Feasibility of Optical Coherence Tomography in Children with Kawasaki Disease and Pediatric Heart Transplant Recipients

Harris et al: Optical Coherence Tomography in Children

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Abstract

**Background**—Optical Coherence Tomography (OCT) is a high-resolution intravascular imaging technique used in adults. We tested the hypothesis that OCT could identify coronary abnormalities not seen by angiography in children with a history of Kawasaki Disease (KD) and pediatric heart transplant (TX) recipients.

**Methods and Results**—KD patients and TX recipients were evaluated between December 2012 and October 2013 with angiography and OCT (Ilumien System, LightLabs, St Jude Medical, Westford, MA). Modifications were made to the adult OCT protocol to adapt this technique for children. Serial cross sectional area (CSA) measurements of the lumen, intima and media were made. Entire imaging data was analyzed for the presence of qualitative changes. Seventeen children were evaluated (5 KD patients; 12 TX recipients). In KD patients angiography was normal. However, OCT imaging revealed that significant vessel wall abnormalities were present in all children including intimal thickening (intima/lumen CSA ratio > 0.4), loss of the normal layered structure of the vessel wall, white thrombus, calcification and neovascularization. There was extensive destruction of the internal elastic lamina. In TX recipients angiography was normal; however, intimal thickening [intima/media (I/M) CSA ratio >1] was seen in 9/12 patients. The median I/M CSA ratio was 1.18.

**Conclusions**—In this initial experience with OCT in children, we have identified significant coronary abnormalities with OCT that are angiographically silent in children with a history of coronary aneurysms due to KD and in pediatric TX recipients.

**Key Words:** coronary disease, intracoronary imaging, pediatrics, transplant vasculopathy, Kawasaki disease
Optical coherence tomography (OCT) is a high-resolution intravascular imaging technique (axial resolution of approximately 10\(\mu m\)), which has gained widespread use in adults with coronary artery disease.\(^1\) It provides detailed anatomic data about the lumen, intima and media.\(^2\) Conventional imaging techniques including echocardiography, computed tomography (CT), magnetic resonance imaging (MRI) and conventional angiography are unable to characterize structural vascular changes in high resolution. The alternative intravascular imaging technique, intravascular ultrasound (IVUS), has inferior spatial resolution (axial resolution approximately 100-150\(\mu m\)) compared to OCT.\(^3\) Additionally, IVUS requires a larger sheath for catheter delivery, which limits its utility in children with small blood vessels.

The high spatial resolution and small size of the imaging catheter make OCT appealing for use in children. While coronary artery pathology is less common in children than adults, cardiac allograft vasculopathy (CAV) is a leading cause of graft failure and mortality in pediatric orthotopic heart transplant (TX) recipients.\(^4\)\(^5\) Additionally, sequelae of coronary artery aneurysms are an important potential cause of long-term morbidity in children with a history of Kawasaki disease (KD).\(^6\) We postulate that these disease processes are well suited to high resolution intravascular imaging because they both involve changes to the blood vessel walls that may not be easily identified with other imaging modalities.

Therefore, we tested the hypothesis that OCT could identify coronary artery abnormalities that would not otherwise be identified with conventional angiography in children with a history of coronary artery aneurysms due to KD and pediatric TX recipients.
Methods

We evaluated all patients with a primary diagnosis of KD or orthotopic heart transplantation who were undergoing cardiac catheterization and selective coronary angiography for clinical purposes between December 1, 2012 and October 31, 2013. Patient charts were reviewed and demographics and clinical data were extracted.

