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ORIGINAL ARTICLE

Technical Feasibility on the Use of Optical Coherence Tomography in the Evaluation of Pediatric Pulmonary Venous Stenosis

Jenny E. Zablah[1] · Barry O'Callaghan[1] · Michael Shorofsky[1] · Dunbar Ivy[1] · Gareth J. Morgan[1]

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Abstract

Pulmonary vein stenosis (PVS) in children is a morbid disease and limited progress has been made in improving outcomes for this heterogenous group of patients. Evaluation is currently limited to imaging techniques that fail to provide an adequate overview of the intraluminal and luminal pathology perpetuating our limited understanding of this condition. Optical coherence tomography (OCT) is an imaging modality which provides intraluminal profiling with microstructural detail through optical reflective technology. We sought to evaluate whether its use was technically feasible in pediatric PVS and whether the imaging data provided potentially useful outputs for clinical utility. Eleven patients were prospectively selected from our cardiac catheterization for OCT evaluation of their pulmonary veins (PV) during elective catheterization for PVS. Measurements were taken both pre and post intervention using both manual and automated tools. Stent morphology was characterized. Eleven patients had evaluation of 34 pulmonary veins, with 7 patients having more than one assessment, for a total of 25 overall catheterizations. Most patients were female (75%). Median age at cardiac catheterization was 35 months (range 5–45 months). Median weight of subjects was 10.6 kg (3.7–14.2) with a median BSA documented at 0.505 m^2 (0.21–0.57). Median number of pulmonary veins involved was 3, (range 1–5 veins) and median contrast volume of 2.9 mL/kg (0.7–3.7) given. Median radiation dose (DAP) was 6095 μGy·cm^2 (1670–12,400). Median number of previous cardiac catheterizations was 7 (range 1–11). All of the vessels with a diameter < 5 mm were adequately visualized. Of all the OCT images acquired, in 15 vessels (44%) contrast was used to clear the vessels from blood as an angiogram was required at the time, in the other 19 vessels (56%), saline was used with adequate imaging. There were no complications related to OCT. OCT is technically feasible to use in pediatric patients without any directly related complications. It provides intraluminal anatomy in children with both native and treated pulmonary venous stenosis when vessel size is less than 5 mm.

Keywords Congenital heart disease · Prematurity · Optical coherence tomography · Pulmonary venous stenosis · Pediatric cardiac catheterization

Introduction

Pulmonary venous stenosis is a complex disorder that affects a small subset of infants and the congenital heart disease population. Disease may be native [1], post-operative, or associated with other disorders such as chronic lung disease of prematurity. Disease may be focal, segmental, or diffuse and venous distribution may be isolated or affect several veins bilaterally [2]. This cohort of patients continue to suffer poor outcomes with respect to long-term survival though we have seen some recent improvements in short-to-medium term survival, particularly, as we have progressed towards more aggressive targeted treatment in the cardiac catheterization laboratory [3, 4]. We continue to have a limited understanding of the evolution of this condition and struggle to define those most likely to benefit from various treatments. It is also difficult to predict those likely to develop aggressive restenosis after balloon angioplasty or stent implantation. Our limited understanding is perpetuated by the inherent difficulty in evaluating intraluminal disease in these small vessels which are precariously accessed by catheterization via the left atrium [5].

Current treatment strategies involve surgical management and catheter-based treatments including balloon angioplasty

✉ Jenny E. Zablah
jenny.zablah@childrenscolorado.org

[1] The Heart Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, Colorado, USA

and stenting [4, 6–8]. These treatments may be paralleled with pharmaceutical strategies including antithrombotic, anticoagulation, and systemic anti-proliferative agents like sirolimus [9–11].

Focused imaging evaluation is currently limited to echocardiography [12], Computed Tomography Angiogram (CTA) & cardiac Magnetic Resonance Imaging (cMRI) [13–15] as well as angiographic evaluation performed during invasive cardiac catheterization [2, 16–18]. These modalities provide an overview of disease distribution and anatomical profiling which can assist with treatment planning and decision making. The intraluminal profile of disease, including both the surface and subsurface characteristics of these vessels, is poorly appreciated on all of the above imaging evaluations. Our current limited understanding of the pathological basis of this disease process is based on histological and pathological specimens from surgical tissue and postmortem evaluation [19, 20]. Preliminary reports of intravascular ultrasound assessment of the pulmonary veins in children have been published and present some interesting findings with respect to the intraluminal profile of disease [21]. Ultrasound assessment is, however, limited in some instances in its ability to produce images of diagnostic resolution thus leaving questions with respect to this disease substrate and potential baseline luminal wall abnormalities in this population.

Optical coherence tomography is a novel imaging technology based on broadband low coherence infrared light combined with interferometry which can produce high-resolution images of opaque human tissues. Its use has been established in adult coronary evaluation facilitating the acquisition of surface and subsurface tissue characteristics [22]. This has facilitated the evaluation of complex coronary plaques and stent vessel relationships and has facilitated more informed practice around specific interventions for complex lesions and decision making [23, 24].

