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Long-term outcome of neonates and infants with permanent junctional reciprocating tachycardia. When cardiac ablation changes natural history

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ABSTRACT

Supraventricular tachycardias (SVT) are the most common arrhythmias in the perinatal period. Permanent junctional reciprocating tachycardia (PJRT) is a rare form of SVT, often incessant and refractory to pharmacological treatments. Our goal was to analyze the clinical features and treatment of PJRT in patients younger than 2 months and to describe their long-term outcomes.

Methods: Retrospective descriptive observational study of patients diagnosed between 2000 and 2015 in the NICU of a referral center for the treatment of pediatric arrhythmias. History of pregnancy, neonatal period, pharmacological treatment, electrophysiological study and long-term follow-up were reviewed.

Results: 129 of the 10.198 (1.26%) patients admitted to the NICU had SVT, sixteen of them (12.3%) being diagnosed as PJRT. Ten cases had a prenatal diagnosis. For those six patients postnatally diagnosed, the tachycardia was detected either during a routine check-up or because of acute hemodynamic instability. The majority of patients required combinations of drugs, despite that the tachycardia was poorly controlled. Fifteen patients underwent cardiac ablation, nine patients (60%) in the neonatal period and six during childhood. The procedure was completely effective in all cases. One patient had a transient complete AV block that resolved spontaneously 24 hours after the procedure. No other complications were seen. After a mean follow-up of 10.9 years, no patient has presented recurrence, cardiac dysfunction, signs of ischemia or EKG abnormalities, they all have a normal life.

Conclusions: When PJRT is refractory to multiple drugs, cardiac ablation should be taken into account at early stages even in very young patients.

Introduction

Supraventricular tachycardias are the most common arrhythmias in the perinatal period [1,2]. They may be present even in fetal life and usually detected between weeks 28–30 of gestation, with an estimated prevalence of 1/200 fetus. Although fetal arrhythmias account for a small percentage (0.6–2.0% of all pregnancies) some of them are associated with a high morbidity and mortality [3]. Permanent junctional reciprocating tachycardia (PJRT) is a rare form of supraventricular tachycardia, also known as Coumel's tachycardia in honor of Philippe Coumel who first described in 1967 together with Gallagher, although it had been originally recognized by Gallavardin [1,4–6].

PJRT is often incessant and refractory to multiple pharmacological treatments. The mechanism for the tachycardia is an exclusively retrograde conduction accessory pathway with slow and decremental properties, similar to those seen in the atrio-ventricular node. Usually, this accessory pathway is located in the right posteroseptal region, right in the opening of the coronary sinus [7,8].

PJRT usually appears in childhood, but it can occur in the neonatal period and even during fetal life. It typically presents in a repetitive incessant mode, with relatively slow rates (100–180 beats per minutes), although in neonates can reach rates aver 200 bpm, sometimes alternating with one or two normal sinus beats. Indeed, this "slow" rate makes this tachycardia often asymptomatic in terms of palpitations, but it is

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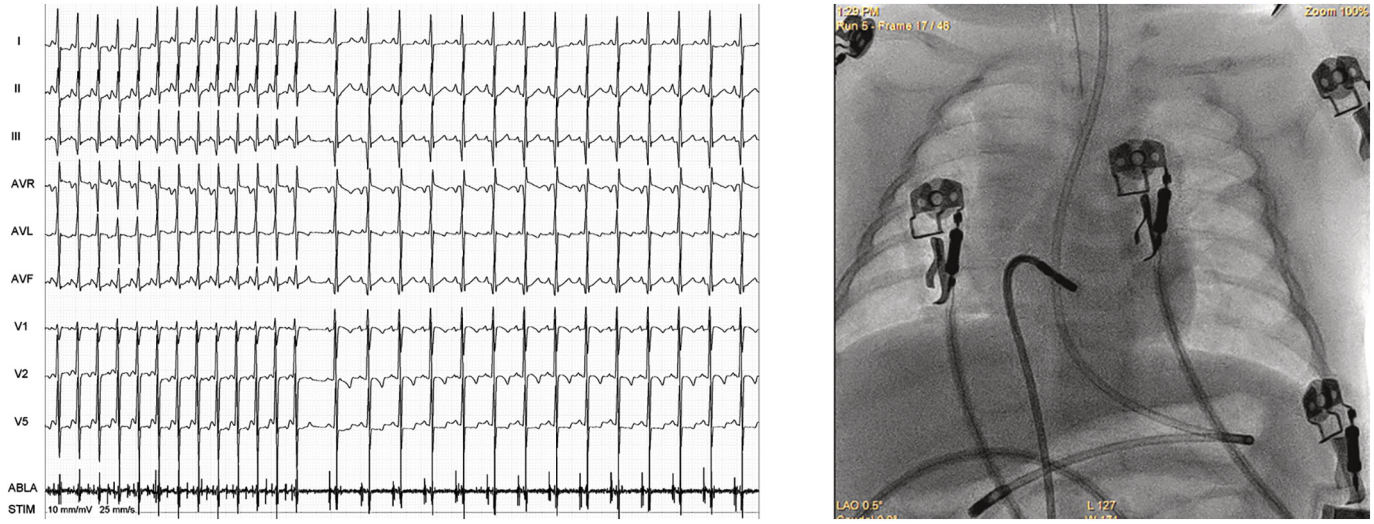

