PACE〜〜 WILEY

Patient-activated anti-tachycardia pacing in adult congenital heart disease

Thomas Carberry MD[1] | **Sabrina Tsao MBBSFHRS**[2] | **Ahmad Sami Chaouki MDPhD**[1]

[1]Division of Cardiology, Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

[2]Division of Cardiology, Hong Kong Children's Hospital, The University of Hong Kong, Ngau Tau Kok, Hong Kong

Correspondence
Thomas Carberry, MD, Division of Cardiology, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 East Chicago Avenue, Box 21, Chicago, IL 60611, USA.
Email: tcarberry@luriechildrens.org

Abstract

Introduction: In adults with congenital heart disease, intra-atrial reentrant tachycardia (IART) is a common arrhythmia that causes significant morbidity and mortality. One treatment option for IART is antitachycardia pacing. Atrial antitachycardia pacing algorithms deliver therapy for IART with $\geq$2:1 conduction, but most algorithms will not recognize IART with 1:1 conduction. Temporary Patient Activated Rx (TPARx) is Medtronic software that can be installed in antitachycardia pacemakers allowing patients to deliver therapies on demand for IART with 1:1 conduction.

Methods: Retrospective chart review at a single institution of all patients who had TPARx installed into their pacemaker.

Results: Four adults with single ventricle congenital heart disease and IART underwent Fontan conversion, arrhythmia surgery, and placement of an epicardial dual-chamber antitachycardia pacemaker. They had recurrent IART with a long cycle length and 1:1 conduction that failed to trigger antitachycardia pacing therapies. TPARx software was programmed into their pacemakers to allow recognition and treatment of IART with 1:1 conduction. Mean follow-up duration after TPARx programming was 4.9 years. Each patient received at least one successful antitachycardia pacing therapy via TPARx – range 0.4–26 treated IART episodes per year. There were no atrial or ventricular arrhythmias induced with antitachycardia pacing. Two patients were able to discontinue anticoagulation after TPARx installation.

Conclusion: This series demonstrates the use of TPARx software as part of a long-term IART management strategy in select patients with IART who have failed more conventional therapies.

KEYWORDS
ACHD, anti-tachycardia pacing, atrial tachycardia, Fontan, pacemaker

- -

1 | INTRODUCTION

Intra-atrial reentrant tachycardia (IART) is a common arrhythmia in adult congenital heart disease (ACHD) patients and is associated with significant morbidity and mortality, including increased risk for sudden cardiac death and thromboembolic events.[1,2] Management of IART is challenging. The primary treatment options for IART include medical therapy and procedural therapy (cardiac ablation via transcatheter or surgical approach). These treatment options have limited success and high rates of arrhythmia recurrence.[3–7] A third management strategy is atrial antitachycardia pacing (ATP). When ATP technology was first developed, many ATP devices required patient activation to delivery therapy,[8–10] but as technology advanced, most included automatic tachycardia detection. Early experience with atrial ATP in pediatric and congenital heart disease was complicated by proarrhythmic effects and inability to provide rate-responsive pacing or AV sequential pacing.[7,11] More recently, ATP has been shown to be a relatively safe and effective therapy for many ACHD patients with IART.[12–14]

The programmed antitachycardia pacemaker algorithm for Medtronic devices is designed to deliver therapy for atrial arrhythmias with ≥2:1 atrioventricular (AV) conduction. The pacemaker will not recognize IART with 1:1 AV conduction, which is seen in many adults with congenital heart disease. There are multiple reasons for this programming, including diagnostic specificity (sinus tachycardia vs. atrial tachycardia with 1:1 conduction) and risk of inducing atrial or ventricular arrhythmias with atrial overdrive pacing.

Temporary Patient Activated Rx (TPARx) is a Medtronic software that can be installed in ATP devices allowing patients to deliver ATP on demand. With this software, if the patient recognizes symptoms of IART, they can activate the TPARx software via a handheld patient activator device (Model 2696 InCheck Patient Assistant, Figure 1). Once activated, the pacemaker will recognize and deliver ATP therapy for atrial tachycardia with 1:1 AV conduction below a set atrial CL, which may be higher than the programmable CL without the software. TPARx has been described in three prior case reports with relatively short follow-up duration.[15–17] We describe the safe and effective long-term use of Medtronic TPARx software for management of IART in four ACHD patients.