We surmised that due to the small caliber of pulmonary veins, similar in dimension to coronary arteries, that this invasive imaging modality may have useful application in the evaluation of both diseased and treated pulmonary venous stenosis in children.

Here, we report our experience with the use of OCT in a small cohort of patients and its feasibility to be used in pediatric patients with pulmonary vein stenosis.

Materials and Materials

We performed a single-center retrospective review of all patients who underwent pulmonary venous assessment with OCT from October 2020 to April 2021. The objectives were to determine the feasibility of performing OCT in pediatric pulmonary veins, evaluate if whether OCT can visualize the lumen, vessel walls, and stent characteristics (when applicable). The secondary objective was to identify any adverse events related directly to OCT. This study was approved by the institutional review board with a waiver of informed consent due to its retrospective nature.

OCT was performed at the time of cardiac catheterization at the discretion of the operator without a standard protocol. No patients had a cardiac catheterization for the sole purpose of performing OCT. Indications for cardiac catheterization included clinical symptoms, echocardiographic findings, and/or CTA findings of new or worsening pulmonary vein stenosis.

OCT was performed with a Dragonfly Optis Imaging catheter (Abbott Vascular, Santa Clara, CA, USA) into the pulmonary vein of interest. The Dragonfly catheter was advanced over a 0.014″ wire via either a *5Fr or 6Fr Judkins Right (JR) guide catheter* (Terumo©) or a *4Fr long sheath*. Layered contrast (2 mL)/saline (5 mL) was used to displace blood (which causes infra-red scatter attenuating the signal and limiting image acquisition) from the vascular area of interest, only when an angiogram was required. Seven mL of saline was used instead of contrast when an angiogram was not required. Imaging acquisition was achieved through automatic pullback, the system has two modes for image acquisition: "Survey" mode (rapid pullback of 75 mm over 2.1 s at 180 frames per second) and "High Resolution" mode

Table 1 Technique description

Catheter used	≥ 5Fr Guide catheter or ≥ 4Fr sheath
Flush to clear blood	7 ml of saline **or** 2 mL contrast + 5 mL saline injected over the acquisition time
Average time from catheter insertion to image acquisition:	Average of 4 min
Maximum vessel/stent lumen diameter	5 mm
Sites of injection for blood clearance	**Wedge injection** for ostial anatomy **Direct Pulmonary Vein injection** for vessel luminal anatomy
OCT modes	Survey mode: rapid pullback of 75 mm over **2.1** s High Resolution mode: 54 mm segment over **3 s**
Stent 3D reconstruction available	Stent diameters ≤ 3.5 mm

(54 mm segment at the same frame rate over 3 s). Modes were selected as per operator's preference (Table 1).

First, the veins were categorized as native veins or post stent implantation. Then these veins were divided based on adequate or inadequate visualization, this referred to the ability to see the vascular lumen and wall architecture enough to do measurements. For patient with prior stents in the vessel, we evaluated the ability to identify stent strouts and the stent lumen. A subgroup of the stented vessels was evaluated to identify which ones could obtain a 3D reconstruction of the stent (Figs. 1 and 2).

Three-dimensional (3D) reconstructions of the region of interest were also post processed to evaluate the distribution of disease and its relationship to stent struts (Fig. 2). The OCT OS automatically registered stent anatomy through struct identification technology and performed automated measurements of area and diameter. These were repeated manually, and neo-intimal thickness was measured at the largest diameter from stent to neo-lumen (Fig. 3).

Further data collection involved the collection of patient demographics, cardiac diagnosis, hemodynamic and angiographic data as well as index and prior procedural data. Continuous data were reported as median (range) or mean (SD) and categorical data were reported as frequencies.

Results

Thirty-four pulmonary veins in 11 patients during 25 cardiac catheterizations underwent OCT evaluation. Patient demographics, clinical data, procedural data, and OCT