We performed selective coronary angiography. We then performed OCT (Ilumien System, LightLabs, St Jude Medical, Westford, MA) on one or more coronary arteries based on patient size and technical factors. Two important modifications were made to the traditional OCT protocol used in adults to adapt this technique for children. First, we used a 5Fr coronary guide catheter with a 0.056” lumen and standard adult curves (Vista brite tip, Cordis, Bridgewater, NJ) for children ≤40kg and a 6Fr coronary guide catheter with a 0.070” lumen (Vista brite tip, Cordis, Bridgewater, NJ) for children >40kg. At present there are no 5Fr coronary guide catheters with pediatric specific curves that will permit OCT imaging. We often were more successful in engaging the right coronary artery with a JR 3.5 or 4 than the left with a JL 3.5 or 4. We typically used a 0.014” Asahi Grand Slam wire (Abbott Laboratories, Abbott Park, IL) which was advanced via the coronary guide catheter. A Dragonfly Duo OCT imaging catheter (St Jude Medical, Westford, MA) was then positioned in routine fashion over the guidewire and 2-5 cm of imaging was obtained depending on patient size. The second modification we made to accommodate pediatric patients was diluting the contrast with saline in a 2:1 (contrast:saline) ratio. Thus we were able to reduce the contrast load associated with imaging in small children. We performed hand injections of 0.25mL/kg of the diluted contrast to a maximum of 12ml. The hand injection was terminated when the imaging catheter was inside the guide catheter. Therefore, in small children in whom the imaging length was limited based
on anatomic factors, the total contrast injection volume was further reduced. We performed repeated OCT imaging until we obtained qualitatively excellent images with minimal artifact.

Serial measurements of the cross-sectional area (CSA) of the lumen, intima and media were made along the length of the coronary vessel using digital planimetry. Cross-sectional frames containing artifacts or side-branches comprising >25% of the image were excluded.\(^1\) In KD patients, the distal margin of the media was frequently not visible for >50% of the circumference of each frame, thus only the lumen and intima CSA were measured. We calculated the intima/lumen CSA ratio (I/L) and defined an I/L > 0.4 as abnormal based on a large pathology series of coronary dimensions in children.\(^7,8\) For TX recipients, we measured the intima/media CSA ratio (I/M) and provided a distribution of values for all datapoints. An I/M ratio of >1 is defined as abnormal in the adult literature.\(^9\) In some TX patients the distal margin of the media was visible for >50% but <75% of the circumference of each frame. In such cases, a sub-group analysis was performed including measurements from the intima and media CSA at exactly 50% of the vessel circumference. The reliability of this estimate was verified by using the same technique to evaluate a subset of patients in whom complete circumferential data was available. The I/M CSA ratio calculated with this technique was comparable to full-frame data and was therefore included in our analysis.

For all patients, entire imaging data was qualitatively analyzed for the presence of mural thrombus, intimal thickening, intima-media changes, loss of the normal layered structure of the vessel wall, calcification, and neovascularization. The qualitative analysis was performed according to the consensus standards for image interpretation\(^1\) with an emphasis on the descriptive imaging characteristics observed. Coronary angiography was independently reported by a cardiac radiologist who was blinded to the OCT findings. Angiographic findings were
compared to OCT findings from the same vessel at the same procedure. Manual co-registration
of the angiograms with OCT images was performed and sites of pathologic findings were
compared. For children with KD in whom previous angiograms were available for review, the
site of the original aneurysm was compared to the present angiogram and OCT findings. The
previous aneurysms were co-localized to the current imaging based on the coronary branching
pattern.

Quantitative and qualitative data analysis was performed and the data were summarized
descriptively. Frequency tables were generated for all categorical data. A univariate procedure
was used to analyze all continuous variables with the median (range) reported.

OCT image quality was independently analyzed by an OCT expert (HB) at a core
laboratory. To determine the interobserver reliability of digital planimetry, the OCT
measurements were performed independently by 3 investigators (KH, AM, and MH) on a subset
of images. Investigators were blinded to the clinical status of the patient. Intraclass correlation
was determined for the lumen diameter, lumen CSA, intima CSA and media CSA.

Statistical analysis was performed using SAS Statistical Software version 9.3 (SAS
Institute, Cary, NC). Ethics approval for this study was given by The University of British
Columbia Children's and Women's Health Centre's Clinical Research Ethics Board.

Results

We studied 17 children including 5 children with a history of coronary artery aneurysms
secondary to KD and 12 TX recipients.
Kawasaki Disease

KD patients ranged from 13 months to 18.4 years at the time of evaluation and were a median of 8.9 years (range, 11 months to 17.6 years) from their initial diagnosis (Table 1). All 5 patients had previously documented coronary artery aneurysms and were treated medically at the time of presentation with intravenous gammaglobulin ± steroid therapy. Two patients had documented extra-cardiac aneurysms (KD-01 and KD-04). Three of five patients were maintained on antiplatelet therapy with aspirin and one was also receiving anticoagulation with enoxaparin.