Fig. 1. Left image: electrophysiological findings during PJRT ablation with a single-catheter approach. Note the long RP tachycardia with inverted P waves in the inferior leads corresponding to concealed accessory pathway located in the posterior septal region. Right image: Fluoroscopic image showing a single-catheter approach in a 1-month-old newborn with successfully ablated PJRT.

not rare that patients present as a tachycardiomyopathy. In fact, heart failure can be the first symptom for this tachycardia [1,2].

Antegrade conduction occurs through the atrioventricular node in this type of tachycardia, so that the QRS complex is narrow, with retrograde P waves (typically negative in inferior leads and lateral wall leads) and a longer RP than PR interval [7] (Fig. 1).

In pediatrics, pharmacological treatment is usually based on flecainide and/or beta-blockers alone or in combination, sometimes associated with digoxin. In some centers though, amiodarone is the preferred treatment [9]. Percutaneous cardiac ablation using radiofrequency is a therapeutic option to take into consideration at an early stage when drug treatments are not rapidly effective and ventricular function worsens. Spontaneous accessory pathway regression has been documented in up to 20% of children with PJRT [10–13].

Objective

The aim of this study is to analyze the clinical characteristics and treatment in PJRT patients younger than 2 months of age and to describe their long-term outcomes.

Methods

We undertook a retrospective descriptive observational study of patients younger than 2 months of age diagnosed with PJRT between 2000 and 2015 in the neonatal intensive care unit (NICU) of a referral center for the treatment of pediatric arrhythmias. Typical EKG (tachycardia with a narrow QRS complex, retrograde P waves and a longer RP than PR interval) or electrophysiological confirmation made diagnosis of PJRT. Information about pregnancy, neonatal period, electrophysiological study (if performed) and the long-term follow-up in the arrhythmia unit were reviewed. Clinical data are presented in tables and figures, and quantitative data are presented as median values and interquartile range (IQR). All procedures have been performed after parental inform consent signature. Protocols for standard of care have been approve by Clinical Research and Ethic Committee of our institution.

Results

Between 2000 and 2015, 129 of the 10,198 (1.26%) patients admitted to the NICU had supraventricular tachycardia, sixteen of them (12.3%) being diagnosed with PJRT.

Of the sixteen patients diagnosed with PJRT, ten of them had been referred from another hospital due to fetal or neonatal tachycardia. Table 1 shows the characteristics of the patients. There were slightly more boys than girls (10/16; 62.5%).

Ten cases (62.5%) were prenatally diagnosed at a median gestational age of 29 weeks (IQR 22 to 35 weeks). Eight mothers (80%) received pharmacological therapy: digoxin alone in four, flecainide alone in one and flecainide in addition to digoxin or labetalol in the remaining three cases. The inability to control the tachycardia was determinant in the decision for an elective early delivery in 4 of the 10 cases (40%), leading to prematurity. Six of the newborns presented with tachycardia within the first 24 h and the other four patients before the first week of life.

The remaining six patients were diagnosed postnatally and were born with no significant complications. No evidence of fetal tachycardia was found when charts were analyzed retrospectively. Onset of tachycardia took place between the first hours and 56 days of life, presenting either with acute hemodynamic instability or asymptomatic tachycardia detected during a routine visit to the primary care pediatrician.

