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Innovations in medicine

Hybrid Sinus Node-Sparing Ablation in Drug-Refractory Inappropriate Sinus Tachycardia and Postural Orthostatic Tachycardia Syndrome: A Novel Approach Implemented at PIM MSWiA

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Abstract

Inappropriate sinus tachycardia (IST) and postural orthostatic tachycardia syndrome (POTS) are complex autonomic tone disorders that affect predominantly young women, often leading to debilitating symptoms such as palpitations, fatigue, and exercise intolerance. Despite pharmacologic and conservative therapy, many patients remain symptomatic. Sinus node-sparing (SNS) hybrid ablation represents a novel strategy combining thoracoscopic epicardial ablation and endocardial 3D mapping. This approach is designed to selectively interrupt arrhythmogenic conduction pathways while preserving sinus node integrity. This article reviews our institutional protocol and first experience at PIM MSWiA, discusses underlying mechanisms, mapping tools, and outlines results from international studies including the HEAL-IST trial and SUSRUTA-IST registry. Hybrid SNS ablation appears to be a promising solution for refractory IST and POTS, meriting consideration among referring physicians and multidisciplinary teams.

Streszczenie

Nieadekwatna tachykardia zatokowa (IST) oraz zespół posturalnej tachykardii ortostatycznej (POTS) to złożone zaburzenia regulacji autonomicznego układu nerwowego, które dotykają przede wszystkim młode kobiety i często prowadzą do uporczywych objawów, takich jak palpitacje, zmęczenie oraz nietolerancja wysiłku fizycznego. Pomimo stosowania terapii farmakologicznej i leczenia zachowawczego, wielu pacjentów pozostaje objawowych. Hybrydowa ablacja oszczędzająca węzeł zatokowy (SNS) stanowi nowatorską strategię leczenia, łączącą torakoskopową ablację epikardialną z endokardialnym mapowaniem 3D. Metoda ta ma na celu selektywne przerwanie arytmogennych dróg przewodzenia przy jednoczesnym zachowaniu integralności węzła zatokowego. W niniejszej publikacji przedstawiamy protokół postępowania oraz pierwsze doświadczenia z wdrożenia tej nowatorskiej metody w PIM MSWiA. Omawiamy mechanizmy patofizjologiczne, technologię mapowania, a także prezentujemy wyniki międzynarodowych badań, w tym HEAL-IST oraz SUSRUTA-IST. Hybrydowa ablacja SNS wydaje się obiecującą metodą w leczeniu opornego IST i POTS, zasługującą na uwagę lekarzy kierujących oraz zespołów wielodyscyplinarnych.

Keywords *SNS, IST, POTS, hybrid ablation*
Słowa kluczowe *SNS, IST, POTS, ablacja hybrydowa*

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Introduction

Inappropriate sinus tachycardia (IST) and postural orthostatic tachycardia syndrome (POTS) are two overlapping but distinct forms of autonomic dysfunction that predominantly affect young, otherwise healthy individuals, with a marked female predominance [1–3]. Although traditionally considered rare, recent data suggest that these syndromes may be underrecognized contributors to chronic fatigue, exercise intolerance, and functional disability, particularly in post-viral contexts such as long COVID [4–5]. Patients with IST frequently present with palpitations, fatigue, chest discomfort, and anxiety-like symptoms, which can significantly impair quality of life. In POTS, symptoms also include orthostatic intolerance, lightheadedness, tremulousness, cognitive dysfunction ("brain fog"), and exercise-induced tachycardia. Though pathophysiologically distinct, IST and POTS often coexist, complicating diagnosis and treatment. Conventional management includes lifestyle modification, increased fluid and salt intake, compression garments, and structured reconditioning programs [6]. Pharmacologic therapies such as ivabradine, beta-blockers, and fludrocortisone are often employed, with mixed results [7,8]. For these challenging cases, invasive therapies have emerged. Traditional sinus node modification or ablation using endocardial radiofrequency approaches carries high recurrence rates and a significant risk of pacemaker implantation (up to 50%) [9]. In contrast, a novel hybrid sinus node-sparing (SNS) ablation technique - combining thoracoscopic epicardial ablation with endocardial 3D electroanatomic mapping - has shown encouraging early results in IST/POTS cohorts [10-13]. This approach targets strategic autonomic and conductive regions while preserving sinus node function. Initial multicenter data, including from the SUSRUTA-IST registry and HEAL-IST IDE trial, report acute success rates >90%, significant heart rate reduction, and a low pacemaker requirement (~4–10%) [9,14]. Moreover, European single-center experiences—such as those from Brussels and Warsaw—have supported the safety, durability, and symptom resolution achievable with this approach, particularly when integrated into multidisciplinary care pathways [11,15,16].

