

## **Parasympathetic Denervation by the Infusion of Ethanol into Vein of Marshall.**

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Myocardial fibers and nerves adjacent to the vein of Marshall (VOM) have been implicated as a source of ectopic beats initiating paroxysmal atrial fibrillation (AF), as a connection pathway of left atrium (LA) and left pulmonary veins (PVs), and as a source of arrhythmogenic autonomic innervation. These various complex functionalities of the LOM can constitute the genesis of atrial fibrillation (AF). It has recently been reported that VOM ethanol infusion creates a low-voltage area in the LA adjacent to the VOM modulate autonomic tone. Intrinsic cardiac nerves (ICN) can modulate atrial muscle physiology in a pro-fibrillatory manner. ICN ablation has been proposed as an adjunctive or stand-alone therapy for AF. The vein of Marshall is considered part of the ICN: it has been shown to contain sympathetic and parasympathetic innervation and it coincides with regions known to harbor ICN. It becomes the VOM caudally as it connects with the coronary sinus. Animal and human surgical open-chest studies have shown that high-frequency electrical stimulation (HFS) at the VOM area may induce parasympathetic responses characterized by significant slowing of atrioventricular (AV) nodal conduction and AF induction. We have developed a technique for retrograde VOM ethanol infusion and have shown its feasibility, safety, and clinical usefulness in terms of curing AF in humans. We hypothesized that: 1) HFS performed within the VOM can elicit parasympathetic responses; and 2) the VOM can be used as a vascular route to target these epicardial ICN and regionally denervate the LA with chemical ablation which includes ethanol infusion into the VOM.