At the time of cardiac catheterization and OCT, selective coronary angiography was normal in 4/5 and showed mild irregularity of the proximal RCA in the remaining patient. Despite the normal lumen size there were marked abnormalities in vessel wall architecture in all five patients (Supplementary Video 1). There was evidence of localized calcification (Figure 1-B), white thrombus (Figure 1-C) and neovascularization (Figure 1-D). A range of intima media changes were noted and the spectrum of these changes are demonstrated in Figure 2. Figure 2-A demonstrates marked concentric intimal thickening, which was segmentally or globally present in 3 patients. Figure 2-B shows eccentric intimal thickening, which was seen segmentally in all 5 patients. Figure 2-C demonstrates a focal signal-rich distinct region that exceeds the intensity of background speckle noise (consistent with possible macrophage infiltration), which was seen in one patient. Figure 2-D shows signal-poor regions with poorly defined borders, consistent with possible lipid-pool containing plaque, and was seen in 3/5 patients. Table 2 summarizes the angiographic and quantitative OCT findings and Figure 3 demonstrates the qualitative intima-media changes in children with KD. The location of OCT abnormalities was independent of the subtle angiographic findings in the only patient that did not have normal selective coronary angiography (Figure 4). In all patients with baseline angiography available for review, the OCT
findings were not limited to the site of original aneurysm formation based on co-registration of OCT findings with angiographic data and co-localization to the original angiograms. The median intima-media thickness for all 5 patients was 0.45mm (maximum 1.77mm, normal in adults < 0.35mm\textsuperscript{10}) and the I/L ratio was 0.60 (range, 0.06 to 5.30). The measured intima-media thickness was maximal in patients KD-01 (median, 0.80mm) and KD-02 (median, 0.99mm), who had OCT imaging performed less than 2.5 years after the KD diagnosis. The range of qualitative changes observed is the greatest in patients KD-01 and KD-04, both of whom had extra-cardiac aneurysms documented at the time of diagnosis.

Transplant Recipients

The median age of TX recipients at the time of evaluation was 11 years (range, 6.7 to 17.2 years). The median time from transplantation was 6.8 years (range, 7 months to 16 years). At the time of evaluation, selective coronary angiography was normal in all patients with no angiographic evidence of CAV. Cardiac biopsy was performed in 11/12 patients, showing ISHLT rejection Grade 0 in 7/11 patients and Grade 1R in 4/11 patients. None of the patients had evidence of antibody mediated rejection.

Table 3 presents the qualitative and quantitative OCT findings in all 12 TX patients. Concentric intimal thickening was identified in 7 patients (Supplementary Video 2), either globally (2 patients) or segmentally (5 patients). Two patients had segmental eccentric intimal thickening. Three patients had normal OCT findings. None of the TX patients had thrombus, calcification, loss of the normal layered structure of the vessel wall, neovascularization or any other intima-media changes. The median I/M CSA ratio was 1.18 (range, 0.74 to 2.02). The individual median I/M CSA ratio was \( \geq 1 \) in 9/12 patients, \( \geq 1.5 \) in 4/12 patients and \( \geq 2 \) in 1/12
patients. Co-registration of the OCT findings with the angiography demonstrated no angiographic abnormalities in areas of intimal thickening (Figure 5).

Image Quality and Interobserver Variability

Image quality was independently reported as excellent in all cases (HB). In order to obtain excellent images repeated pullback were needed in some cases. Overall 37 pullback attempts were performed to obtain high quality image data in the 22 vessels analyzed. This corresponds to an average of 1.7 attempts per vessel. Qualitative interpretation was corroborated by an independent OCT expert (HB). Interobserver variability was determined based from analyses in 4 patients with a total of 30 measurements analyzed. The intraclass correlation coefficient for lumen diameter was 0.999 (n=8), for lumen CSA was 0.996 (n=8), for intima CSA was 0.999 (n=8), and for media CSA was 0.997 (n=6).