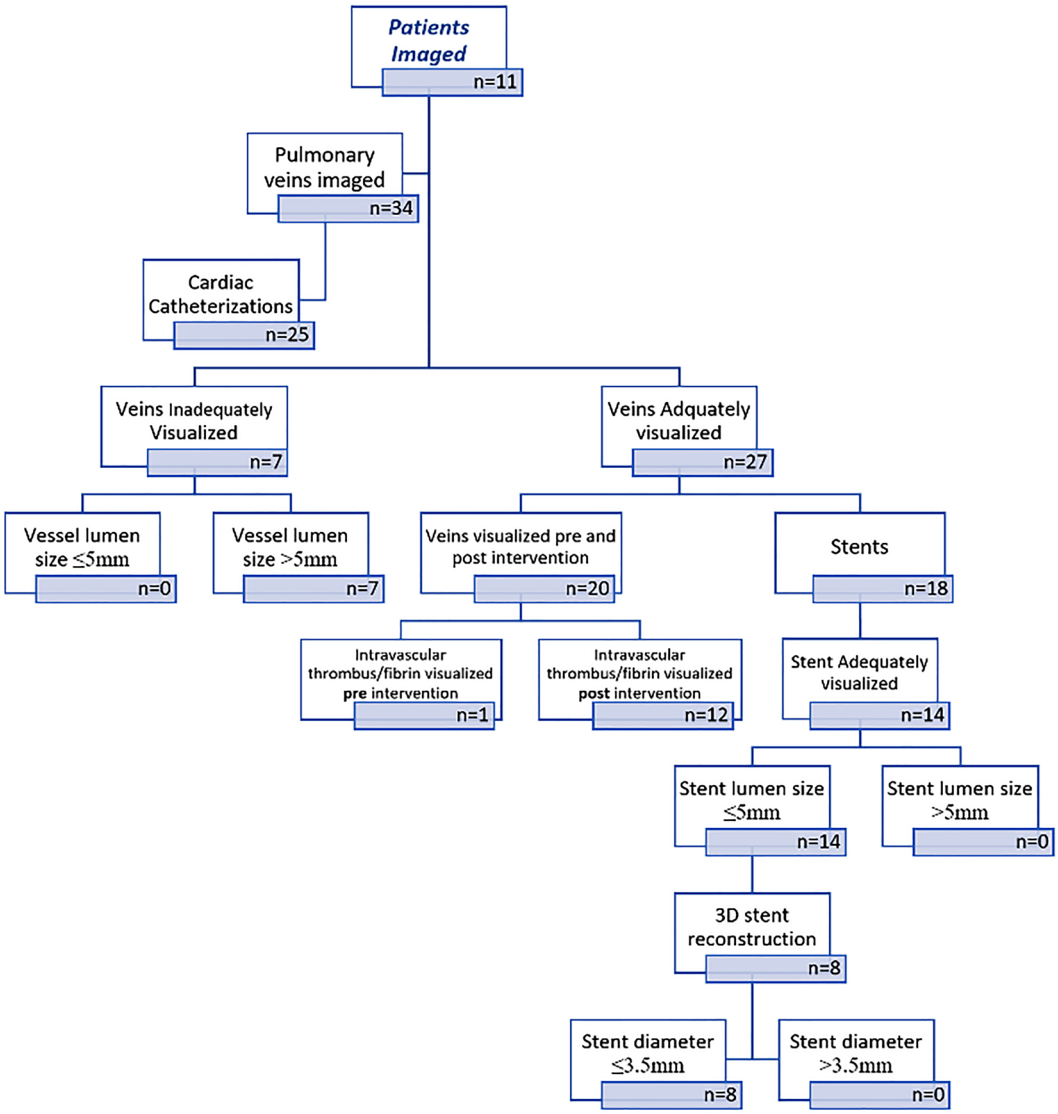

Fig. 1 Description of pulmonary veins assessed with OCT

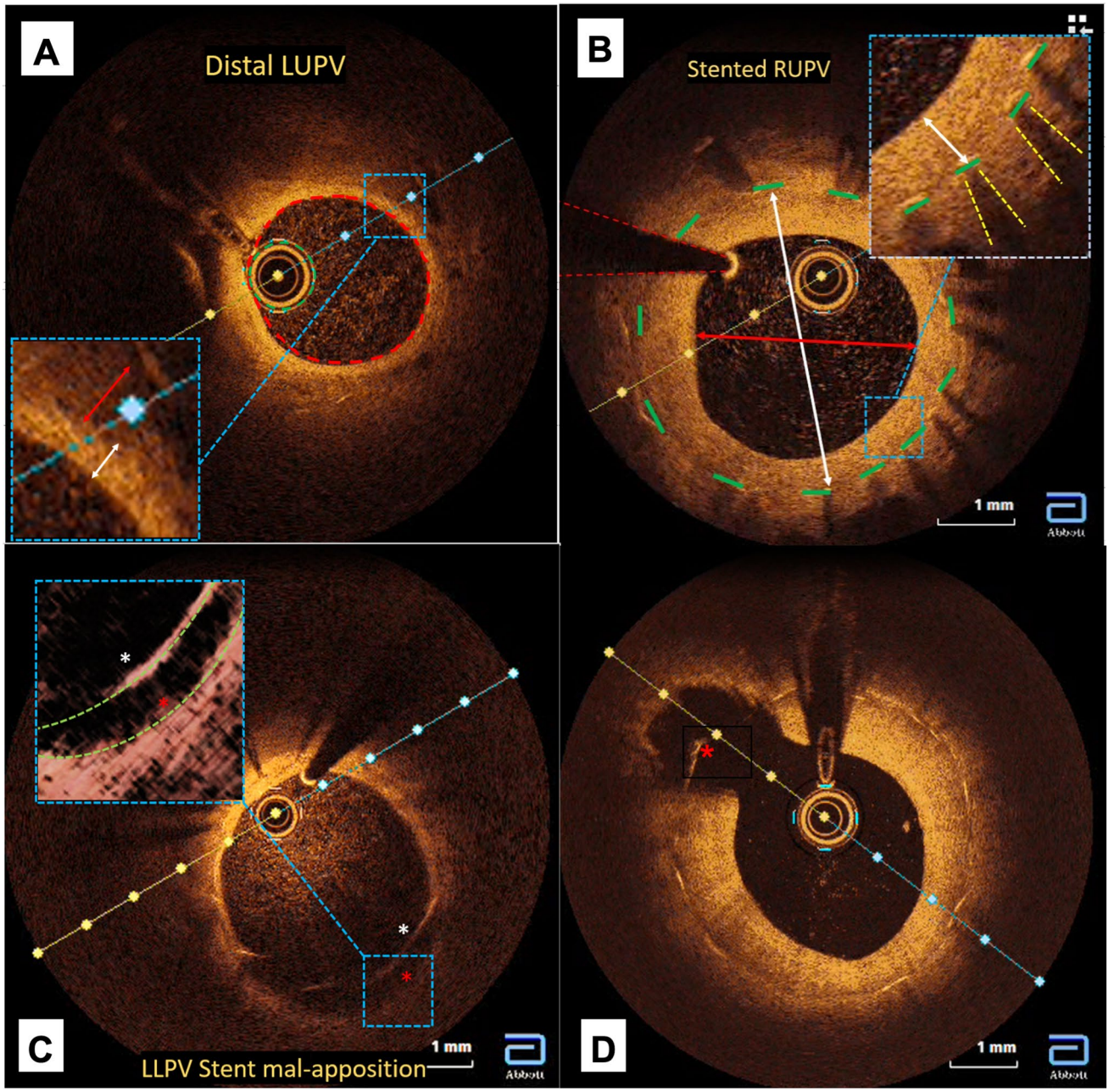

Fig. 2 Native and stented pulmonary vein images. **A** OCT acquisition of normal pulmonary venous lumen (red) with OCT catheter (green) on a wire sitting at 9 o'clock. Intimal and medial/adventitial layer labeled with white and red arrows, respectively (LUPV: left upper pulmonary vein, OCT: optical coherence tomography). **B** OCT acquisition with wire artifact depicted with red dashed lines at 9 o'clock, stent struts individually labeled in green producing peripheral optical artifact (dashed yellow lines), red arrow depicting the diameter of the neo-lumen, and white arrow depicting the diameter of the true stent lumen. There is significant neo-intimal proliferation present (RUPV: right upper pulmonary vein, OCT: optical coherence tomography). **C** OCT acquisition in a stented LLPV distal from the more peripheral lesion. The resolution is more limited peripheral from the OCT catheter, however, post processing of the image in the zoomed window demonstrates the stent in white and the vessel wall in red allowing identification, localization, and quantification of stent mal-apposition. **D** Demonstrates a tributary branch vessel (red asterisk) merging with a stented pulmonary vein with stent struts crossing the confluence, wire artifact is noted at 12 o'clock. The OCT catheter is placed coaxially with the stented vessel of interest

data are presented in Table 2. Most patients were female (75%). Median age at cardiac catheterization was 35 months (range 5–45 months). Median weight of subjects was 10.6 kg (3.7–14.2) with a median BSA documented at 0.505 m^2 (0.21–0.57).