This report aims to provide an evidence-based synthesis of the evolving understanding of IST and POTS, critically examining the role of hybrid SNS ablation in the management of drug-refractory or drug-intolerant cases, and outlining current gaps, controversies, and future directions in treatment paradigms.

Pathophysiology of IST and POTS

The pathophysiology of IST and POTS remains incompletely elucidated. However, emerging evidence points toward a multifactorial dysregulation of autonomic control, with both intrinsic and extrinsic contributions to abnormal heart rate dynamics.

In IST, the central feature is an increased resting and diurnal heart rate in the absence of physiological demand. Electrophysiologic studies have shown enhanced automaticity of the sinoatrial node (SAN), abnormal sinus node re-entry, and even focal micro-reentrant circuits near the crista terminalis or within the SAN tissue [6,8]. Autonomic imbalance - particularly increased sympathetic tone and reduced vagal input - plays a central role [1]. In some patients, β-adrenergic receptor hypersensitivity or autoantibodies to β-receptors have been proposed as potential contributors, although these remain inconsistently validated [17].

On a structural level, recent mapping studies using high-density endo-epicardial electroanatomical techniques have demonstrated that the earliest SAN activation ("exit zones") typically originate from the epicardium, with endo-epicardial delays (mean ~20 ms) and reversed polarity bipolar electrograms, suggesting spatial conduction abnormalities within the SAN and surrounding atrial musculature [8]. These findings support the hypothesis of segmental SAN dysfunction or conduction block, creating susceptibility to inappropriate chronotropic responses even at rest.

In contrast, POTS is largely characterized by a positional HR increase due to impaired autonomic regulation during orthostatic stress. The proposed mechanisms include excessive sympathetic activation, hypovolemia, impaired baroreflex sensitivity, and small fiber neuropathy affecting lower extremity vasculature, which leads to venous pooling and compensatory tachycardia. Some patients demonstrate low blood volume, while others show elevated plasma norepinephrine levels when upright, consistent with a hyperadrenergic phenotype.

Recent attention has focused on post-infectious autonomic dysfunction, particularly after COVID-19, as a trigger for new-onset POTS or exacerbation of underlying dysautonomia [4,5]. Mechanisms may involve inflammatory damage to autonomic ganglia, viral persistence, or immune-mediated injury.

Notably, IST and POTS can coexist, with overlapping symptoms and shared features of autonomic instability. Many patients exhibit a “mixed” phenotype - displaying inappropriate resting tachycardia with an exaggerated orthostatic HR rise - complicating diagnosis and management.

Thus, both conditions represent clinical expressions of autonomic dysregulation, but with different predominant patterns: IST driven by intrinsic SAN dysfunction, and POTS by orthostatic circulatory compensation failure. Understanding these mechanisms is essential for guiding targeted therapy, including the use of hybrid SNS ablation in selected cases.

Diagnostic Pathways and Differential Diagnosis

Diagnosing IST and POTS requires a structured and exclusion-based approach (Fig. 1). Both entities share symptoms such as palpitations, fatigue, orthostatic intolerance, and exertional dyspnea, but their defining characteristics differ, necessitating comprehensive autonomic and cardiovascular evaluation.

