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CASE REPORT

CLINICAL CASE: DAVINCI CORNER

Myoarchitecture of the Sinoatrial Node and its Relevance for Catheter Ablation

Anatomy and Histology

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Anatomical work in the early 20th century led to the description of the sinoatrial node (SAN) as a distinct structure responsible for pacemaker function in mammals and humans, first described by Keith and Flack[1] as "a small condensed area of tissue, just where the cava sinks into the right auricle." Their observation of the reliable presence of this unique structure in all the specimens examined led to an assertive deduction of its importance as the myocardial tissue responsible for initiation of cardiac impulses.[1] This hypothesis was later confirmed by translational anatomical experiments and observations.[2]

Anatomical studies of the SAN have great relevance in electrophysiology when considering invasive management of arrhythmias arising within or in proximity to the SAN region. This editorial has 2 parts: the first part summarizes key anatomical and histologic concepts of the SAN myoarchitecture and its surrounding structures, whereas the second part integrates these anatomical concepts with modern electroanatomical mapping and imaging guidance techniques to facilitate spatial understanding for safe and effective ablations.

LEARNING OBJECTIVES

- To understand how the unique myoarchitecture of the SAN and its cellular composition is responsible for cardiac pacemaker function.
- To learn common and uncommon variants of SAN anatomy, blood supply and innervation in order to guide safe and effective ablation of arrhythmias arising within or near the SAN.

ANATOMICAL CONSIDERATIONS

The SAN is a crescent-shaped structure located subepicardially within the sulcus terminalis of the right atrium (RA), lying inferior to the crest of the right atrial appendage (RAA), also known as the arcuate ridge. The SAN is covered by epicardial fat along the terminal groove, thus making it invisible by gross examination unless its adjacent tissue is dissected.[3] SAN anatomical variations in shape, extent, and location within the sulcus terminalis and anatomical proximity to the phrenic nerve (**Figures 1A to 1C**, Videos 1 and 2) have relevance for ablation therapy of atrial arrhythmias in this region.[4,5]

When describing the SAN using an attitudinal orientation, its body (wide and short) is located cranially near the superior vena cava (SVC) orifice, whereas its tail portion (narrow and long) extends caudally toward the inferior terminal crest (TC) and the Eustachian valve of the inferior vena cava. The

