Mechanism of arrhythmia: biological VT ablation

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Ventricular tachycardia (VT) arises from zones of slow conduction around regions of fibrosis in the myocardium. This consideration of mechanism highlights the possibility that VT may be suppressed by biological substrate modification to decrease fibrosis and increase healthy tissue. In the process of mechanistic investigations into cell therapies for heart disease, we discovered a central role for extracellular vesicles (EVs) as paracrine mediators of therapeutic bioactivity. EVs reproduce the benefits of cells, and they are easy to isolate, store and deliver, making them viable cell-free therapeutic candidates. EVs work by delivering RNA and protein payloads to target cells, and they are known to suppress fibrosis. We therefore mapped VT in pigs and injected cardiac EVs into zones of slow conduction. Two weeks later, the amount of fibrous tissue was decreased, and slow conduction (as gauged by late potentials) was virtually eliminated. Likewise, animals previously susceptible to VT induction by programmed stimulation were rendered non-inducible after local injection of EVs. The next generations of cell-free biologics (EVs) may provide new means of treating refractory VT.