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CASE REPORT

ADVANCED

CLINICAL CASE

First-in-Human Percutaneous Circumferential Annuloplasty for Secondary Tricuspid Regurgitation

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ABSTRACT

Transcatheter therapies to treat tricuspid regurgitation are being developed, but few have attempted the gold standard of surgical repair: ring annuloplasty. We describe the first-ever fully percutaneous implantation of a circumferential, semirigid annuloplasty ring to treat massive secondary tricuspid regurgitation. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2020;2:2176–82) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

We describe the first human implantation and adjustment of a 2-stage Percutaneous Annuloplasty System (Cardiac Implants LLC, Tarrytown, New York) to treat tricuspid regurgitation (TR).

LEARNING OBJECTIVES

- To recognize that the surgical gold standard to treat secondary TR can be converted to a fully percutaneous procedure.
- To appreciate the importance of multimodality imaging in the pre-procedural and intraprocedural stages of TV interventions.

HISTORY OF PRESENTATION

A 69-year-old woman with a history of symptomatic right-sided New York Heart Association class III heart failure with maximal medical management was considered high risk for surgery.

PAST MEDICAL HISTORY

The patient had a history of stroke, stage II hypertension, atrial fibrillation, hyperlipidemia, and thyroid disease. She was taking spironolactone and warfarin.

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DIFFERENTIAL DIAGNOSIS

The differential diagnosis of secondary TR is broad, including pulmonary hypertension and congestive heart failure. Extensive baseline evaluations, including multimodality imaging, laboratory tests, physical examination, and past medical history, were used to rule out primary TR.

INVESTIGATIONS

Semiquantitative/quantitative color flow and structural measurements from the baseline transthoracic echocardiography (TTE) (**Figure 1A**) were characteristic of massive TR (**Table 1**) (1,2). The tricuspid valve (TV) and leaflets were structurally normal, with no evidence of TV stenosis. Cardiac computed tomography (CT) volume-rendered reconstructions (TeraRecon Aquarius, TeraRecon Inc., Durham, North Caroline) revealed no abnormalities in the TV (medial, anterior, and inferior) papillary muscles or right ventricular moderator band (septomarginal trabecula). HeartNavigator (Koninklijke Philips N.V, Amsterdam, the Netherlands) was used to virtually plan the implant procedure (**Figure 2**), including determining the distance from the right coronary artery (RCA) to the optimal landing zone (**Figure 3A**) and designing a ring delivery system (RDS) customized to the shape and size of the patient's TV annulus (TVA).

MANAGEMENT

In the first procedure, a fully circumferential ring was percutaneously implanted over the TVA (**Figure 3B**). The implant system consists of an RDS and annuloplasty ring (**Figure 1L**). The ring is flexible, with a built-in adjusting cord and 10 barbed 7.5-mm stakes, each with a penetrative depth of 7 mm. Their small profile minimized the potential for adverse atrioventricular nodal impact. Following a standard cut-down technique to the right jugular vein and introduction of a guidewire into the pulmonary artery, the RDS was advanced into the right atrium (Video 1). The proximal balloon of the RDS was inflated to expand the scaffold (Video 2). The scaffold was then maneuvered to align the ring plane, fluoroscopically guided by the radiopacity of the metal ring delivery scaffold. Real-time 3-dimensional transesophageal echocardiography (TEE) (midesophageal and transgastric views) was used to image each launcher and to confirm its contact with tissue. Small adjustments were guided by both imaging modalities, TEE and fluoroscopy, until optimal positioning was achieved (**Figures 1G and 1H**). The ring was then launched into the tissue in a single step (Video 3). Implantation and ring-to-tissue contact were again confirmed by TEE, and the RDS was then retracted (Videos 4 and 5). The adjustment cord tethers were sheathed through a cord protector to prevent tissue overgrowth and thrombus formation during the healing period. Excess cord was coiled and placed into a cord protector pouch below the skin. The time of the procedure (from insertion through removal of the investigational device) was 139 min, including 34 min of fluoroscopy. The patient was discharged with no procedure-related adverse events.