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ABBREVIATIONS AND ACRONYMS

RA = right atrial

RAA = right atrial appendage

RCA = right coronary artery

SAN = sinoatrial node

SVC = superior vena cava

TC = terminal crest

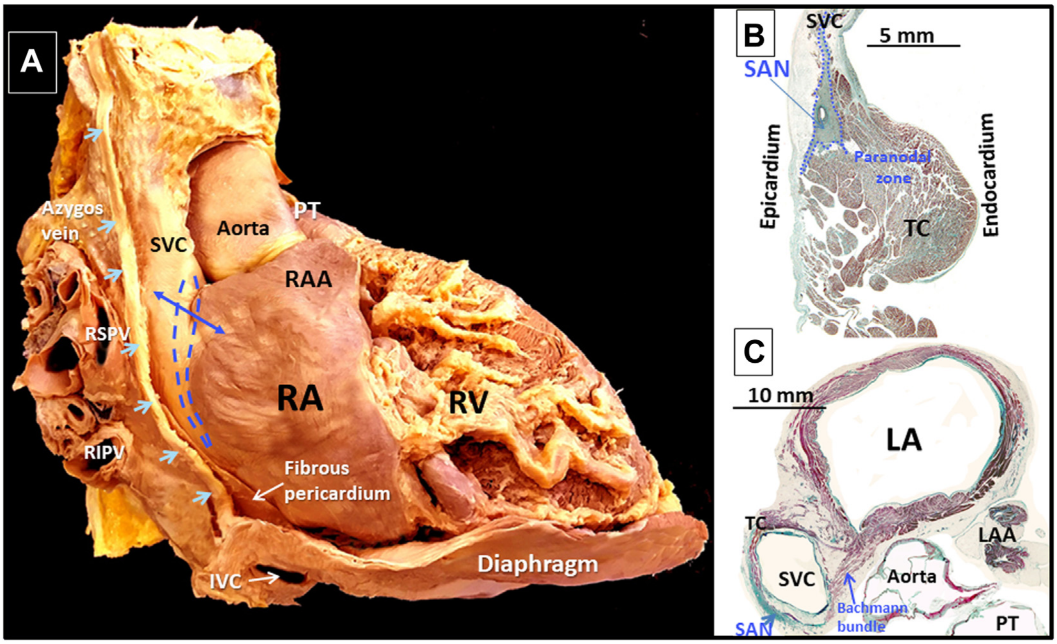
TX = transitional zone

SAN tissue is contained within an area defined by the intersection of the sulcus terminalis, the lateral border of the SVC, and the superior border of the RA. Of relevance is the confluence between the TC at its origin in the interatrial groove and the rightward muscular extensions of the interatrial Bachmann bundle[6] (**Figures 1A to 1C**). An anatomical variant of the SAN has a more anterior position extending across the crest of the RAA in a horseshoe shape.[7] Although the body of the SAN is subepicardial, lying 0.1 to 1 mm deep within the fatty tissue of the sulcus terminalis, as it moves caudally, it gradually penetrates intramyocardially into a subendocardial position[8,9] (**Figures 1A to 1C**).

HISTOLOGY AND ITS RELEVANCE TO PACEMAKER CELL FUNCTION

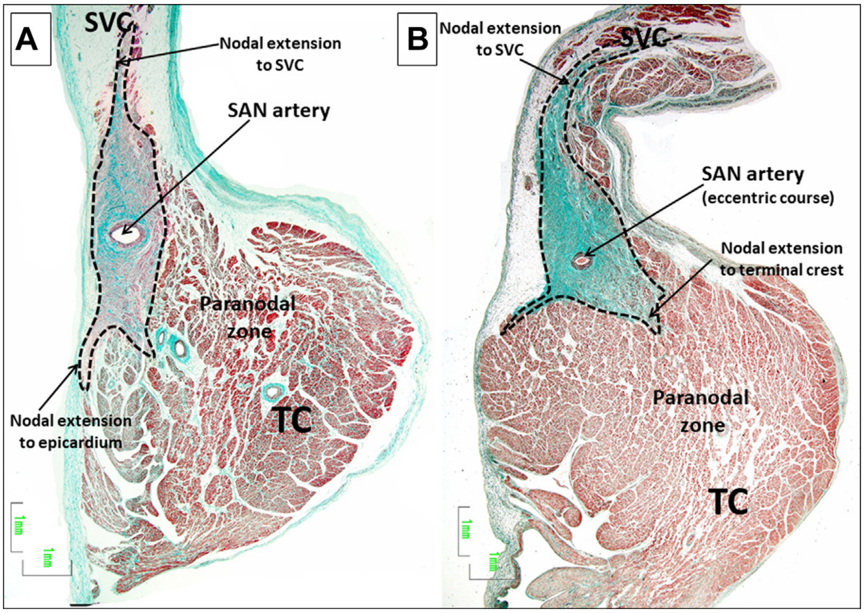
The SAN consists of a dense collection of electrically specialized cells residing within a connective and fibrous matrix, adjacent to the surrounding atrial myocardium by a group of “transitional zone” (TZ) cells with poorly defined borders[10] (**Figures 2A and 2B**). Masson trichrome staining permits a clear distinction between the SAN (poorly stained as a result of an underdeveloped microfilament cytoskeleton) and the surrounding atrial myocardial cells. The highly specialized smaller SAN pacemaker cells lie in the center of the SAN and close to the SAN artery, whereas larger transitional pacemaker cells are located in its periphery (**Figures 1A to 1C and 2A and 2B**). The tail of the SAN exhibits significant fragmentation, with islands of SAN tissue intertwined with subendocardial fibrofatty tissue and atrial myocytes. Moreover, in many hearts, short extensions of nodal tissue have been observed from the head, body, and tail of the node, penetrating the working atrial myocardium toward the epicardium, TC, or SVC[9] (**Figures 2A and 2B**). As one moves toward the outer aspects of the TZ, there is a gradual shift in the ratio of nodal to atrial cells, with a predominance of atrial cell morphology.