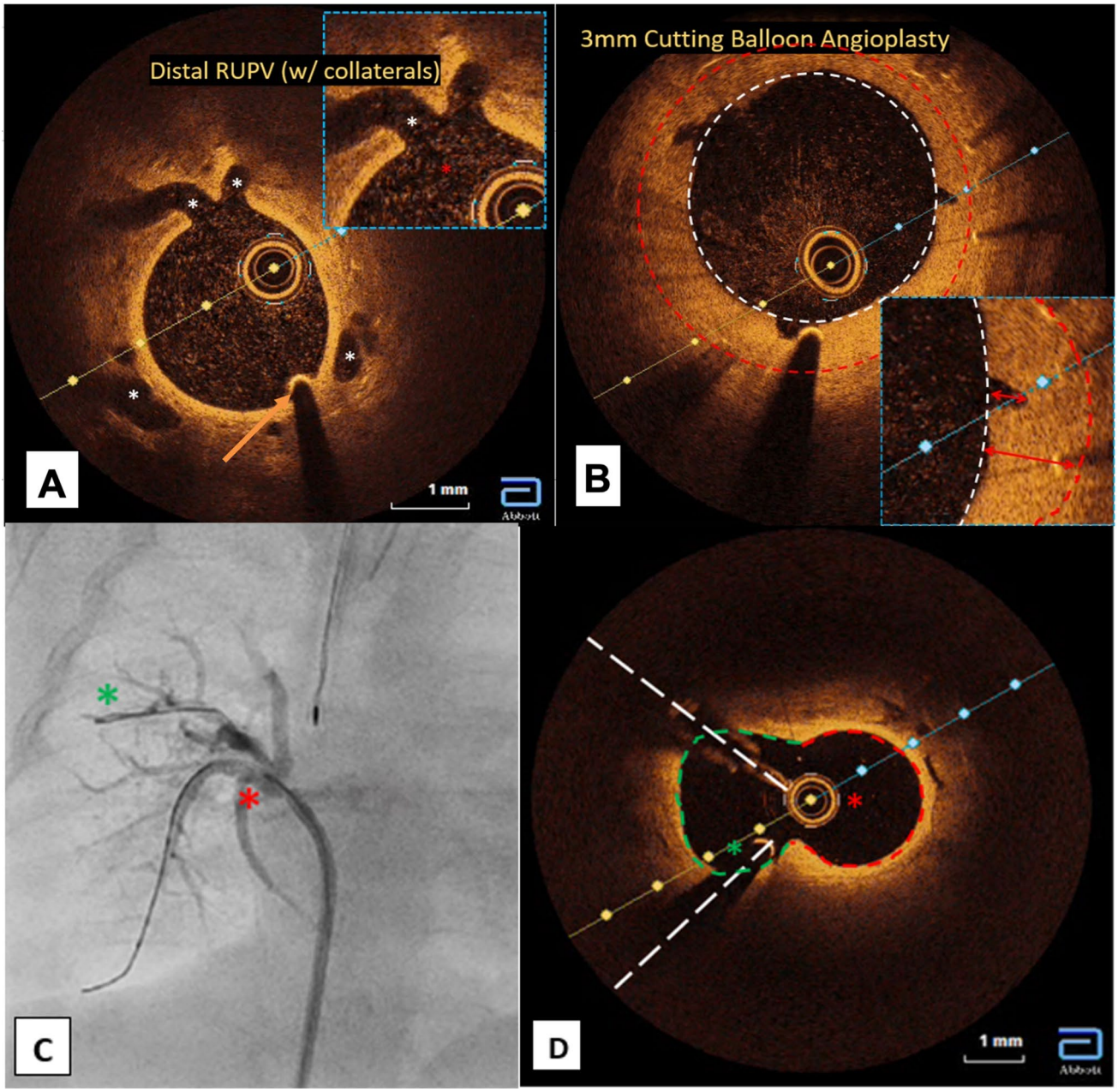

Fig. 3 **A** OCT acquisition of distal RUPV in patient with significant proximal stenosis, white asterisk depicts 2 large collateral vessels entering the lumen (red asterisk), there is wire artifact seen (green arrow) (OCT: optical coherence tomography, RUPV: right upper pulmonary vein). **B** Stented (red) RUPV s/p cutting balloon angioplasty with Boston Scientific Wolverine (3 mm) which contains 3 atherotomes. The neo-lumen is represented in white. The thickness of the atherotome impression is demonstrated in the zoomed window with a small red arrow in comparison to the thickness of the neo-intima (large red arrow) (RUPV: right upper pulmonary vein). **C** and **D** Paired angiography with OCT acquisition. There are two wires placed in two distal tributary branches of the RUPV. The OCT catheter and its supporting wire are sitting in the main RUPV (red) and a second wire sits in a tributary branch (green). The OCT image demonstrates the 2 branches coalescing with both wires producing wire artifact (depicted in white)

All veins accepted the Dragonfly catheter and there were no OCT-related adverse events. Pre- and post-intervention assessment were performed in 20 pulmonary veins (59%). Six patients had more than one OCT assessment 8 to 12 weeks after the index evaluation for comparative assessment. One patient had cardiac catheterization performed every 6 weeks for 6 months, this allowed 4 separate times when OCT was used for pulmonary vein luminal evaluation.

Table 2 Demographics and procedure summary

Patients (*n*)	11
Age, months	35 (5–45)
Sex, female	6 (75%)
Weight, kg	10.6 (3.7–14.2)
Pulmonary veins involved (*n*)	3(1–5)
Number of prior catheterizations	7 (1–11)
Diagnosis	5(46%)
Prematurity	4 (36%)
Congenital Heart Disease	2 (18%)
TAPVR	
Cardiac catheterization metrics	
Procedure time, min	175 (57–236)
Fluoroscopy time, min	64 (35.8–97)
Contrast, ml	2.9 (0.7–3.7)
DAP, μGy·cm^2	6,050 (1670–12,400)
Pulmonary vein assessed with OCT	4 (12%)
Right upper	8 (23%)
Right middle	2 (6%)
Right lower	2 (6%)
Lingular	6 (18%)
Left upper	12 (35%)
Left lower	
OCT features	8
High resolution mode (54 mm)	24
Survey mode (75 mm)	2
Stationary acquisition	

Values are displayed as frequency (%) or median (range)

OCT Optical Coherence Tomography, *TAPVR* total anomalous pulmonary vein return

Median number of pulmonary veins involved was 3 (range 1–5 veins), and median contrast volume of 2.9 mL/kg (0.7–3.7) given. Median radiation dose (DAP) was 6095 μGy·cm^2 (1670–12,400). Median number of previous cardiac catheterizations was 7 (range 1–11). Median procedural time was 190 min (139–236) with a median fluoroscopy time of 64.4 min (35.8–97). 46% of patients had history prematurity. There was no significant difference in procedural times, radiation doses, and contrast dose for each individual patient between the cardiac catheterization when OCT was used and prior catheterizations.