For IST, diagnostic confirmation involves the presence of sinus rhythm with a resting heart rate (HR) >100 bpm and a mean 24-hour HR >90 bpm, in the absence of identifiable secondary causes [2]. The patient should also report persistent symptoms that are not attributable to anxiety or physical deconditioning. For POTS, diagnostic criteria include an increase in HR ≥30 bpm (or ≥40 bpm in adolescents) within 10 minutes of upright posture or tilt, without orthostatic hypotension (i.e., no sustained drop in systolic BP >20 mmHg or diastolic >10 mmHg) [1,3]. Both diagnoses require a symptom duration of ≥6 months and a significant impact on daily functioning.

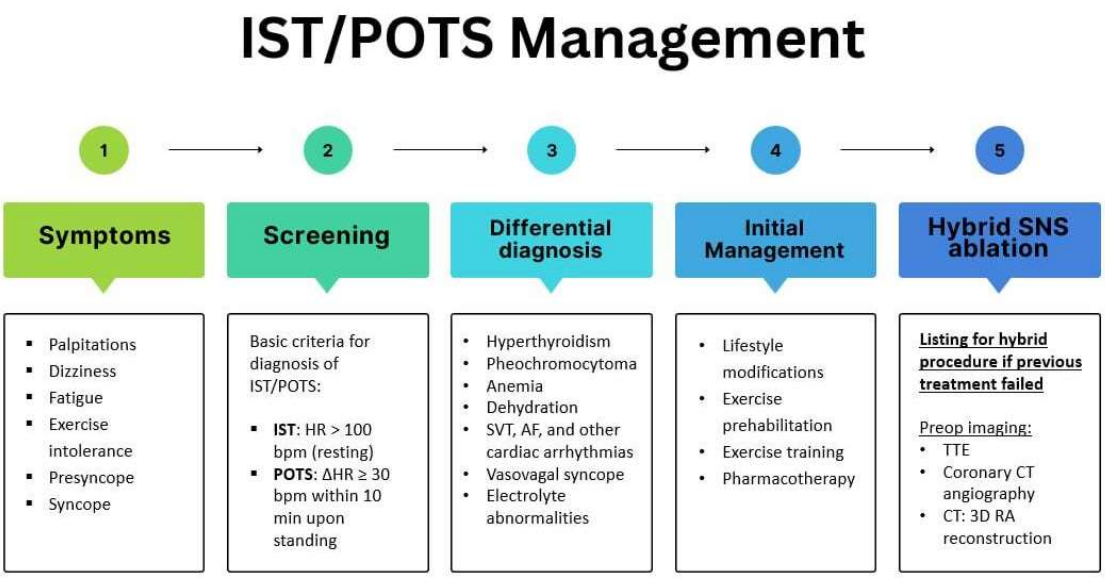

Figure 1 *Graphical summary of IST/POTS management. Abbreviations: AF – Atrial Fibrillation; CT – Computed Tomography; HR – Heart Rate; IST – Inappropriate Sinus Tachycardia; POTS – Postural Orthostatic Tachycardia Syndrome; RA – Right Atrium; SNS – Sinus Node-Sparing; SVT – Supraventricular Tachycardia; TEE – Transesophageal Echocardiography*

Core components of the diagnostic work-up include:

- 12-lead ECG and 24-hour Holter monitoring to assess baseline rhythm, rate variability, and nocturnal trends.
- Echocardiography to exclude structural heart disease and ensure normal ventricular function.
- Head-up tilt table testing with continuous beat-to-beat BP and HR monitoring to objectively measure orthostatic response, including late vasovagal components.
- Laboratory testing to exclude hyperthyroidism, anemia, pheochromocytoma, hypovolemia, or electrolyte imbalance.

Differential diagnosis is extensive and includes:

- Endocrine disorders: hyperthyroidism, pheochromocytoma, diabetes-induced autonomic neuropathy
- Cardiac arrhythmias: supraventricular tachycardia (SVT), inappropriate junctional tachycardia, atrial tachycardia, and atrial fibrillation
- Neurological and autonomic dysfunction: vasovagal syncope, neurally mediated hypotension, and baroreflex failure
- Volume depletion: dehydration, bleeding, adrenal insufficiency
- Medications and stimulants: β-agonists, decongestants, caffeine, or withdrawal states

Invasive electrophysiological studies are helpful in unclear IST presentations to exclude macroreentrant SVT or inappropriate focal atrial tachycardia. High-density 3D mapping with sinus node activation timing can also guide therapeutic decisions, particularly in patients evaluated for hybrid SNS ablation.