Patient #11 presented to the clinic with pallor and sweating and a tachycardia of 250 bpm was evident upon examination. Echocardiography showed a dilated cardiomyopathy with an ejection fraction (EF) below 30%. Electrical cardioversion was attempted with early recurrence of the tachycardia, even after drugs were loaded. Therefore, he was accepted for cardiac ablation. The EF increased after ablation, reaching 64% before discharge 7 weeks after the ablation procedure.

Patient #12 had a tachycardia of 270 bpm in the routine checkup at one month of age. Vagal maneuvers, adenosine and electrical cardioversion were attempted before and after pharmacological treatment.

Patient #13 had a sudden tachycardia with no apparent cause at 8 h of life. It resolved initially with vagal maneuvers, but it reappeared and could be initially managed pharmacologically.

Patient #14 appeared with respiratory distress, poor skin perfusion and feeding refusal. He had tachycardia with ventricular dysfunction and progressed to cardiogenic shock and multiorgan failure. He required advanced life support and cardiopulmonary resuscitation. Tachycardia could be initially controlled with drugs until age of 3 years that reappeared in form of cardiogenic shock. Patient#15 had multiple episodes of paroxysmal tachycardia despite electric cardioversion and combination of drugs, therefore, cardiac ablation was performed.

Patient #16 had an aborted sudden death episode. The EKG on admission was compatible with PJRT. It could be managed with pharmacological treatment until the tachycardia reappeared at 57 days of life.

Table 1
Characteristics of the patients affected with PJRT.

Dx	ID	GA	Gender	WG at diagnose	Maternal treatment	Age at diagnose or debut (days)	Maximum HR	HMD instability requiring ECV	Treatment	Ablation at early age (<2 months)			Treatment at discharge	Ablation at older age (≥ 2 months)			Pathway location	Follow-up
										Age (days)	Efficacy	Complic.		Age	Efficacy	Complic.		
Prenatally	1*	35 + 4	M	35	–	1	200	N	D-P		–	–	D-P	4, 6 m	Y	Y (AVB II)	RPS	17y: *asym*. Without tx
	2	39	M	22	D	2	200	N	D		–	–	D-F	7y	Y	N	LPS	14y: asym. Without tx
	3	35 + 3	M	32	D	1	250	N	D-F	9	Y	N	–	–	–	–	RPS	14y: asym. Without tx
	4	39 + 3	F	26	D-F	6	246	N	P	17	Y	N	–	–	–	–	RPS	13y: asym. Without tx
	5	37 + 5	F	20	D	3	210	N	D-F		–	–	D-F	–	–	–	RPS	11y: asym. Without tx
	6*	40	F	40	–	1	276	N	F	15	Y	N	–	–	–	–	LPS	10y: asym. Without tx
	7*	33 + 4	F	33	D-F	1	245	N	D-F-P	21	Y	N	–	–	–	–	RPS	9y: asym. Without tx
	8*	36 + 5	M	22	F-L	4	280	Y	F-P	20	Y	N	F-P	8 m	Y	N	RPS	6y: asym. Without tx
	9	38 + 6	M	36	D	1	218	N	F-P	16	Y	N	–	–	–	–	LL	5y: asym. Without tx
	10*	38 + 1	M	26	F	1	270	N	D-P-A	–	–	–	Not discharged	5 m	Y	N	RPS	3y: asym. Without tx
Postnatally	11*	39 + 2	M	–	–	48	250	Y	D-F	59	Y	N	–	–	–	–	RPS	18y: asym. Without tx
	12*	40	M	–	–	23	273	Y	D-F	29	Y	N	–	–	–	–	RPS	18y: asym.Without tx
	13	39 + 5	M	–	–	1	220	N	D-P		–	–	D-P	5y (2)	Y	N	RPS	15y: asym. Without tx
	14*	39	M	–	–	56	267	Y	F	–	–	–	F-A	4y	Y	N	RPS	9y: asym. Without tx
	15*	38 + 5	F	–	–	2	310	Y	F-P	34	Y	Y (transient AVB)	–	–	–	–	RPS	8y: asym. Without tx
	16*	39 + 4	F	–	–	27	250	Yes	D-F	–	–	–	D-F	2 m	Y	N	RPS	4y: asym. Without tx