Discussion

In this initial experience with OCT in children we have demonstrated that there are significant abnormalities in the coronary arteries of children with KD in whom overt coronary aneurysms have resolved. The striking changes, including marked intimal thickening with loss of the normal layered structure of the vessel wall, were not seen with conventional angiography. In pediatric TX recipients we observed segmental and global concentric intimal thickening in the majority of children which was angiographically silent. Our results demonstrate that OCT provides important insights to vessel wall changes that are not identified with conventional coronary imaging in children at risk for coronary artery disease.
Kawasaki Disease

OCT imaging in patients with KD revealed a spectrum of abnormal findings within the coronary vessel wall including intimal thickening, loss of the normal layered structure of the vessel wall, calcification, white thrombus, and neovascularization. Additionally, a wide range of changes in the intima-media vessel wall characteristics was seen. These changes share common features with adult type fibrous, lipidic, macrophage and atheromatous plaques,\textsuperscript{1} although presently we do not have pathologic correlates in our population to definitively characterize the changes we have observed. Importantly, there are several pathology studies on children that have died with or from KD that provide some insight regarding the spectrum of histopathologic changes possible in this disease state. Previous pathology studies in children that died within the first year following diagnosis of KD demonstrate histopathology findings that contrasted with those seen in atherosclerosis.\textsuperscript{11} Notably no macrophage infiltration was seen in their 4 patients. Other groups have reported macrophage involvement both early and late in the disease process.\textsuperscript{12} The OCT characteristics of macrophage accumulation include a high density signal at the junction of the intima and lumen with a signal poor region distal to that,\textsuperscript{1} which is remarkably similar to our findings shown in Figure 2(c). However, this is the first OCT study to be performed in the pediatric population and interpretation of the findings in KD subjects is limited by the absence of OCT pathological correlates in children or adults with a history of KD presently.

Distinct pathological processes have been identified in the acute and convalescent stages of KD.\textsuperscript{13} The acute arteritis phase preceding the development of aneurysms is mainly driven by an inflammatory process, which is characterized by infiltration and activation of macrophages, lymphocytes and neutrophils.\textsuperscript{14} In the later stage of the disease, regression of coronary aneurysms over time is the result of intimal thickening caused by destruction of the internal
elastic lamina, migration of smooth muscle cells and accumulation of fibrous tissue into the intima.\textsuperscript{11} The presence of intramural calcifications and thrombus formation are also described.\textsuperscript{15} There is also evidence of active expression of growth factors within the various vessel layers, supporting the hypothesis that active remodeling continues in the later stage of the disease.\textsuperscript{11} Histological studies on coronaries in the late phase of KD reveals a different pattern of expression of growth factor within the coronary vessel wall between KD and adult-onset atherosclerosis, suggesting distinctive underlying disease processes.\textsuperscript{11} Conversely, Takahashi and colleagues demonstrated severe atherosclerotic changes in arteries with aneurysm formation at autopsy in a 39 year-old.\textsuperscript{12} Our identification of striking intima-media changes in patients as young as 2 years old and up to 17 years after the initial diagnosis in our study raises important questions regarding the evolution of these abnormal features over time and the future risk they may confer. In our series, OCT demonstrated more extensive coronary changes in children who had evidence of extracardiac aneurysms at initial KD diagnosis than in those that had isolated coronary involvement. It is possible that extracardiac aneurysms are a marker for more extensive inflammation and, therefore, associated with greater long-term coronary changes; however, given our small sample size this observation may be coincidental. We also noted that, in children in whom there was a longer time interval from initial diagnosis of coronary aneurysms to follow up imaging, there was less intimal thickening, which may be due to ongoing beneficial remodeling. Nonetheless, the observation of sustained neutrophil activation and abnormal endothelial function has raised the concern that functional changes may persist.\textsuperscript{16-18} Although the mortality rates in KD have significantly decreased since initiation of intravenous immunoglobulin therapy, little is known about the long-term cardiovascular risk in these patients in the current era. Particularly, it is not definitively known whether coronary changes confer an
increased risk of early or accelerated atherosclerosis. Other long-term cardiovascular complications such as coronary stenosis, in patients with history of aneurysm, are a well known source of late morbidity.12, 19, 20

*Cardiac Allograft Vasculopathy*

CAV is an important source of morbidity and graft failure in pediatric transplant recipients.21-24 Early diagnosis may alter the management of pediatric transplant recipients emphasizing the importance of regular effective surveillance.23, 25 Conventional angiography is the accepted standard for evaluating pediatric transplant recipients for the development of this condition despite its poor sensitivity.4 Recently other imaging modalities have been used to improve the rate of early diagnosis. In adults, IVUS has been used to improve early identification of coronary changes and has shown important prognostic utility.26 A recent report demonstrated the efficacy of OCT in characterizing intimal thickening in adult cardiac transplant recipients.9 Our results demonstrate that similar coronary changes occur in young children and, in our study, these changes were not related to time from transplantation. We identified important regional differences in the severity of intimal thickening.