Over 90 days, the injury point created by the barbed stakes in the TVA promoted the encapsulation of the ring by tissue. The healing period minimizes the risk of dehiscence, by providing strong holding forces to secure the implant. Indeed, 4-dimensional CT reconstruction demonstrated the ring implant to be encapsulated by TVA tissue (**Figure 1I**).

At 90 days, the ring implant was adjusted in situ during a second procedure. Pre-procedural TTE (**Figure 1B**) demonstrated stabilization of disease without worsening TR. The capsule containing the adjustment cords was removed, and the cords were accessed again. The cord ends were hooked to a CORKNOT system (LSI Solutions Inc., Victor, New York), and it was advanced through the access sheath to the implant. The 3-dimensional TEE before adjustment demonstrated the implanted ring in TVA tissue (**Figure 1J**). Under fluoroscopy and TEE guidance, the implant ring was gradually adjusted by traction on the tethers to reduce the TVA diameter from approximately 42.0 ± 0.5 mm to 37.5 ± 0.5 mm in the septolateral dimension (4-chamber view). A CORKNOT clip was used to secure the adjusted ring, and the tether cords were cut. Total procedure time was 170 min, including 14 min of fluoroscopy.

DISCUSSION

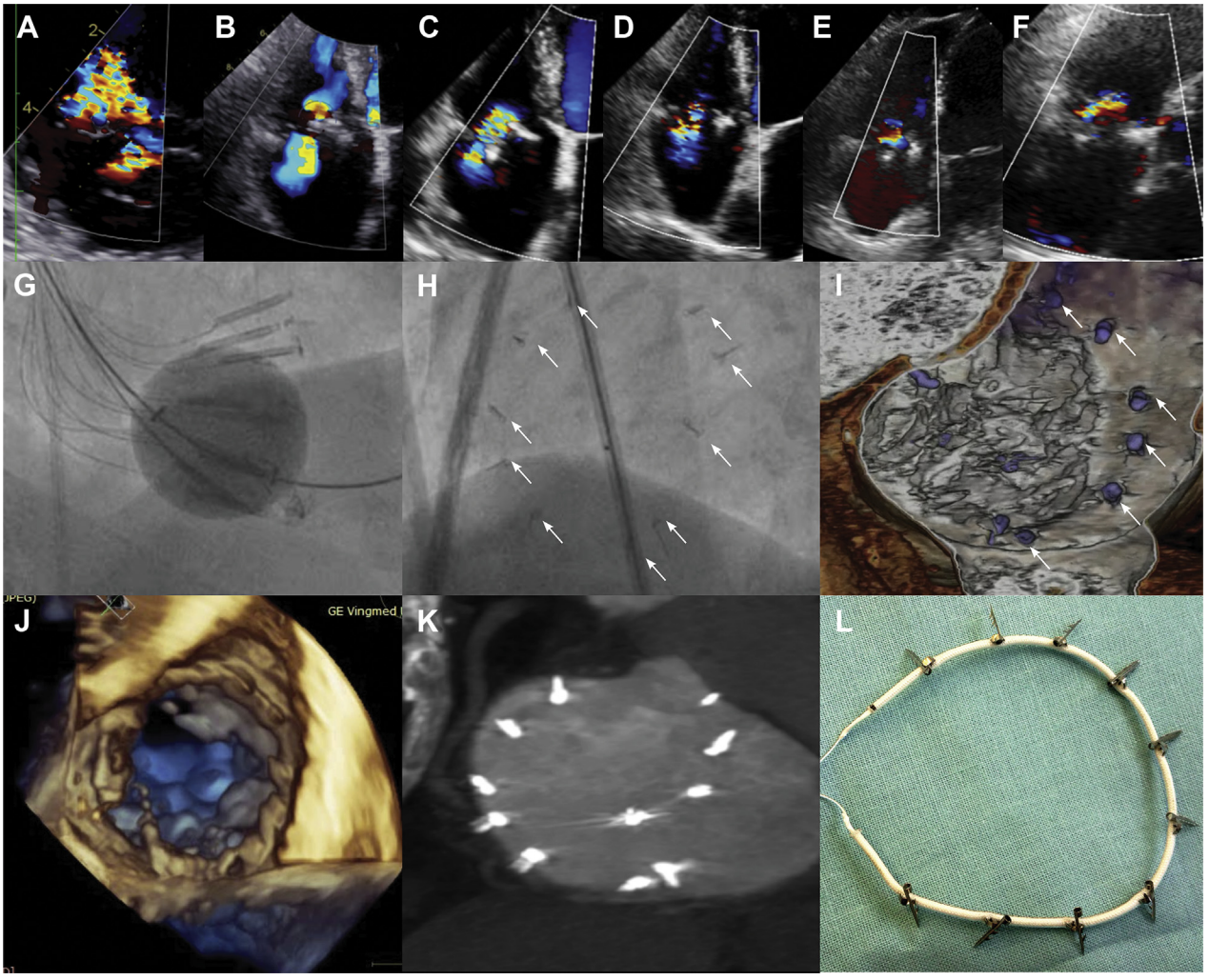
Transcatheter annuloplasty has a mechanism predicated on the gold standard for surgical therapy for TV repair. Surgical rings aim to correct or restore the physiological shape of the TVA and re-establish the 3-dimensional geometry to prevent further annular dilatation (3–5). We describe the first percutaneous, fully circumferential ring annuloplasty for TR therapy (**Central Illustration**).