Treatment Guidelines

The 2015 Heart Rhythm Society (HRS) Expert Consensus Statement provides the most comprehensive guidance on the management of IST and POTS [18]. It emphasizes a multifaceted approach, addressing autonomic dysfunction, physical deconditioning, and symptom control.

Non-pharmacologic strategies are considered first-line for both IST and POTS:

- Structured, progressive aerobic exercise is strongly recommended and has been shown to improve autonomic tone and functional capacity (Class I, Level B evidence).
- Volume expansion via oral fluids and increased sodium intake is advised in POTS patients to mitigate orthostatic intolerance.
- Behavioral and lifestyle modifications, including head-of-bed elevation, avoiding triggers, and wearing compression garments, are universally endorsed.
- Pharmacologic therapy is considered when non-drug measures fail to control symptoms.

In IST, beta-blockers are first-line. However, these often produce side effects such as fatigue, bradycardia, and exercise intolerance, limiting long-term adherence. Ivabradine, an If channel inhibitor has emerged as a preferred agent in IST. Moreover, ivabradine has demonstrated efficacy in reducing HR and improving symptoms without affecting blood pressure [19], yet up to 30–40% of patients remain refractory or intolerant to medical therapy [1,6, 20]. The HRS statement recognizes its potential role, though it remained off-label in 2015. More recent trials and registry data support its use, alone or in combination with beta-blockers [19]. In POTS, agents such as midodrine, pyridostigmine, fludrocortisone, or desmopressin may be trialed, based on phenotype (hypovolemic, hyperadrenergic, neuropathic subtypes). Efficacy remains inconsistent and individualized. The document also emphasizes the need to identify and manage comorbid conditions, such as sleep disorders.

Despite these recommendations, a significant proportion of patients remains refractory. Observational data from SUSRUTA-IST and institutional experience at PIM MSWiA confirm that 30-40% of IST/POTS patients are drug-resistant or intolerant [9,16]. These individuals often suffer from high symptom burden, impaired quality of life, and inability to maintain employment or physical activity. For such patients, hybrid SNS ablation offers a promising interventional option. By targeting the arrhythmogenic substrate while preserving

SN function, it bridges the gap between conservative therapy and traditional catheter ablation, aligning with the individualized, mechanism-based philosophy advocated by the HRS.

Electrophysiological Rationale for Targeting the Sinus Node

The sinus node (SN), anatomically located at the junction of the superior vena cava (SVC) and right atrium (RA), is a complex, heterogeneous structure with variable exit sites, intricate autonomic innervation, and overlapping anatomical zones. Its electrophysiological behavior is governed not only by pacemaker cell automaticity but also by modulation from both sympathetic and parasympathetic systems. In IST and POTS, the SN may be intrinsically abnormal, exhibiting excessive sensitivity to autonomic input or structural remodeling [8].

Histological and electrophysiological studies have identified dysfunctional SN behavior in IST patients, including:

- Multiple or shifting SN exit sites along the crista terminalis
- Accelerated baseline firing rate
- Enhanced sensitivity to catecholamines
- Fibrosis and regional conduction abnormalities surrounding the SN
- Increased activity of SVC sleeves with ectopic atrial foci

Invasive electroanatomic mapping, especially using high-density (HD) grid catheters, has enabled precise localization of earliest atrial activation, often revealing that the dominant pacemaker shifts dynamically depending on autonomic tone or posture [8]. In patients with IST/POTS, such instability suggests a broader arrhythmogenic zone rather than a focal trigger. POTS may also involve central and peripheral dysautonomia that amplifies SN discharge under orthostatic stress.