All patients admitted electively for cardiac catheterization were discharged within 48 h of admission.

Pulmonary veins assessed by OCT are summarized in Fig. 4. All of the vessels with a diameter ≤ 5 mm were adequately visualized. In vessels with diameter larger than 5 mm, there was not enough blood clearance with direct injection or wedge injection, to identify the vessel wall or the vessel lumen diameter. Of all the OCT images acquired, in 15 vessels (44%) contrast was used to clear the vessels from blood as an angiogram was required at the time, in the other 19 vessels (56%), saline was used with adequate imaging.

High resolution mode was used in 8 pulmonary veins, Survey Mode was used in 24 pulmonary veins and Stationary acquisition (no pullback done) was done in 2 pulmonary veins. Of the veins/stents with luminal diameter < 5 mm, only 37% of the veins were visualized when using the High resolution mode; when compared with 100% of the veins that were visualized when using the Survey Mode. The vessels evaluated with the stationary acquisition were all > 5 mm.

Anatomical description of the most relevant OCT images is described in Figs. 1 and 5.

Discussion

We present a novel application of optical coherence tomography (OCT) and the first overview of the practical approach and technical feasibility of pediatric pulmonary venous assessment using OCT. In this study, OCT was successfully performed in patients under 5 years of age, hemodynamically fragile, and with severe congenital heart disease without adverse events.

Current practice with OCT in cardiovascular medicine is mostly limited to its utility in detailed coronary plaque assessment in adults where it guides therapeutic approaches [22–24]. There has been limited experience of the use of OCT in pediatrics and only a couple of publications describing its use outside the coronary scope in congenital heart disease [25–27]. OCT in adult pulmonary veins has been carried out as part of attempting to understand some of the morphological changes in patients with atrial fibrillation, some of whom have complex myofibrillar changes beginning at the venoatrial confluence [28, 31].

In pediatric practice, IVUS was been shown to be feasible and safe in pediatric patients with pulmonary vein stenosis [21] and can adequately visualize pulmonary vein lumen and walls. However, although OCT and IVUS may have similar applications, their technologies have clear differences. The axial and lateral resolutions of OCT are 70–90 μm which is enhanced from IVUS. The resolution of OCT (to 10–20 μm) is about tenfold higher than that of IVUS (to 100–150 μm), but the maximum depth of tissue penetration is lower with OCT (1–3 mm) than with IVUS (4–8 mm). More differences are included in Table 3.

One of the more relevant technical differences is related to the strong attenuation of light (for OCT) by blood, this is why blood must first be removed during an OCT examination to eliminate massive scattering of light by red blood cells. In the adult practice, this is performed using contrast. Due to the difficulty to clear the blood in these short pulmonary veins in pediatric population with elevated heart rates, the OCT "Survey Mode" was the most commonly used by our team due to the shortest acquisition time.