Dx: diagnosis. ID: patient identification. *patients referred from other hospitals after birth. GA: gestational age. Gender: M-male, F-female. WG: weeks of gestation. D: digoxin. F: flecainide. L: labetalol. P: propranolol. A: amiodarone. HR: Heart Rate. HMD: Hemodynamic. ECV: electrical cardioversion. Complic.: Complications. AVB: atrioventricular block. Age: m: moths; y: years. RPS: right posteroseptal. LPS: left posteroseptal. LL: left lateral. Asym: asymptomatic. Tx: treatment. Y: Yes. N: No.

Six of the 16 patients (37.5%) required initial electrical cardioversion due to hemodynamic instability at the onset of tachycardia. Digoxin, flecainide, propranolol, labetalol and amiodarone were used for treatment at different moments, with the majority of patients (75%) requiring drug combination; insufficient control of the tachycardia during the neonatal period in nine of the 16 patients (56.3%) led to cardiac ablation being performed after parental consent.

The procedure was performed during the neonatal period in 9 cases at a median age of 20 days (IQR 16 to 29), with a median weight of 3.4 kg (IQR 2.7 to 3.6), using a simplified single catheter ablation technique. Median duration of the procedure was 40 min (IQR 27.5 to 57.5), with a median radiation time (fluoroscopy) of 7 min (IQR 6 to 19), median PDA 300mGycm2 (IQR 150 to 710), using a usual setup of 55 °C and 30 W of radiofrequency energy with a median radiofrequency time 1.4 min (IQR 1 to 4.6). TABLE 2.

Ablation was effective in all 9 cases, eliminating the tachycardia and leaving no detectable residual conduction through the accessory pathway in the final electrophysiological study. The patient with tachycardiomyopathy (patient #11) showed gradual improvement after controlling the tachycardia, with normalization of the left ventricular ejection fraction after 7 weeks. In one patient (patient #15), transient complete AV block developed during the procedure, in spite of the region of application being far more posterior than the His system. Atrioventricular conduction was spontaneously recovered 24 h later. No other complications were detected. One of the patients requiring neonatal ablation (patient #8), suffered from early recurrence of the tachycardia 7 days after the procedure. He was put under pharmacological treatment and discharged home without tachycardia; however, the arrhythmia reappeared at the age of 8 months and he required a second cardiac ablation, which was effective.

All the seven patients who did not require cardiac ablation during the neonatal period needed a combination of drugs, under which they were discharged. Despite receiving maximal recommended doses, six of them (85.7%) experienced a progressive deterioration and consequently underwent cardiac ablation at 2 months, 4 months (and again at 6 months due to early recurrence), 5 months, 4 years, 5 years (twice) and 7 years old respectively, with final full effectiveness in six cases and with no complications in any of them.

Post neonatal cardiac ablation was performed at a median age of 8 months of life (IQR 5 to 60), with a median weight of 22 kg (IQR 22 to 27), using a simplified single catheter ablation technique. The median duration of the procedure was 17.5 min (IQR14.5 to 26.3), with a median radiation time (fluoroscopy) of 4.5 min (IQR 4 to 9), median PDA 524 mGycm2 (IQR 230 to 720), using a usual setup of 55 °C and 40 W of radiofrequency energy with a median radiofrequency time of 1.1 min (IQR 0.8 to 1.9). TABLE 2.

Patient #1 had a complete atrioventricular block for several hours during the first ablation at 4 months of age, and recovered spontaneously. A second catheterization was performed at 6 months of life and the atrioventricular block reappeared even though the ablation was far from the atrioventricular node. In the follow-up, he shows Wenckebach phenomenon at low heart rates that normalizes at heart rates above 90 bpm. He has a normal active life.

Patient #10 was referred from another country at 5 months of age (due to bureaucratic issues) for failure to control his tachycardia despite simultaneous combination of four drugs. When he arrived at our center, he had severe ventricular dysfunction and severe left ventricle dilation. He underwent cardiac ablation at his arrival. Heart function was completely restored at discharged, 2 weeks later.

Patient #14 was discharged with pharmacological (flecainide and amiodarone initially, then only flecainide). However, at age 3 he was admitted with cardiogenic shock due to uncontrollable tachycardia and he was ablated.