Standard transcatheter sinus node modification, typically performed via the endocardial approach using radiofrequency (RF) ablation, is associated with multiple limitations [9]:

- Difficulty accessing the full anatomical SN area due to the convex shape of the crista terminalis and posterior RA
- Incomplete lesion sets and residual conduction through SN exit sites
- High recurrence rates due to reinnervation or inadequate substrate modification
- Elevated risk of iatrogenic sinus node dysfunction, resulting in pacemaker implantation

These shortcomings have prompted the development of hybrid SNS ablation, which combines:

- Thoracoscopic epicardial ablation for direct visualization and lesion delivery over the crista terminalis, SVC, and inferior vena cava regions
- Intraoperative 3D endocardial mapping to confirm SN location and validate conduction block

Epicardial access allows safe, transmural lesions using bipolar RF clamps, ensuring electrical isolation of perinodal tissue without destroying the SN itself. By avoiding direct SN ablation, this approach preserves chronotropic competence while modulating the arrhythmogenic substrate responsible for inappropriate sinus acceleration.

Lesion set during SNS

ure 2 illustrates the targeted areas. Clinical data from de Asmundis et al., the SUSRUTA-IST registry, and our own Polish cohort support this electrophysiological model [9,15,16]. Long-term outcomes demonstrate significant heart rate reduction, improved variability, and low rates of pacemaker dependence [10]. The HEAL-IST IDE trial is designed to further validate this strategy in a multicenter, prospective fashion [14].

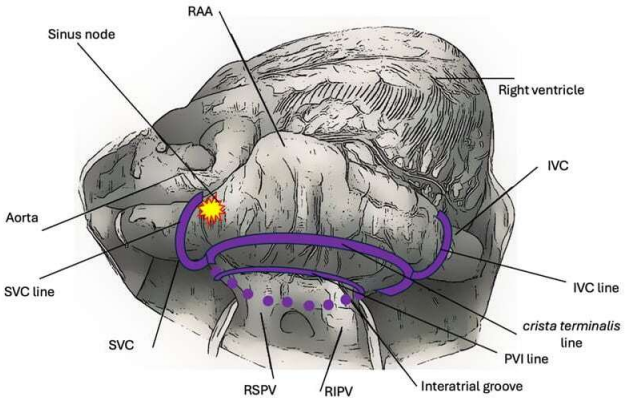

Figure 2 *Lesions set during hybrid Sinus Node Sparing ablation. Abbreviations: IVC – Inferior Vena Cava; PVI – Pulmonary Vein Isolation; RAA – Right Atrial Appendage; RIPV – Right Inferior Pulmonary Vein; RSPV – Right Superior Pulmonary Vein; SVC – Superior Vena Cava*

In summary, targeting the electrophysiologic substrate around the SN - not the node itself - via a hybrid epicardial approach appears to be a safe and mechanistically rational intervention for drug-refractory IST and POTS.

Hybrid Sinus Node-Sparing Procedure: Step-by-Step

The hybrid procedure involves combined epicardial and endocardial approaches (Fig. 3A-3E). Under general anesthesia, thoracoscopic access is gained via three ports on the right chest. The pericardium is opened anterior to the phrenic nerve. A 3D electroanatomic endocardial map is created via femoral venous access to localize the sinus node.

Bipolar RF clamps are applied to isolate the SVC, inferior vena cava, and crista terminalis, sparing the SN marked intraoperatively. The lesion set is completed with confirmation of the conduction block. In some cases, touch-up endocardial ablation is required for complete isolation. The goal is to interrupt reentry and autonomic pathways without damaging the sinus node.

Recently, the first two cases in Europe were performed with the novel Isolator Synergy EnCapture Clamp (AtriCure Inc, Manson, Ohio, USA) which is approved by the FDA and CE-mark-pending within the EU. Its design allows for safe grasping at the level of crista terminalis, ensuring direct ablation, while avoiding LA posterior wall dissection and going around pulmonary veins (Fig. 4).

