Title Page: LETTERS TO THE EDITOR

**Myocardial inflammation in brugada syndrome**

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To the editor,

We read with interest the provocative work by Pieroni et al. (1) describing the relationship between electroanatomic abnormalities and the pathological substrate in Brugada syndrome. In particular we noted that right ventricular (RV) biopsy guided by 3-dimensional RV electroanatomic mapping identified histopathological abnormalities including fibrosis in 15/20 cases and lympho-mononuclear infiltrates in 12/20 cases. The presence of inflammation was associated with significantly greater areas of low voltage present on unipolar and bipolar maps.

Although we commend Pieroni et al. for their important work toward understanding Brugada syndrome and its purported structural basis, we would exercise caution in implicating myocardial inflammation in its pathogenesis based upon these data. Fibrosis alone would explain the areas of low voltage seen in their patients. Indeed, we have reported previously, in this *Journal*, pathological findings from a series of 12 cases of Brugada syndrome, six diagnosed *in vivo* and six following a sudden death with direct comparison to a control of non-cardiac deaths (3). In line with the observations of Pieroni et al., the Brugada syndrome group showed increased epicardial and interstitial fibrosis, particularly within the right ventricular outflow tract, with quantification of collagen content further supporting the observation. However, there was no evidence of increased myocardial inflammatory cells among the Brugada group compared to controls. This is concordant with our extensive experience of hearts from sudden cardiac and non-cardiac deaths at a large UK cardiac pathology centre. Minor lympho-mononuclear infiltrates as observed by Pieroni et al. in figure 1 of their article may be seen in otherwise normal myocardial tissue. We propose that future histopathological and immuno-histochemical research into inflammation and fibrosis in BrS should include a blinded control sample with objective quantification of signal and interpretation in this context.

**References**

(1) Pieroni M, Notarstefano P, Oliva A, Campuzano O, Santangeli P, Coll M, et al. Electroanatomic and Pathologic Right Ventricular Outflow Tract Abnormalities in Patients With Brugada Syndrome. J Am Coll Cardiol 2018 Dec 4;72(22):2747-2757.

(3) Nademanee K, Raju H, de Noronha SV, Papadakis M, Robinson L, Rothery S, et al. Fibrosis, Connexin-43, and Conduction Abnormalities in the Brugada Syndrome. J Am Coll Cardiol 2015 Nov 3;66(18):1976-1986.