As in surgical ring annuloplasty, this study device aims to re-establish the physiological shape of the annulus and prevent further dilatation. Following the healing period, the implanted ring and thus also the TVA are reduced in size, thereby restoring leaflet

ABBREVIATIONS AND ACRONYMS

CT = computed tomography
RCA = right coronary artery
RDS = ring delivery system
TEE = transesophageal echocardiography
TR = tricuspid regurgitation
TTE = transthoracic echocardiography
TV = tricuspid valve
TVA = tricuspid valve annulus

FIGURE 1 Multimodality Imaging at Baseline and Follow-Up



(A) Baseline transthoracic echocardiography. **(B)** Transthoracic echocardiography 90 days post-implantation and pre-adjustment. Post-adjustment transthoracic echocardiography: **(C)** at 30 days; **(D)** at 90 days; **(E)** at 180 days; (**F**) at 365 days. Intraprocedural fluoroscopy: **(G)** side view of the ring implant on a scaffold before deployment; **(H)** en face view of the ring implant in tissue post-deployment; **arrows** indicate stakes of the ring implant. **(I)** Post-implantation 4-dimensional computed tomography; **arrows** indicate the stakes of the ring implant (not all stakes are visible in this view). **(J)** 3-dimensional transesophageal echocardiography post-implantation and pre-adjustment. **(K)** Computed tomography of the tricuspid valve annulus and the ring **implant (white trigones)** at 180 days post-adjustment. **(L)** The Percutaneous Annuloplasty Ring (Cardiac Implants LLC, Tarrytown, New York).

coaptation. Among surgical therapies, ring annuloplasty is preferred given its superior long-term mortality outcomes and freedom from recurrent TR (3-7). Our patient had no evidence of disease worsening, with improvement in TR grade sustained out to 1-year post-intervention. Her heart failure status improved at 180 days post-adjustment, and it was also maintained to 1 year. Echocardiographic and CT evaluation at 1 year confirmed an unchanged TVA diameter, with no recurrence of annular dilatation or failure of the therapy. Moreover, there were no device- or procedure-related adverse events over 1-year post-adjustment.

Pre-procedural, multimodality imaging has been recommended during percutaneous TR interventions to assess the vena cava for delivery, assess ventricular size and function, define the TVA, and determine the proximity of adjacent structures (i.e., RCA) (8). In this case, the use of multimodality imaging was crucial for both pre-procedural planning and real-time guidance.