2 | CASE SERIES

We performed a retrospective chart review at a single institution of all patients who had TPARx software installed into their pacemaker. Cardiology inpatient and outpatient notes were reviewed for surgical history, medical therapies, pacemaker settings, and patient-activated ATP events. IRB approval and FDA compassionate use exemption were obtained for each patient prior to TPARx software installation.

Four patients had TPARx software installed into their pacemaker over the last 10 years. All patients were adults with single ventricle congenital heart disease and IART who underwent Fontan conversion, arrhythmia surgery, and placement of an epicardial

dual chamber antitachycardia pacemaker. They had recurrent IART with a long CL and 1:1 AV conduction that failed to trigger ATP therapies. TPARx software was installed into their pacemakers to allow recognition and treatment of IART with 1:1 AV conduction. Prior to TPARx installation, each patient had demonstrated successful termination of 1:1 IART with manual atrial overdrive pacing without complications. Atrial tachycardia CL detection and atrial ramp/burst pacing settings were individualized for each patient based on previous pace terminated IART episodes and/or noninvasive pacing studies. Atrial tachycardia CL detection ranged from 350 to 500 ms.

Mean follow-up duration after TPARx installation was 5.4 years. Each patient received at least one successful ATP therapy via TPARx – range 0.4–26 treated IART episodes per year (Table 1). All but one episode of 1:1 IART was successfully terminated with TPARx (141/142, 99%). The one episode of IART that was not terminated with TPARx was the result of a patient activator that had run out of battery. Some IART episodes required more than one ATP attempt for successful termination. The incidence of IART requiring multiple ATP attempts for termination cannot be accurately reported due to inconsistent documentation in the medical record. Two patients were able to discontinue anticoagulation after installing TPARx. No patients had changes to their antiarrhythmic medications after installing TPARx. No patients experienced atrial fibrillation or ventricular arrhythmias from ATP via TPARx (141 total treated IART episodes). Ventricular high rate detection was set at 150−200 bpm to monitor for potential proarrhythmic effect of ATP. All devices were set to disable ATP therapies for acceleration of the ventricular rate.

2.1 | Patient 1

A patient with a history of transposition of the great arteries, ventricular septal defect, pulmonary atresia, and hypoplastic right ventricle underwent a staged palliation ending with a classical Fontan operation at 9 years of age. At age 22, she underwent a Fontan conversion to lateral tunnel cavopulmonary connection, modified right atrial maze, and single chamber epicardial atrial pacemaker placement. Her pacemaker was converted to a dual chamber antitachycardia pacemaker 5 years later (Model P1501DR Medtronic EnRhythm). She was medically managed with multiple antiarrhythmic drugs including atenolol, digoxin, and sotalol. She continued to have breakthrough IART with 1:1 AV conduction. She underwent a noninvasive pacing study that demonstrated inducible sustained IART with 1:1 AV conduction on isoproterenol (CL 300 ms) that terminated with atrial ATP at CL of 220 ms without complication. TPARx software was installed into her device at age 35, with atrial tachycardia detection set to CL ≤ 350 ms and burst+ therapy programmed. In the year preceding TPARx installation, she had two inpatient admissions for IART with 1:1 AV conduction. She has been followed for 9.5 years since TPARx installation, during which time she has used TPARx to successfully treat 22 episodes of IART – mean 2.3 per year. After software installation, she sought emergency medical care

FIGURE 1 Model 2696 InCheck Patient Assistant device (9.6 × 5.6 × 2.2 cm). Left panel: photo of the physician assistant device. Right panel: diagram of physician assistant device with the symbols displayed for reference. Explanation of device buttons: "AF?": The patient can press this button to query for atrial arrhythmia detection. If the device detects a median atrial rate for the last 12 beats that is faster than the set CL, then the "lightning bolt" button will light up. "Lightning bolt": Pressing this button activates the TPARx application to temporarily allow ATP for 1:1 atrial tachycardia that satisfies all other criteria. "Sad face": Pressing this button records symptoms without delivering ATP therapy. The device will display "OK" if there is no atrial tachycardia and "AF" if atrial tachycardia is detected [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Characteristics of patients with Temporary Patient Activated Rx