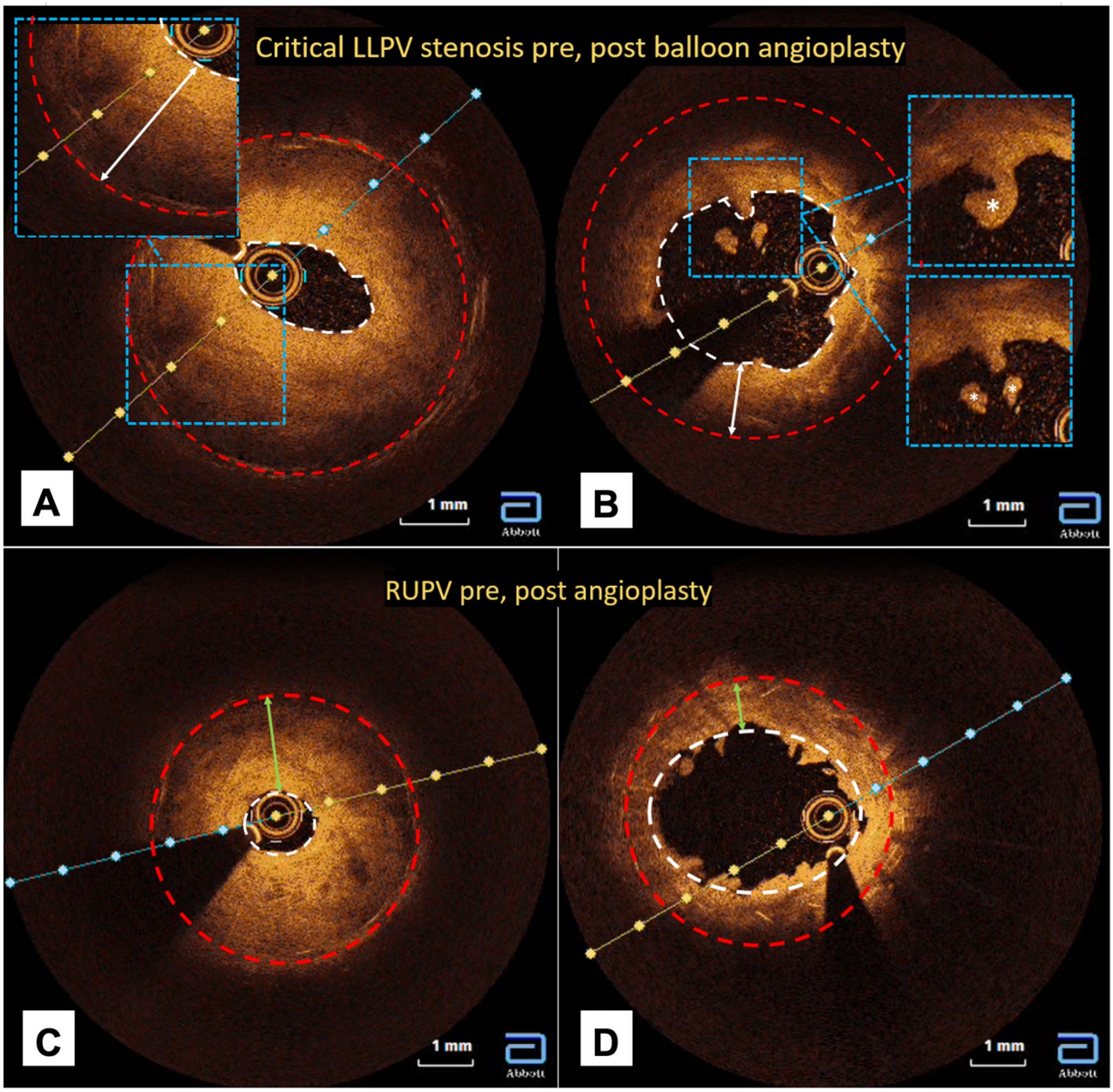

Fig. 4 **A** and **B** Pre- and post-angioplasty images of a patient with an LLPV stent and critical neo-intimal proliferation (white arrow), the stent is demonstrated in red and the neo-lumen in white. The zoom windows demonstrate both attached and mobile thrombus within the neo-lumen (white asterisk) after successful balloon angioplasty (LLPV: left lower pulmonary vein). **C** and **D** Aggressive neo-intimal proliferation (green arrow) in a stented (red) RUPV. The neo-lumen is depicted in white both pre and post angioplasty with a significant lumen gain demonstrated. Ragged edges of the neo-intima are seen adjacent the white line in the post-angioplasty image

In our experience, contrast or saline can be used, delivered with a 5F or 6F Guide catheter or a 4F sheath positioned at the pulmonary vein ostia. We used contrast exclusively when an angiogram was required, then OCT interrogation can be obtained at the same time. This allows automatic registration of the OCT catheter, the intraluminal image, and the angiographic appearance of the vessel. Otherwise, our preference is to use saline solution and keep the contrast doses as low as possible in our already fragile population. There is still registration to catheter position with the live fluoroscopic acquisition and the intraluminal appearance. The quality of the images was not related to the use of contrast or saline in our experience. Co-registration with cine-angiography (Fig. 5C and D) facilitates angiographic labeling and targeting at the time of intervention.