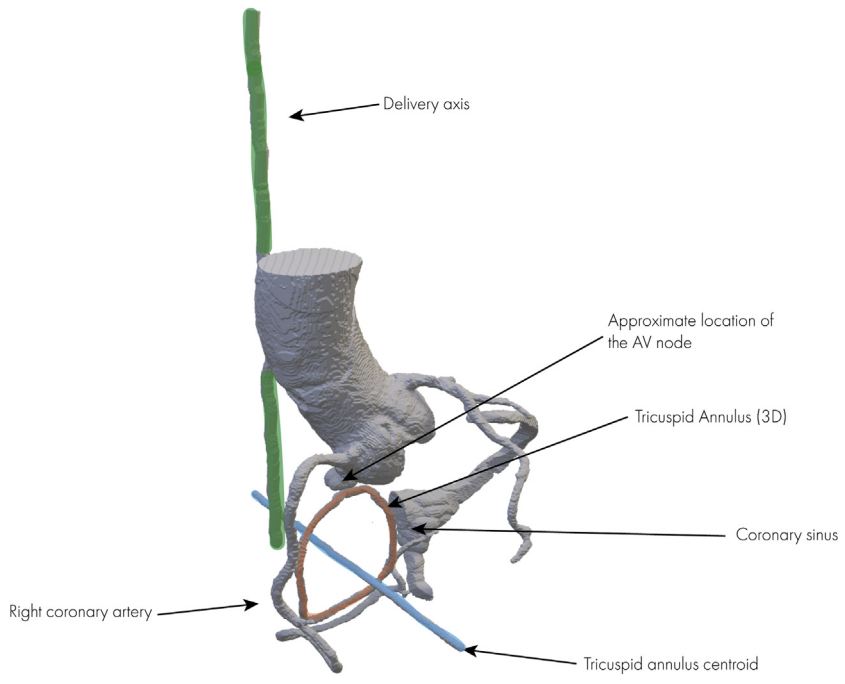
TABLE 1 NYHA Functional Classification and TTE Findings at Baseline and Follow-Up

	Baseline	Adjustment Procedure	30 Days Post-Adjustment	60 Days Post-Adjustment	90 Days Post-Adjustment	180 Days Post-Adjustment	365 Days Post-Adjustment
NYHA functional classification	III	III	III	III	III	II	II
Structural and hemodynamic							
RV length (mm)	57.0	–	–	–	–	60.0	59.0
RV end-diastolic diameter (mm)	40.0	39.0	42.0	–	42.0	36.0	36.60
LV end-diastolic diameter (mm)	46.0	43.0	–	–	45.0	46.0	45.0
sPAP (mm Hg)	55.0	–	–	–	-	38.0	35.0
Semiquantitative							
VCW (cm)	0.80	0.60	0.30	0.30	–	0.30	0.40
PISA radius (cm)	1.00	0.90	–	–	–	0.35	0.30
Quantitative							
TV annular diameter (mm)	44.0	42.0	36.0	32.0	–	38.5	34.0
PISA EROA (cm^2)	0.70	0.50	–	–	–	0.10	0.16
TV tenting height (cm)	0.60	0.20	–	–	–	–	–
Grading							
Tricuspid regurgitation	Massive	Severe	Mild	Mild	Mild	Mild-moderate	Mild-moderate
Mitral regurgitation	Mild-moderate	Trace	Mild-moderate	Mild-moderate	Mild-moderate	Mild-moderate	Mild

EROA = effective regurgitant orifice area; LV = left ventricular, NYHA = New York Heart Association; PISA = proximal isovelocity surface area; RV = right ventricular; sPAP = systolic pulmonary artery pressure; TTE = transthoracic echocardiography; TV = tricuspid valve; VCW = vena contracta width.