FIGURE 1 **Gross Anatomy and Histology of RA Structures and Anatomical Relationships**



(A) Lateral view of a human heart specimen showing the course of the right phrenic nerve (arrows) relative to the right atrium (RA). The location of the sinoatrial node (SAN) is outlined (blue dotted line). The double-headed arrow represents the sectioning plane used for making the histologic cross sections through the sinoatrial node and the terminal crest (TC) shown in B. (Masson trichrome stain). (C) Histologic cross-section (Masson trichrome stain) showing the Bachmann bundle bridge across the anterior interatrial groove and its rightward extension toward the sinoatrial node. IVC = inferior vena cava; LA = left atrium; LAA = left atrial appendage; PT = pulmonary trunk; RAA = right atrial appendage; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein; RV = right ventricle; SCV = superior vena cava.

FIGURE 2 **Histology of the SAN Body (Masson Trichrome Stain)**



(A and B) Histologic sections of the sinoatrial node (SAN) and its nodal artery within a dense matrix of connective tissue (green) and nodal extensions to the superior vena cava (SVC), epicardium, and terminal crest (TC). Note the irregular myoarchitectural contours of the Paranodal zone. (A) Normal density of connective tissue (green); (B) replacement of normal sinoatrial node myocytes with connective tissue (darker green).

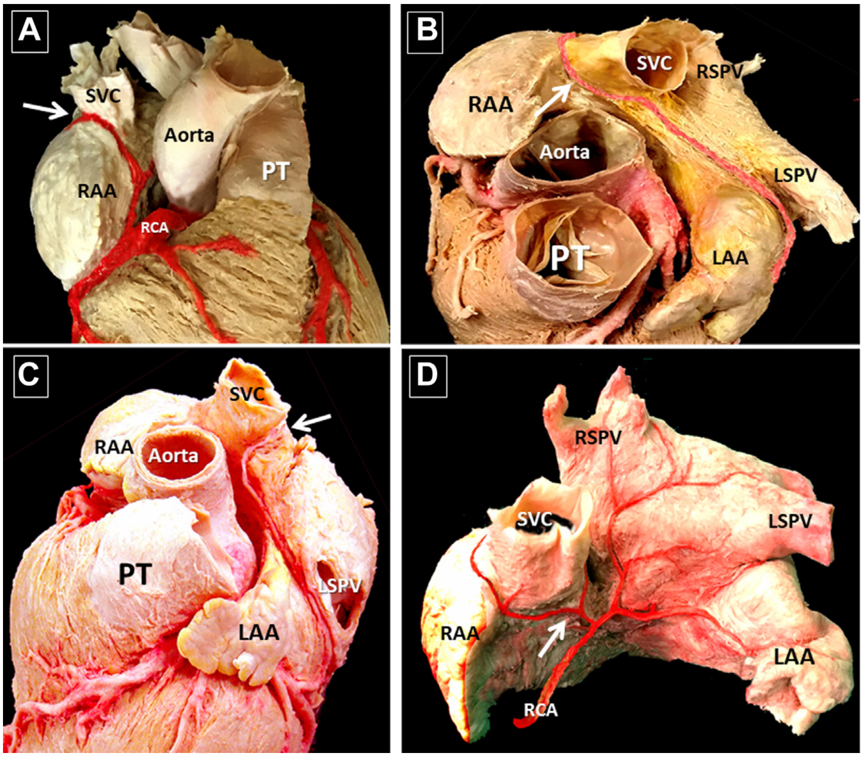
A key aspect of the myoarchitecture of the SAN and its unique arrangement is that the specialized pacemaker cells of the SAN must remain electrically insulated from the larger mass of hyperpolarized atrial myocytes surrounding it to achieve their automatic pacemaker behavior. The TZ cells therefore act as a region of functional and anatomic block and allow for exit pathways of SAN impulse conduction. Thus, anatomical and functional characteristics of TZ cells favor antegrade conduction of nodal impulses. A combination of cell coupling, electrotonic interaction, and differing intrinsic properties between nodal cells and atrial myocytes provides the framework for the electrophysiological characteristics of the SAN as the governing pacemaker region of the heart.[11]

