consequence of a stress-mediated mechanism.

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### 1. Introduction

Wall stress exceeding physiological level has been linked to left ventricular remodeling after a myocardial infarction (Savoie et al., 2006; Yoshiyama et al., 2005; McKay et al., 1986). Consequently, wall stress reduction is an important goal in the treatment of heart failure, its benefits ranging from reduced oxygen consumption to control of adverse remodeling (Grossman et al., 1975; Aikawa et al., 2001). The same paradigm, vis-a-vis the importance of wall stress, is true for the atrium (O'Brien et al., 2000).

Atrial fibrillation (AF) is the cardiac arrhythmia most commonly encountered in clinical practice and a leading cause of stroke (Wolf, 1998; Wolf et al., 1991a, 1991b, 1978, 1998). AF affects approximately 6% of the population over the age of 65 (Heeringa et al., 2006) and it is estimated that more than 900,000 strokes/year are due to AF alone in North America and Europe, a number that is expected to rise (Heeringa, 2010). AF is characterized by disorganized electrical activation, which greatly

reduces the ability of the atria to fill the ventricles (Wang et al., 1996). Although a clear etiology has not been identified, AF results from the synergic action of electrophysiological, biochemical and structural remodeling (Kourliouros et al., 2009; Schoonderwoerd et al., 2005).

AF is commonly associated with various cardiac pathologies, including congestive heart failure, hypertension and mitral valve disease (Gerdtts et al., 2002; Gottdiener et al., 2006). All these pathologies increase the pressure in the atrial chambers. Animal models of ventricular tachypacing (VTP), where the left ventricle is continuously paced at a high rate, have been successfully used to reproduce the relevant features observed in patients suffering from AF, such as increased atrial pressure, ion-channel alterations, fibrosis, and atrial dilatation (Burstein et al., 2009; Shiroshita-Takeshita et al., 2007; Cardin et al., 2003). Chronic pressure overload induces modifications in the shape and structure of the atria, as well as electrical changes and a state of reduced contractility (Eiras et al., 2006; Greiser et al., 2009; Chang et al., 2007). The process affects the individual regions of the atrium differently due to the heterogeneity of the atrium itself in terms of electrical as well as mechanical properties, i.e. ion channel densities, wall thickness, fiber orientation, material properties.

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