Postoperative Care and Rehabilitation

Following the hybrid procedure, patients are monitored in the Intensive Care Unit with telemetry and frequent ECGs. Pericardial drains are removed after ensuring no effusion. Routine prophylaxis

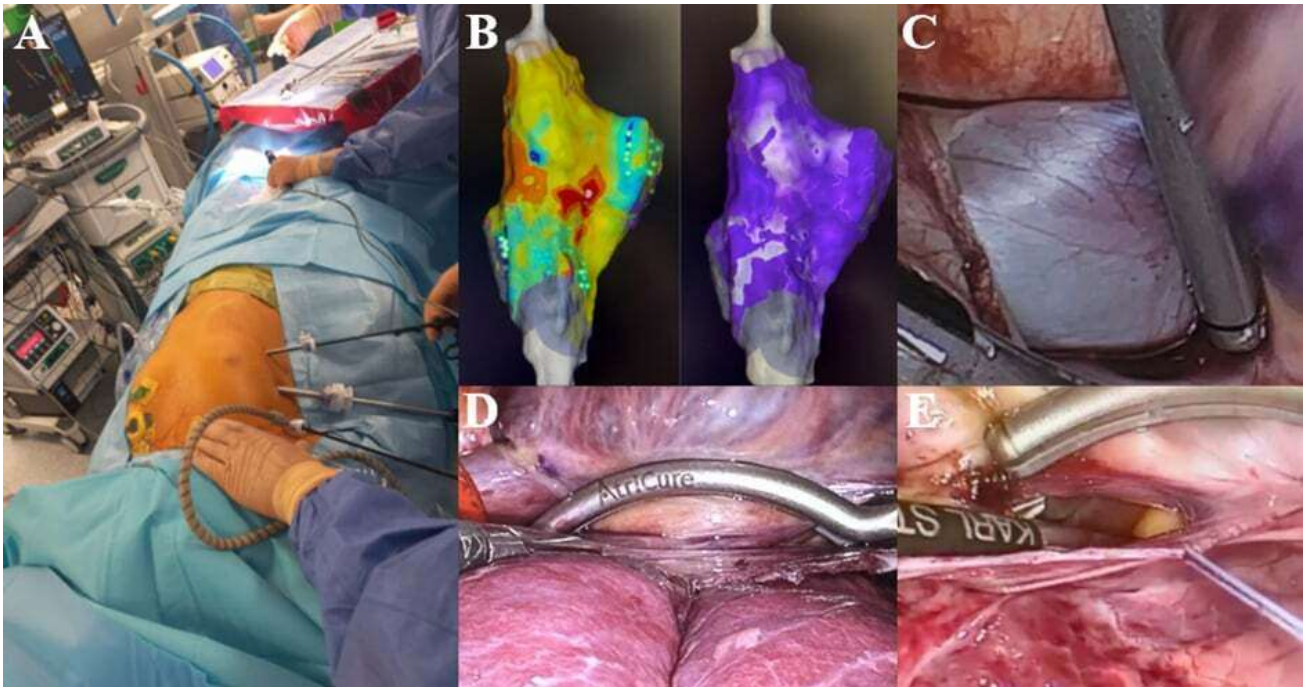

Figure 3 *A: Procedure setup B. Endocardial 3D-mapping (EnSite NavX/PrecisionTM; Abbott, St. Paul, MN, USA) and validation of the sinus node's earliest activation site C. Superior vena cava ablation (AtriCure Inc, Manson, Ohio, USA) D. Crista terminalis ablation E. Inferior vena cava ablation.*

Figure 4 *EP-Heart-Team: more than 30 specialists, nurses, and other professionals involved in hybrid treatment and perioperative care.*

with colchicine and NSAIDs is implemented to prevent pericarditis, a common post-ablation complication. A structured rehabilitation program begins during hospitalization and continues through telemedicine support.

Cardiac rehabilitation focuses on gradual reconditioning, fluid management, and orthostatic training. Patients typically undergo 6-minute walk tests, Holter monitoring, and quality-of-life assessments at 1, 3, and 6 months post-op. Device interrogation is scheduled for those with implantable monitors. Multidisciplinary follow-up ensures early detection of recurrence or complications. Patients are advised on activity resumption, fluid intake, and medication tapering as appropriate.

Results and Registry Data

Data from the SUSRUTA-IST registry showed that hybrid SNS ablation resulted in >90% success in restoring normal sinus rhythm, with significant HR reduction and symptom relief. Compared to radiofrequency sinus node ablation, hybrid procedures showed superior outcomes in peak HR control, fewer redo procedures (8% vs 100%), and lower pacemaker implantation (4% vs 50%) [9].