Structural changes within the SAN myoarchitecture affect its function. In aging hearts, for example, connective and fibrofatty tissue encapsulates the SAN, and in infants with congenital heart block, the SAN may be completely absent and replaced by fibrous tissue[8,9] (**Figures 2A and 2B**). Conditions that lead to loss of SAN cells, gap junction dysfunction, and increase in fibroblasts, collagen, and elastin content may cause pacemaker dysfunction and damage of functional exit sites. These structural changes are likely responsible for varying degrees of SAN dysfunction.

BLOOD SUPPLY AND INNERVATION

The SAN is supplied by the sinoatrial nodal artery, and in 60% of specimens this vessel arises as the first branch of the right coronary artery (RCA), coursing along the interatrial groove before reaching the SAN anteriorly (precaval disposition).[12] Topographic variations include posterior (retrocaval) and circumferential (around the cava) dispositions[13] (**Figures 3A to 3D**). In the remainder,[12] the sinoatrial nodal artery arises from the left coronary system (**Figures 3A to 3D**), usually the left circumflex, arising as a branch of the left anterior atrial or left lateral atrial artery. SAN arteries arising from the left system traverse from the anterior LA following the Bachmann bundle into the RA in a superior direction (**Figures 3A to 3D**), before reaching the SAN. Uncommon variants include a dual blood supply from the right and left systems or from lateral atrial arteries found in the lateral wall of the RAA. Although in most hearts the SAN artery branches

FIGURE 3 Gross Anatomical Specimens Showing Arterial Blood Supply Variations of the SAN