Only one of the 16 patients could be successfully managed in the long term with medical treatment, with no need for cardiac ablation. He received double therapy with flecainide and digoxin (due to respiratory

Table 2
General characteristics of the radiofrequency ablation.

ID patient	RFA age	Weight at RFA, Kg	Procedure duration, minutes	Fluoroscopy duration, minutes	Radiofrequency energy exposure			PDA (mGycm2)	Ablation site	Number and characteristics of catheters
					T, °C	W	Time (*sec*)			
1	4 m	7	40	8	60	25	23	288	RPS	1, Medtronic 5Fr
	6 m	8.3	35	6	55	20	119	201	RPS	1, Medtronic 5Fr
2	7y	34	30	15	56	50	116	806	LPS	1, Cordis 6Fr, curve B
3	9d	2.5	35	5	55	20	273	133	RPS	1, Cordis 6Fr, curve B
4	17d	3.2	35	6	50	30	43	221	RPS	1, Medtronic 5Fr
6	15d	3.4	45	9	55	30	86	299	LPS	1, Medtronic 5Fr
7	21d	2.2	15	5	55	25	84	137	RPS	1, Medtronic 5Fr
8	20d	2.7	70	26	50	40	473	885	RPS	1, Medtronic 5Fr
	8 m	7.8	15	5	45	38	90	237	RPS	1, Cordis irrigated curve B
9	16d	3.6	25	17	45	40	60	606	LL	1Medtronic 5Fr- > Cordis irrigated, curve B (30 W)
10	5 m	7.2	20	12	45	35	410	441	RPS	1, SJM 5Fr
11	59d	5.3	30	19	55	30	388	709	RPS	1, Medtronic 5Fr
12	29d	3.5	45	7	65	35	35	304	RPS	1, Medtronic 5Fr
13	5y	22	25	4	55	25	57	768	RPS	1, Cordis 6Fr curve B
	5y (2°)	22	15	4	55	35	66	705	RPS	1, Medtronic 5Fr
14	4y	27	13	3	45	35	38	608	RPS	1, Cordis Irrigated 7Fr, curve B
15	34d	4.2	75	7	55	35	70	302	RPS	1, Medtronic 5Fr
16	2 m	4.5	15	4	52	30	49	149	RPS	1, SJM 5Fr

ID: identification. RFA: radiofrequency ablation. Kg: kilograms. T: temperature. °C: degrees Celsius. W: watt. Sec: seconds. PDA: product dose area. RPS: right postero-septal. LPS: left postero-septal. LL: left lateral.

intolerance to beta-blockers) for 3 years and the treatment could be gradually withdrawn thereafter without new episodes during the 11-years follow-up.

None of the 16 patients had cardiac malformations. In 13 of them (81.3%) the accessory pathway was located right posteroseptal. There was only one complication (5.5%) in 18 ablations, with a type II AVB that normalizes at high heart rates. The ablation was completely effective in 14 out of the 15 patients who underwent the procedure (93%).

All images were stored with an acquisition of 3.75 fps. Catheters used for the ablation procedure were 5F Mariner Radiofrequency catheter (Medtronic®) and 6F non-irrigated and 7F irrigated catheters (Cordis®), and lately 5F FlexAbility™ (SJM, Abbott).

After a median follow-up of 10.4 years (IQR 7.6 to 14.4 years), no recurrence has been detected and no patient has neither cardiac dysfunction or EKG abnormalities, including criteria for ischemia (neither at rest nor during the exercise stress test performed at the age of 7 years). All of them have currently a good quality of life, attend school normally and practice sport regularly without having complained of palpitations, dizziness or chest pain. Serial echocardiographic exams show normal indexed chamber sizes and cardiac function, with no valve regurgitations.

Discussion

PJRT is an uncommon form of paroxysmal supraventricular tachycardia, but accounts for the most common cause of incessant tachycardia in children. The mechanism for the tachycardia is an exclusively retrograde conduction accessory pathway with slow and decremental properties. Consistent with prior reports, the most frequent location of the accessory pathway in our series was the right posteroseptal region [14].