	Patient 1	Patient 2	Patient 3	Patient 4
Sex	Female	Male	Male	Male
Age at TPARx installation (years)	35	25	41	31
Procedural arrhythmia therapies	Right atrial maze	Bi-atrial maze	Transcatheter RF ablation, bi-atrial maze	Transcatheter RF ablation, bi-atrial maze
Anti-arrhythmic drug(s)	Sotalol	Sotalol, digoxin	Atenolol, digoxin	Amiodarone
Duration of TPARx (years)	9.5	8.1	1.5	2.3
Total successfully treated IART episodes with TPARx	22	79	39	1
Mean treated IART episodes per year with TPARx	2.3	9.8	26.0	0.4
TPARx atrial tachycardia detection cycle length (ms)	350	450	500	480
Anticoagulation after TPARx	Yes	No	No	No

for one episode of IART where the cardiologist discovered that the battery life had expired on her patient's activator device. Besides this, she has had no other hospital admissions or emergency department visits for IART. She was continued on anticoagulation for history of two prior thromboembolic strokes.

2.2 | Patient 2

A patient with a history of pulmonary atresia, ventricular septal defect, and hypoplastic right ventricle underwent a staged palliation ending with a classical Fontan operation at 2 years of age. At age 22,
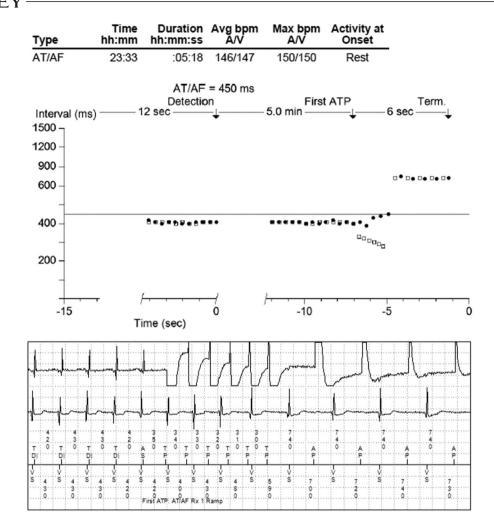
FIGURE 2 Example of pace-termination of IART via TPARx software (Patient 2). Top panel: Atrial and ventricular CL trends. There is a 1:1 atrio-ventricular relationship and a tachycardia CL of 420–440 ms (less than the AT/AF detection of 450 ms). After the first attempt at antitachycardia pacing, there is termination of atrial tachycardia and resumption of atrial-paced rhythm. Bottom panel: Atrial and ventricular electrograms during tachycardia demonstrating successful pace-termination of IART with atrial ramp pacing (A-S1 Interval 81%, interval decrement 10 ms, 6 initial S1 pulses)

he underwent Fontan conversion to extracardiac total cavopulmonary connection, biatrial maze, and epicardial dual chamber antitachycardia pacemaker implantation (Model P1501DR Medtronic EnRhythm). He was medically managed with multiple antiarrhythmic drugs including atenolol, digoxin, sotalol, and amiodarone. He continued to have break-through IART with 1:1 AV conduction. A noninvasive pacing study demonstrated inducible sustained IART (CL 440 ms), and he had clinical episodes of IART that were manually pace terminated with atrial over-drive pacing at a CL of 370 ms without complication. TPARx software was installed into his device at age 25, with atrial tachycardia detection set to CL ≤ 450 ms and ramp/burst+ therapies programmed. He has been followed for 8.1 years after TPARx installation. In the year pre-ceding TPARx installation, he had four inpatient admissions for IART with 1:1 AV conduction. In the first 2 years after installing TPARx, he was admitted twice for observation after IART had been successfully terminated with TPARx at home. Over time, he stopped seeking emer-gency medical care for IART that terminated with TPARx at home. He has used TPARx to treat 79 total episodes of IART – means 9.8 per year

(Figure 2). Anticoagulation was discontinued shortly after installing TPARx.