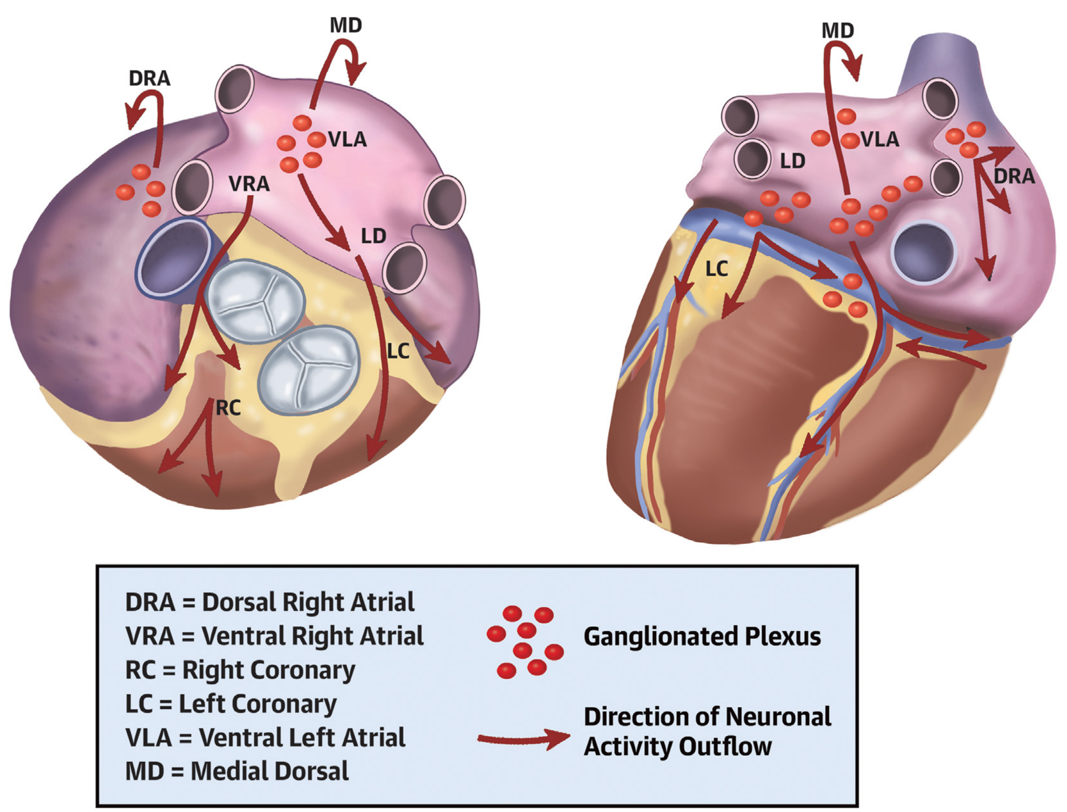


(A) Sinoatrial node (SAN) artery (arrow) originating from the right coronary artery (RCA) and located between the right atrial appendage (RAA), superior vena cava (SVC), and aorta. (B) Sinoatrial node artery originating from the circumflex artery and lying on the Bachmann bundle, in a precaval location (arrow) toward the sinoatrial node. (C) Sinoatrial node artery originating from the circumflex artery and located over the Bachmann bundle, in a retrocaval location (arrow) toward the sinoatrial node. (D) Sinoatrial node artery arising from the proximal segment of RCA, coursing to the SVC, and dividing with a circumferential disposition (arrow) around the superior vena cava-right atrial junction. Abbreviations as in Figure 1.

out inside the SAN body, in some specimens, the SAN artery branches out before reaching the SAN body, and occasionally there is a dual supply from an arterial circle entering the SAN cranially and caudally.[8,9] Thus, although in most cases the body of the SAN is penetrated by the nodal artery and maintains a central position throughout the length of the SAN, in some specimens the nodal artery penetrates either its head or tail portion, with an eccentric course alongside the SAN[9] (Figures 2A and 2B).

The SAN is densely innervated by sympathetic and parasympathetic ganglionated fibers, responsible for regulation of the sinus rate through modulation of ionic currents within nodal cells.[14] Animal studies[15] have demonstrated that vagal efferent postganglionic neurons innervating the SAN are located in discrete epicardial ganglionic structures within fat pads, originating from either the 10th cranial or vagus nerve, thus resulting in short postsynaptic parasympathetic nerve fibers. By contrast, the neural body of postganglionic sympathetic neurons is located far from the heart. Sympathetic innervation of the SAN occurs through fibers arising from the first 4 thoracic spinal nerves. Once inside the heart, they are distributed to form the intrinsic cardiac nervous system, one of which is the dorsal right atrial subplexus, located between the posterosuperior region of the RA, the root of the SVC, and part of the interatrial septum. This subplexus extends widely over the posterior and lateral aspects of the RA,

FIGURE 4 Schematic Representation of Cardiac Autonomic Subplexuses in the Human Heart



Arrows represent the neuronal activity output direction. The dorsal right atrial (DRA) subplexus is of particular relevance for sinoatrial node function.

including the region of the SAN and the superior surface of the RAA[14] (**Figure 4**). This dual autonomic innervation and the balance between sympathetic and parasympathetic inputs determine heart rate values within the SAN pacemaker cell hierarchy. Increased vagal tone leads to caudal migration of dominant pacemaker cells within the SAN, whereas sympathetic activation causes cranial activation of SAN automaticity.[8]

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APPENDIX For supplemental videos, please see the online version of this paper.