In the Central European series, 20 female patients with drug-resistant IST/POTS underwent hybrid SNS ablation. All showed post-operative HR reductions (mean -26 bpm) and symptom resolution. No patient required permanent pacing. Complications were minimal, with only one case of transient pericardial effusion [16]. The HEAL-IST registry (NCT05280093) aims to further assess long-term safety and efficacy in larger multicenter cohorts [14].

Redo Procedures, PPM Risk, and Long-Term Rhythm Control

Redo procedures are required in 10–15% of patients, primarily due to reconnection or incomplete isolation at the crista terminalis [10]. Mapping during redo shows conduction gaps in prior lines, often in the crista terminalis region (Fig. 5). Most redos are successful with additional touch-up ablation.

Pacemaker implantation is rare in hybrid SNS ablation, reported at 4–10%, typically in patients with sinus node dysfunction post-procedure or planned nodal modification [9,10]. Compared to traditional RF ablation, this represents a significant safety improvement. At long-term follow-up, freedom from IST recurrence is approximately 85%, with sustained HR control and improved quality of life metrics [10].

Discussion and Future Direction

The emergence of hybrid SNS ablation has transformed the interventional landscape for drug-refractory IST and POTS. Unlike traditional endocardial sinus node modification, this approach enables targeted substrate modulation with high efficacy and