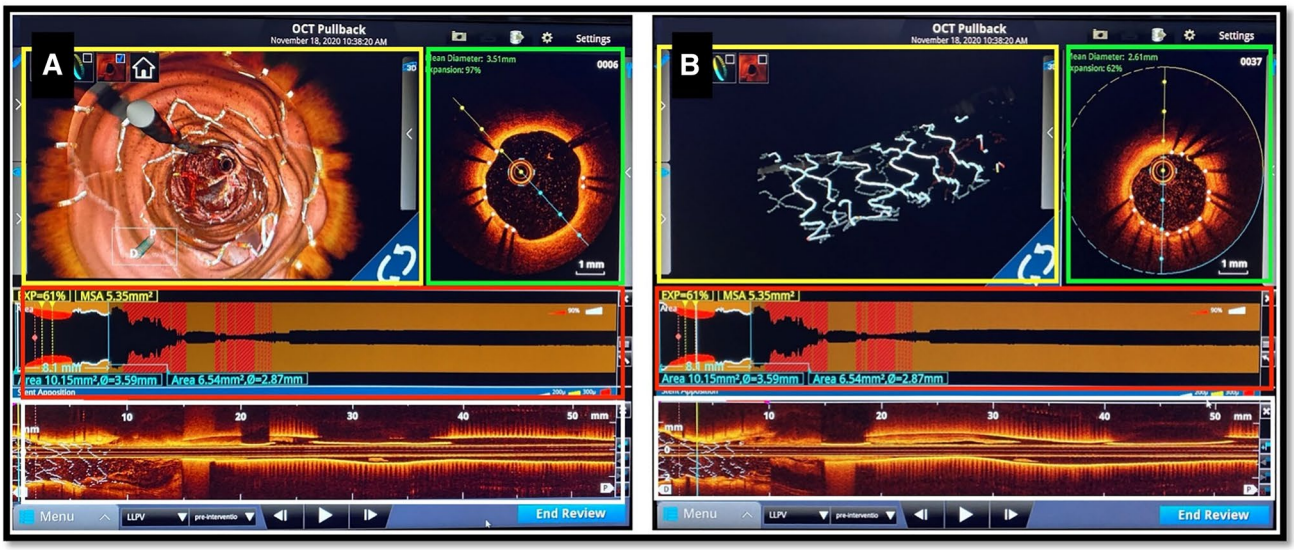

Fig. 5 Advanced stent analysis features with yellow windows demonstrating the vessel tissue characterization and "fly through" with 3D reconstructed stent (**A**) and reconstructed image of the stent morphology without related tissue (**B**). Green windows demonstrate the live OCT image with automatic stent strut identification software labeling struts adjacent to the intimal layer (white dots). The struts create significant sono-artifact which is usual. Red windows in A, B demonstrate L mode mapping of the diameter variability throughout the long axis of the vessel with stent vessel apposition and expansion auto-registration and automatic identification of zones of area loss (target zones). White windows in **A**, **B** represent standard reconstructed L mode images of the vessel with superimposed stent imaging. Legend: (OCT: optical coherence tomography)

Table 3 Comparison between IVUS and OCT

	IVUS	OCT
Method	Sound	Infrared Light
Type of Pullback	Mechanical or Manual	Mechanical
Catheter size (Fr)	3.2–3.5	**2.4–2.7**
Axial Resolution	100–200 µm	**10–20 µm**
Depth Tissue Penetration	**4–8 mm**	1–3 mm
Frame rate	30 frames/s	**180 frames/s**
Pullback Speed	0.5-1 mm/s	20 mm/s
Max. Scan Dia	15 mm	10 mm
Lines per frame	256	**500**
Blood clearing	**Not required**	Required
Lateral sampling (3 mm vessel)	225 µm	**19 µm**

IVUS Intravascular Ultrasound, *OCT* Optical Coherence Tomography, *Fr* French

The pulmonary veins that were not adequately visualized by OCT in our study were all larger than 5 mm or the High resolution mode was being used. The reason behind this is due to several factors that include heart rate of the patients being evaluated, the time of image acquisition, and the fact that the blood flow is towards the tip of the OCT catheter (and not the opposite as in the coronary arteries); all of these factors, intimately related to the time that the contrast or saline stays in the vessel to clear the blood. When the blood is not completely clear, the lumen is obscured, and the luminal walls cannot be identified.

For patients with vessels or stents larger than 5 mm, we obtained stationary acquisition. With this technique, we evaluated a 1 mm segment of a specific area of the vessel with a quick injection of saline. The acquisition is fast enough that works in larger vessels but is limited to an extremely small section. The information obtained was not felt to be clinically useful to the operator.

If the area of interest is the pulmonary vein ostia, a pulmonary wedge angiogram can be performed if a second venous access is available. This would allow antegrade flow of contrast in levophase to the pulmonary vein and clears the blood enough for a good quality image. The 3D reconstruction tools and intraluminal assessment with OCT are relevant for small patients for procedural planning, especially for stent placement in very short segments of pulmonary veins (Fig. 2).

Pulmonary veins in children fall within the appropriate size range and wall thickness for OCT image evaluation, particularly in patients with diseased vessels [29, 30]. Established luminal geometric assessment in OCT evaluation has been really useful in our practice and includes minimal lumen area (mm^2), lumen obstruction (%), stent apposition, stent expansion, minimal stent cross sectional area (mm^2), lumen gain (%), late lumen loss (%), and restenosis quantification (%). Geometric assessment of the entire short and long axis (L-mode) of the pulmonary veins may be relevant

to qualify the exact area of narrowing requiring treatment, identify targets for healthy vessel diameters as well as for decision making on balloon or stent sizing and design. Strut analysis can decipher stent vessel relationships [22] allowing adequate stent vessel apposition relationships in several of our patients (Fig. 1). Relationships of the stent to the native vessel and its intima in pulmonary venous stenosis may assist in identifying those most likely to suffer from aggressive restenosis [31].

OCT has brought to our practice all the known advantages of IVUS in pulmonary vein stenosis patients with significantly enhanced features that allow a high-definition image with 3D reconstructions and analysis of the wall vessel.

Limitations

This was a single-center study on a small number of complex patients and carried out with no standardized approach to acquisition. There is no normal data on OCT imaging in pediatric pulmonary venous disease nor does this disease bear similarity to adult coronary artery disease. The interpretation of imaging data obtained by OCT evaluation may be interpreted with caution and is not currently validated for diagnostic utility.

Conclusion

OCT is technically feasible and safe to use in pediatric patients for pulmonary veins evaluation. It provides intraluminal anatomy in children with both native and treated pulmonary venous stenosis when vessel size is less than 5 mm.

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Declarations

Conflict of interest Jenny E. Zablah and Gareth Morgan are consultants/speakers for Abbott.

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