Heart rate is usually lower than in other types of tachycardias and it often alternates with periods or isolated beats of sinus rhythm. Because of these characteristics it can appear unnoticed and progress to tachycardiomyopathy [10–13]. In fact, the first sign of the disease may be heart failure, as was the case in three of our patients [11].

In our data, the mean maximum heart rate reached was 240 bpm in the prenatal cases and surprisingly higher (mean 260 bpm, up to 300 bpm) for those diagnosed after birth, which is not characteristic of a PJRT.

It should be noticed that some patients presenting with fetal tachycardia are free of rhythm abnormalities during first days of life (up to a week). This might be related to persistence of plasmatic therapeutic levels in the newborn of the drugs received during gestation. When drug concentrations decrease, tachycardia might reappear (usually 2–4 days after) if no treatment is given. Individual variations in drug metabolism may lead to a delayed diagnosis if the patient is discharged too early and increase the risk of morbidities due to an inadvertent tachycardia.

As it has shown in our series, the therapeutic approach is very heterogeneous both during the fetal and neonatal periods 10. This can be explained by several reasons: 1) there is no ideal treatment for this type of tachycardia. Some authors consider beta-blockers as first line drugs, while other published pediatric series show high rates of success with other drug combinations like amiodarone and beta-blockers [13,15]; 2) due to the long time span covered by this series (15 years) therapeutic trends might have changed throughout this period. Digoxin was the first option for treatment before 2010, while patients were started on flecainide after this date; 3) most of the patients were referred to our hospital from other centers due to failure to control tachycardia, and had therefore received several and variable treatments before being admitted in our center.

Fetal tachycardia with rates under 230 bpm does not usually associate complications such as cardiac dysfunction or fetal hydrops and are usually controlled with maternal pharmacological treatment [16]. Accordingly, newborns with heart frequencies lower than 230 bpm in our series could usually be managed with pharmacologic treatment. Patients with higher heart frequencies benefited from cardiac ablation in the neonatal period.

In our review, failure to control the tachycardia with medical therapy was the rule. The most commonly prescribed regime was flecainide and digoxin, with others being flecainide or digoxin with propranolol. Some patients received up to four treatment combinations before stabilization. Several pharmacologic regimes have been proposed to treat refractory supraventricular tachycardias; sometimes a combination therapy is required to control the arrhythmia. The growing experience in simplified percutaneous techniques has brought cardiac ablation to the front line of the therapeutic arsenal in hemodynamically unstable patients with incessant tachycardia, even for those with low weight [17]. In our series, the mean weight of the patients who required ablation in the neonatal period was 3.4 kg, with the smallest one being 2.2 kg, and the total procedure was carried out in a mean of 43 min. The total effectiveness rate was 93%, consistent with a multicenter cohort study by Kang et al., which described a 90% success rate for pediatric PJRT ablations [18].

These procedures can be carried out with high effectiveness and few complications, especially if using the minimum possible number of

catheters (often one or maximum two), and minimizing procedural, radiation and anesthetic times [10,17]. In our series, the incidence of complications was similar to that reported in other recent studies (1/18, 5.5%), with transient AV block being the most remarkable [18–20]. Even when ablation was only partially effective, it benefited patients making tachycardia episodes, less frequent, less intense and less hemodynamically significant. It allows for a better pharmacological control of the arrhythmia with fewer drugs and lower doses, to the extent that some patients can even go without.

Previous use of simplified percutaneous techniques for cardiac ablation in pediatric patients (>1500 cases up to date) has helped build the necessary experience to extend this knowledge into the neonatal field with no major complications due to the radiofrequency ablation.

Our study has some limitations: 1) it is a retrospective collection of data and the long duration of the study period, with the consequent change in treatment protocols. 2) Incidence and prevalence of tachycardias our neonatal unit cannot be extrapolated to general hospital as our is a National reference center, that could be a bias.

However, the strength of our study relies on the analysis of the bigger series of very young patients and the evidence that cardiac ablation can be a safe and effective technique even in newborns.

Conclusions

PJRT, when refractory to pharmacological treatment, can lead to ventricular dysfunction and hemodynamic instability. Pharmacological therapy using multiple drugs is often ineffective in controlling the tachycardia and cardiac ablation should be taken into account at early stages even in very young patients. This can be performed safely using simplified single catheter ablation techniques, but this technique requires a learning curve in order to minimize complications and radiation time.

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