2.3 | Patient 3

A patient with a history of double inlet left ventricle underwent a staged palliation ending with a classical Fontan operation at 14 years of age. At age 40, he underwent Fontan conversion to extracardiac total cavopulmonary connection, biatrial maze, and epicardial dual chamber antitachycardia pacemaker implantation (Model A2DR01 Medtronic Advisa). Prior to his Fontan conversion, he had had four transcatheter ablation attempts at a different institution. All four procedures con-sisted of radiofrequency ablation of multiple different IART substrates. His IART was medically managed with multiple antiarrhythmic drugs including atenolol, metoprolol, digoxin, sotalol, and amiodarone. He continued to have breakthrough IART with 1:1 AV conduction. He had multiple episodes of 1:1 IART that were manually pace terminated with

atrial overdrive pacing at a CL of 360 ms without complication. TPARx software was installed into his device the following year at age 41, with atrial tachycardia detection set to CL $\leq$ 500 ms and ramp/burst+ therapies programmed. In the year preceding TPARx installation, he had two inpatient admissions for IART with 1:1 AV conduction. He was followed for 1.5 years, during which he had 39 total episodes of IART treated with TPARx – mean 26.0 per year. Many of the episodes of IART treated with TPARx occurred while he was admitted for heart failure management. Anticoagulation was discontinued shortly after installing TPARx. He died in at age 43 from complications related to heart, liver, and kidney failure, which were unrelated to his arrhythmia.

2.4 | Patient 4

A patient with heterotaxy, unbalanced AV septal defect, and double outlet right ventricle underwent a staged palliation ending with a classical Fontan operation at three years of age. At age 26, he underwent Fontan conversion to extracardiac total cavopulmonary connection, biatrial maze, and epicardial dual chamber antitachycardia pacemaker implantation (Model A2DR01 Medtronic Advisa). Prior to his Fontan conversion, he had one unsuccessful transcatheter ablation attempt at a different institution. His IART was medically managed with multiple antiarrhythmic drugs including digoxin, metoprolol, dofetilide, sotalol, and amiodarone. He had multiple episodes of 1:1 IART that were manually pace terminated with atrial overdrive pacing without complication. TPARx software was installed into his device at age 31, with atrial tachycardia detection set to CL $\leq$480 ms and ramp/burst+ therapies programmed. In the year preceding TPARx installation, he had three inpatient admissions for IART with 1:1 AV conduction. Two weeks after installing TPARx, he had an episode of IART that was successfully pace terminated with TPARx. Since then, he had limited cardiology follow-up, but no atrial tachycardia had been detected by his pacemaker. He underwent a generator change for low battery 26 months after TPARx installation. TPARx was not installed into the new device due to a software limitation.

3 | DISCUSSION

Management of IART in adults with congenital heart disease can be challenging. Many patients continue to have refractory IART despite multiple therapies including antiarrhythmic drugs, transcatheter ablation, surgical ablation, and antitachycardia pacemaker implantation. Refractory IART results in frequent hospital admissions, thromboembolic risk requiring long-term anticoagulation, and increased risk for sudden cardiac death. Medtronic TPARx software can be a useful addition to the armamentarium of therapies for IART with 1:1 AV conduction and a long CL. TPARx software allows patients to manually terminate symptomatic episodes of 1:1 IART without needing to seek medical care and disrupt their lives. In addition, this treatment modality may allow for reconsideration of long-term anticoagulation. TPARx has some limitations, including the need for patients to recognize symp-

toms of IART. Additionally, rapid atrial pacing for an atrial arrhythmia with 1:1 AV conduction carries a risk of inducing atrial fibrillation or ventricular arrhythmias. We believe this risk can be mitigated by programming the device with settings previously shown to convert IART safely in a controlled environment. In this series, we did not encounter any atrial fibrillation or ventricular arrhythmias induced by ATP, which includes a total of 141 episodes of IART converted with TPARx. In addition to our TPARx experience outlined above, there are three other case reports in the literature.[15-17] These cases describe the successful use of TPARx in ACHD patients with no reported proarrhythmic complications. However, the follow-up duration in these case reports is limited – 9 months,[15] unreported.[16,17] Although there may be an increased incidence of atrial fibrillation in adults with structurally normal hearts and antitachycardia pacemakers,[18] the ATP literature in congenital heart disease has not demonstrated an increase in atrial fibrillation.[12-14] In addition, increased atrial fibrillation was not observed in our case series or the TPARx case reports referenced above.

This case series provides examples of Medtronic TPARx software being used effectively to manage IART in select ACHD patients with no observed complications over a relatively long follow-up duration.