A recent study of explanted hearts in patients undergoing retransplantation for CAV demonstrated pathologic findings of intimal thickening and prominent mural infiltrates.27 The fibromuscular proliferation contrasts histologically with atherosclerotic plaques and is consistent with our finding of circumferential and often concentric intimal hyperplasia. The optimal metrics for assessing intimal changes in CAV is not presently known. The IVUS literature suggests using the maximal intimal thickness. Others using OCT in adults to evaluate CAV, have suggested that an average I/M ratio >1 is abnormal.9 In our study 9/12 children had a median
I/M ratio > 1. The median I/M ratio was >1.5 in 33% of our patients. We noted an I/M ratio >2 in at least one data point in 5/12 children. None of these changes were detected with conventional angiography as there was no luminal narrowing seen. We did not identify any calcification in this group. As expected, given the age of our population, there were no qualitative atherosclerotic changes confounding our evaluation of CAV. We postulate that the changes we observed may represent the early changes of CAV although the natural history of these early changes requires prospective longitudinal evaluation. In one patient the changes were so striking that the transplant cardiologists altered the medical management of the patient based on the OCT findings. The opportunity for early intervention is a key potential benefit of early diagnosis given that recent medical advances have shown promise in the management of CAV.28

This study is limited by its cross-sectional nature. The observations we have made demonstrate there are clear changes in the coronary arteries that may not be seen with other forms of non-invasive or intravascular imaging. At this stage it is not clear what the prognostic significance of these coronary changes are in children. The vessel wall changes seen in children with KD and pediatric transplant recipients were striking; however, given the lack of pathologic correlates of OCT images in children, the findings are not robust enough to draw inferences about the underlying pathophysiology of these changes. While the technical modifications to the OCT protocol we have used allows us to image children with a smaller guide catheter which is better suited to children, the image quality can be somewhat variable due to slower contrast injections through the narrower guide lumen. In some cases this necessitated repeat imaging to acquire a complete data set. The standard curves available on 5Fr guide catheters are not well suited to engaging the coronary ostia in small children, which can present technical challenges in performing OCT. The development of 5Fr guide catheters with pediatric curves (2.5 and 3)
would improve the feasibility of this technique in imaging the left and right coronary arteries in children.

OCT is an important new intravascular imaging modality which is well-suited to use in children due to its small catheter size, rapid automated pullback and high resolution imaging. The technical modifications we have made to obtain OCT images using a 5Fr catheter provide unique diagnostic and investigational opportunities in children. The very low interobserver variability of OCT has been demonstrated in this and other studies and represents an important advantage of OCT over IVUS, which has been shown to be less precise. Our results confirm that OCT is feasible in children and provides important image characterization of coronary vessel wall changes. There is a need for pathologic correlates to determine the biological processes underlying these changes and longitudinal studies will be helpful to define the natural history of the observed changes in each of these disease states.

Disclosures

Dr. Anthony Fung is a Proctor for St. Jude Medical. Dr. Hiram Bezerra is a Medical Advisor for and holds a research grant from St. Jude Medical.

References


Table 1. Demographics*  

<table>
<thead>
<tr>
<th></th>
<th>Kawasaki Disease N = 5</th>
<th>Transplant Recipient N = 12</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male (%)</strong></td>
<td>5/5 (100%)</td>
<td>7/12 (58%)</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>50.7 (13.8-74)</td>
<td>32.5 (20.6-70.6)</td>
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<td><strong>Age at incident event (years)</strong></td>
<td>0.8 (0.2-8.6)</td>
<td>2.9 (0.1-12.6)</td>
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<tr>
<td><strong>Age at OCT (years)</strong></td>
<td>16.2 (1.1-18.4)</td>
<td>11.0 (6.7-17.2)</td>
</tr>
<tr>
<td><strong>Time since incident event† (years)</strong></td>
<td>8.9 (0.9-17.6)</td>
<td>6.8 (0.6-16)</td>
</tr>
</tbody>
</table>