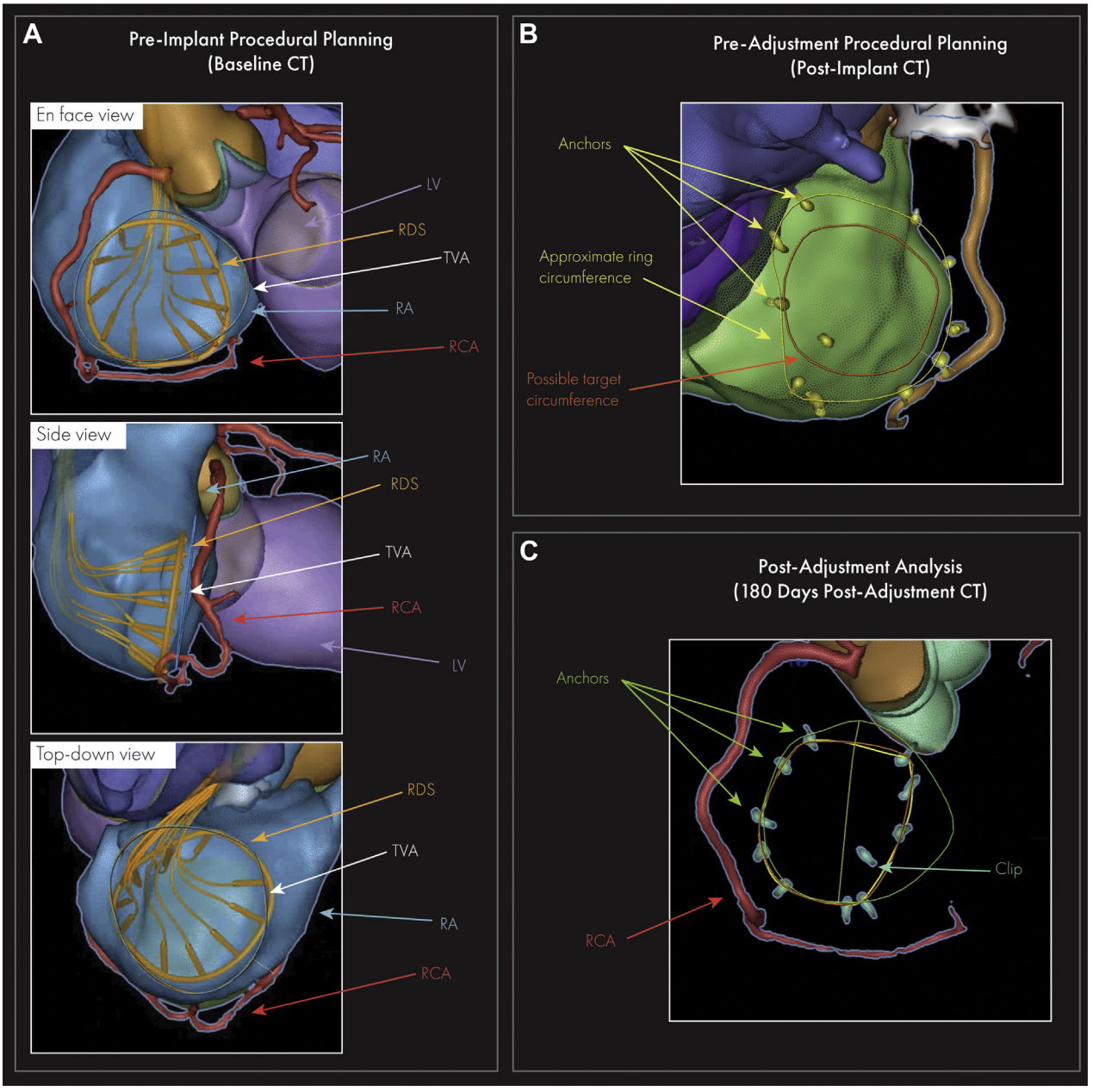
Fluoroscopy guided the planar alignment of the RDS with the TV. TEE confirmed tissue-to-launcher contact before deployment of the launchers. Post-procedural and follow-up imaging provided an understanding of the relative depth and angles of the ring stakes (Figures 3B and 3C). Through fluoroscopy, the position, relative motion, and relationship between the stake and the ring attachment bracket were

FIGURE 2 Pre-Procedural Planning Using 3D Reconstructions



3-dimensional (3D) Reconstruction from baseline cardiac computed tomography to plan the axis of delivery. AV = atrioventricular.