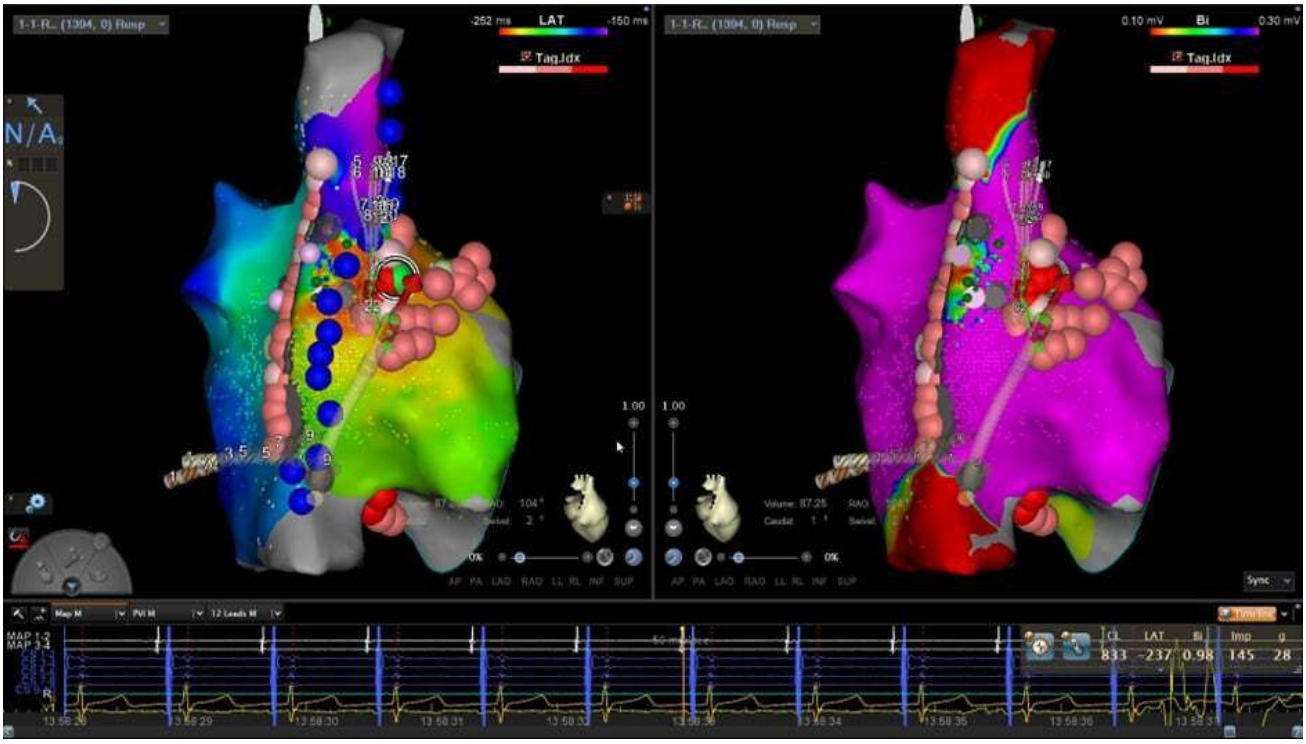

Figure 3 *Redo procedure.*

reduced procedural risk. Clinical data from single-center series and multicenter registries demonstrate favorable safety profiles, durable rhythm control, and low device dependency [10,16]. However, limitations persist. The majority of current data stem from observational studies without randomized controls. Patient selection criteria are not fully standardized, and operator experience influences outcomes. Long-term follow-up beyond two years is limited. Comparative cost-effectiveness and access to hybrid ablation centers remain hurdles in broader implementation.

Future directions include expanded prospective registries like HEAL-IST, incorporating diverse populations, including male and post-viral dysautonomia patients. Ongoing studies should examine neurohormonal and electrophysiologic predictors of response. The development of standardized lesion sets and intraoperative endpoint definitions will refine procedural consistency. Integration of wearable monitors, remote rehabilitation platforms, and autonomic testing may enhance postoperative management and personalization. Hybrid ablation may also be explored in conjunction with cardioneuroablation in overlapping syndromes.

The emergence of hybrid SNS ablation for patients with drug-refractory IST and POTS not only represents a procedural innovation but also underscores the critical importance of a well-integrated electrophysiology (EP) Heart Team. The complexity of these disorders, both diagnostically and therapeutically, necessitates a model in which decision-making and execution are shared across domains of expertise. EP Heart Team brings clarity to the diagnostic process through advanced autonomic testing, long-term rhythm surveillance, and - where necessary - invasive electrophysiological studies. Such diagnostic precision is essential in appropriately selecting patients for a hybrid intervention and avoiding over-treatment in those with psychogenic or poorly characterized syndromes.

The procedural workflow itself depends on the synchronized efforts of both cardiac surgeons and electrophysiologists. The epicardial component, involving thoracoscopic ablation of the crista terminalis and intercaval tissue, requires careful anatomical dissection, phrenic nerve protection, and deliberate lesion planning based on preoperative imaging and mapping. The electrophysiologist's role begins well before the incision, through high-density 3D mapping to define the earliest activation zones, often using HD-grid catheters. During the case, intraoperative endocardial access permits real-time lesion validation, pacing thresholds, and if necessary, complementary touch-up ablation. Without this real-time interplay between surgical and EP modalities, the procedure risks either under-treatment or inadvertent damage to the sinus node itself.

Beyond the operating room, the Heart Team model ensures comprehensive post-procedural follow-up. Monitoring for late pericardial effusion, managing the weaning of rate-control medications, and assessing for symptom recurrence all fall within this shared domain. Furthermore, rehabilitation professionals and autonomic specialists may contribute to early mobilization and retraining of cardiovascular reflexes - particularly relevant in POTS patients who exhibit deconditioning-related dysautonomia.

In our institutional experience, the multidisciplinary nature of the EP Heart Team proved essential not only for technical success but also for patient satisfaction and long-term rhythm control. It allowed us to implement a consistent procedural protocol, conduct systematic follow-up, and adapt to complications in real-time. Importantly, the Heart Team structure fosters accountability and transparency, two essential qualities in the adoption of a novel and somewhat invasive treatment for a previously pharmacologically managed condition. The scalability of this approach across centers will depend on the presence of such collaborative frameworks. As hybrid procedures become more standardized through ongoing trials such as HEAL-IST, the role of the EP Heart Team may emerge

as a central quality marker for procedural success, patient safety, and clinical outcomes in this challenging patient population.

Ultimately, hybrid SNS ablation represents a tailored, physiology-driven therapy for a select but growing population. As diagnostic accuracy and procedural expertise improve, this approach could become a first-line strategy in advanced IST and complex POTS care pathways.

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