CONFLICT OF INTEREST
The authors have no conflicts of interest to report.

REFERENCES

1. Janson CM, Shah MJ. Supraventricular tachycardia in adult congenital heart disease: mechanisms, diagnosis, and clinical aspects. *Card Electrophysiol Clin*. 2017;9:189-211.
2. Weipert J, Noebauer C, Schreiber C, et al. Occurrence and management of atrial arrhythmia after long-term Fontan circulation. *J Thorac Cardiovasc Surg*. 2004;127:457-464.
3. Natale A, Newby KH, Pisanó E, et al. Prospective randomized comparison of antiarrhythmic therapy versus first-line radiofrequency ablation in patients with atrial flutter. *J Am Coll Cardiol*. 2000;35:1898-1904.
4. Triedman JK, Alexander ME, Love BA, et al. Influence of patient factors and ablative technologies on outcomes of radiofrequency ablation of intra-atrial re-entrant tachycardia in patients with congenital heart disease. *J Am Coll Cardiol*. 2002;39:1827-1835.
5. Triedman JK, Bergau DM, Saul JP, Epstein MR, Walsh EP. Efficacy of radiofrequency ablation for control of intraatrial reentrant tachycardia in patients with congenital heart disease. *J Am Coll Cardiol*. 1997;30:1032-1038.
6. Yap SC, Harris L, Silversides CK, Downar E, Chauhan VS. Outcome of intra-atrial re-entrant tachycardia catheter ablation in adults with congenital heart disease: negative impact of age and complex atrial surgery. *J Am Coll Cardiol*. 2010;56:1589-1596.
7. Kannankeril PJ, Fish FA. Management of intra-atrial reentrant tachycardia. *Curr Opin Cardiol*. 2005;20:89-93.
8. Peters RW, Shafton E, Frank S, Thomas AN, Scheinman MM. Radiofrequency-triggered pacemakers: uses and limitations. A long-term study. *Ann Intern Med*. 1978;88:17-22. Jan.
9. Aonuma K, Rozanski JJ, Barold SS, et al. Externally activated antitachycardia pacemaker with noninvasive electrophysiologic re-testing capability. *Pacing Clin Electrophysiol*. 1985;8:215-224. Mar.
10. Hartzler GO, Holmes DR Jr, Osborn MJ. Patient-activated transvenous cardiac stimulation for the treatment of supraventricular and ventricular tachycardia. *Am J Cardiol*. 1981;47:903-909. Apr.

11. Rhodes LA, Walsh EP, Gamble WJ, Triedman JK, Saul JP. Benefits and potential risks of atrial antitachycardia pacing after repair of congenital heart disease. *Pacing Clin Electrophysiol*. 1995;18:1005-1016. May.

12. Kamp AN, LaPage MJ, Serwer GA, Dick M, Bradley DJ. Anti-tachycardia pacemakers in congenital heart disease. *Congenit Heart Dis*. 2015;10:180-184.

13. Kramer CC, Maldonado JR, Olson MD, Gingerich JC, Ochoa LA, Law IH. Safety and efficacy of atrial anti-tachycardia pacing in congenital heart disease. *Heart Rhythm*. 2018;15:543-547.

14. Stephenson EA, Casavant D, Tuzi J, et al. Efficacy of atrial anti-tachycardia pacing using the Medtronic AT500 pacemaker in patients with congenital heart disease. *The Am J Cardiol*. 2003;92:871-876.

15. Weber S, Jeron A, Schneider HJ, Muders F. Efficacy of patient activated anti-tachycardia pacing therapy using the Medtronic AT500 pacemaker. *Europace*. 2006;8:413-415.

16. Batra AS. Patient-activated anti-tachycardia pacing to terminate atrial tachycardias with 1:1 atrioventricular conduction in congenital heart disease. *Pediat Cardiol*. 2008;29:851-854.

17. Balaji S, Mandapati R, Webb GD. *Arrhythmias in Adult Congenital Heart Disease : a Case-Based Approach*. St. Louis, MO Elsevier. 2019:101-111. Chapter.

18. Gillis AM, Morck M, Exner DV, et al. Impact of atrial antitachycardia pacing and atrial pace prevention therapies on atrial fibrillation burden over long-term follow-up. *Europace*. 2009;11:1041-1047. Aug.