FIGURE 3 Pre- and Post-Procedural CT Reconstructions

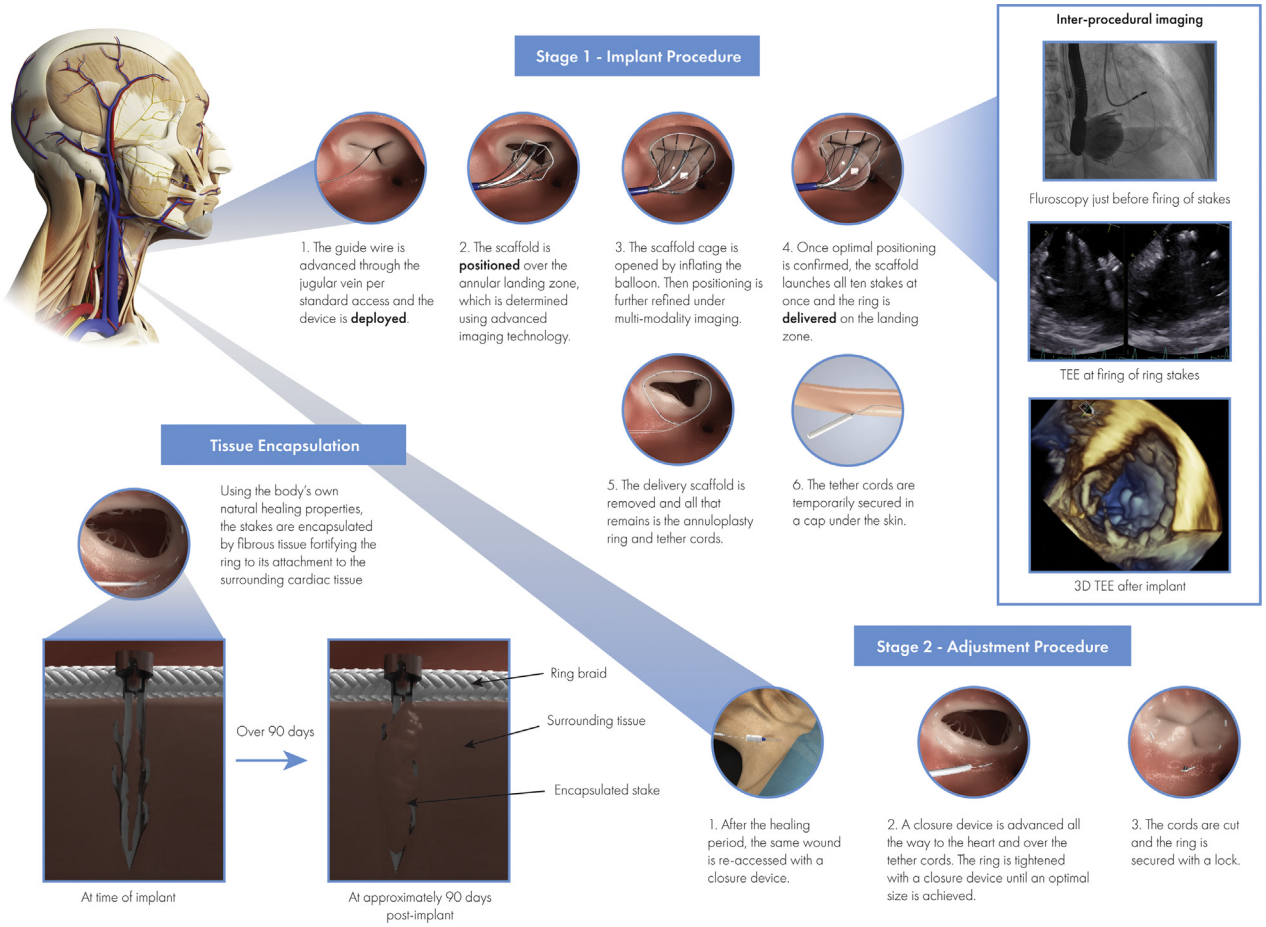


(A) Pre-procedural planning for the implantation procedure using baseline computed tomography (CT) data with the approximate circumference of the tricuspid valve annulus (TVA), scaffold of the ring delivery system (RDS), proximity to right coronary artery (RCA), and surrounding anatomy (right atrium [RA], left ventricle [LV]). **(B)** In a view from the right atrium, post-implantation pre-adjustment planning. **(C)** In a view from the right ventricle, post-adjustment analysis at approximately 180 days post-implantation.

assessed. The stakes were directly visualized by TEE along the imaging slices. At 30 days post-implant, multiphase CT was used to determine the exact positioning and implantation depth.

Post-operative imaging also revealed that 2 stakes on the posteroseptal aspect of the TV were sub-optimally implanted (Figure 3B). Despite this complication, an adjustment was successfully

CENTRAL ILLUSTRATION **Fully Percutaneous, Circumferential Ring Annuloplasty for Secondary TR**



Reddy, V.Y. et al. J Am Coll Cardiol Case Rep. 2020;2(14):2176–82.

The 2-stage approach for a fully percutaneous ring annuloplasty to treat severe tricuspid regurgitation (TR). Stage 1 is the implant procedure followed by the 90-day tissue encapsulation period, at which point stage 2 is the adjustment of the implanted ring.

completed (Figure 3C). After weighing the potential risks and benefits of attempting greater or lesser annular adjustment, and given the patient's valvular morphology and dysfunction and the early experience with this device, we chose a strategy of lesser adjustment. Nonetheless, an adjustment of approximately 5 mm resulted in a change of TR by 2 grades. Further refinement of multimodality imaging practices will likely help minimize suboptimal stake placement in future cases.

There is a risk of pull-through in implantable TR devices, especially when the tissue is frail or diseased. Unlike in other percutaneous interventions, the implanted ring is allowed to be encapsulated with fibrous tissue before applying any traction. In preclinical experiments, 30 days allowed sufficient time for tissue encapsulation of stakes and subsequent successful adjustment without pull-through or dehiscence (D. Alon and A. Siefert, unpublished data, September 2015). Indeed, by the end of 90 days, the holding strength of the annular stakes was superior to that of surgical sutures (D. Alon and A. Siefert, unpublished data, September 2015).

Similarly, some devices may pose a risk of kinking the RCA. With this device, however, no force or motion (i.e., twisting or turning) is applied directly to the stakes; instead, the ring is circumferentially tightened by pulling on the tether cords. Therefore, the risk of kinking the RCA appears minimal.

Given the mode of delivery and the characteristics of the implant system, rigorous patient selection is key to the success of this procedure. An adequate

acoustic window is necessary for the implant procedure because the procedure cannot be guided by fluoroscopy alone. Additionally, the current design of the RDS precludes patients with right ventricular leads from receiving this device.

FOLLOW-UP

Various functional and imaging assessments were performed to 1-year post-adjustment (Table 1). There were no procedure- or device-related serious adverse events. The New York Heart Association functional class improved to class II, and post-procedure TR improved to mild by 1 month (Figures 1C and 1D). The adjustment of the ring was maintained at 6 months post-adjustment, as confirmed by CT (Figure 1K) and TTE (Figure 1E). At 1-year post-adjustment, this patient's TR remained mild to moderate (Figure 1F).

CONCLUSIONS

We describe the first successful implantation of the Percutaneous Annuloplasty System in a patient with massive TR and severe annular dilatation. Both the implantation and the adjustment procedures were successfully and safely performed, with consequent improvements in heart failure symptoms and TR. The implanted ring maintained its adjusted diameter out to 1-year post-adjustment, with no evidence of ring failure. The ongoing first-in-human study will provide additional feasibility data to determine the safety profile for this device.

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AUTHOR DISCLOSURES

This report discusses a case from a study funded by Cardiac Implants LLC. Dr. Reddy has consulted for Cardiac Implants LLC; and has an equity interest in Cardiac Implants LLC. Dr. Abbo has an equity interest in Cardiac Implants LLC; and has been employed by Cardiac Implants LLC. Drs. Ruiz and Kerner has consulted for Cardiac Implants LLC; and has an equity interest in Cardiac Implants LLC. Mr. Kipshidze is employed by Cardiac Implants LLC. Dr. Avisar is employed by Cardiac Implants LLC. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS 3-dimensional, electrocardiogram, right ventricle, treatment, tricuspid valve, valve repair

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