*Continuous data are presented as median (min-max).  
† Incident event for Kawasaki Disease is the date of diagnosis of coronary artery aneurysms; incident event for Transplant Recipients is the date of orthotopic heart transplantation.  
OCT = Optical coherence tomography
**Table 2. Summary of KD patients**

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<tr>
<th></th>
<th>KD-01</th>
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<td>1.1</td>
<td>17.5</td>
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<td>18.4</td>
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<td><strong>Weight (kg)</strong></td>
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<td>13.8</td>
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<tr>
<td><strong>Sex</strong></td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
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<td><strong>Age at Dx (years)</strong></td>
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<td>0.2</td>
<td>8.6</td>
<td>0.2</td>
<td>0.8</td>
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<tr>
<td><strong>Extra-cardiac aneurysms</strong></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td><strong>Time from Dx to OCT (years)</strong></td>
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<td>0.9</td>
<td>8.9</td>
<td>16</td>
<td>17.6</td>
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<td><strong>Medical Rx at time of OCT</strong></td>
<td>ASA</td>
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<tr>
<td><strong>Coronary Evaluated</strong></td>
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<td>RCA</td>
<td>RCA</td>
<td>RCA, Cx, LAD</td>
<td>RCA, LAD</td>
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<td><strong>Angiographic Findings</strong></td>
<td>Mild irregularity of proximal RCA</td>
<td>Normal</td>
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<td><strong>Lumen diameter median (mm)</strong></td>
<td>(1.75)</td>
<td>(1.65)</td>
<td>(3.11)</td>
<td>(2.74)</td>
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<tr>
<td><strong>(min:max)</strong></td>
<td>(1.16:2.59)</td>
<td>(1.29:1.88)</td>
<td>(2.98:3.21)</td>
<td>(2.43:3.19)</td>
<td>(2.09:2.97)</td>
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<td><strong>Intima thickness median (mm)</strong></td>
<td>0.80</td>
<td>0.99</td>
<td>0.26</td>
<td>0.36</td>
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<td><strong>(min:max)</strong></td>
<td>(0.34:1.77)</td>
<td>(0.38:1.61)</td>
<td>(0.09:0.50)</td>
<td>(0.17:0.45)</td>
<td>(0.09:0.24)</td>
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<td><strong>Intima:Lumen CSA ratio median (min:max)</strong></td>
<td>1.01</td>
<td>1.49</td>
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<td>(0.43:5.30)</td>
<td>(0.51:3.69)</td>
<td>(0.06:0.34)</td>
<td>(0.26:0.70)</td>
<td>(0.06:0.24)</td>
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ASA = Aspirin; Cx = Circumflex coronary artery; CSA = Cross-sectional area; Dx = Diagnosis; KD = Kawasaki disease; LAD = Left anterior descending coronary artery; OCT = Optical coherence tomography; RCA = Right coronary artery; Rx = Treatment
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<p>| I/M CSA ratio (% Datapoints that exceed each cut-off value) | &lt; 1 | 46 | 0 | 0 | 80 | 0 | 0 | 50 | 29 | 0 | 100 | 80 | 0 |
| ≥1 &lt; 1.5 | 46 | 22 | 64 | 20 | 8 | 20 | 50 | 57 | 9 | 0 | 20 | 67 |</p>
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* Most prominent in proximal portion of vessel

AMR = Anti-body mediated rejection; Bx = Biopsy; Cx = Circumflex coronary artery; F = Female; I/M = Intima-to-media; ISHLT = International Society for Heart and Lung Transplantation; LAD = Left anterior descending coronary artery; M = Male; MMF = Mycophenolate mofetil; Neg = Negative; OCT = Optical coherence tomography; RCA = Right coronary artery; TX = Transplant or transplantation
Figure Legends

**Figure 1.** A. Normal coronary artery; intima (white arrow) and media (white arrowhead) are well delineated; B. (KD-01) Circumferential intimal thickening with diffuse loss of the normal layered structure of the vessel wall and calcification (white arrow); C. (KD-01) Circumferential intimal thickening with white thrombus (white arrow); D. (KD-02) Circumferential intimal thickening with neovascularization (white arrow).

**Figure 2.** A. (KD-02) Severe concentric intimal thickening with loss of the normal layered structure of the vessel wall inferiorly (white arrow); B. (KD-01) Eccentric intimal thickening with non-obstructive luminal narrowing (white arrow); C. (KD-04) Signal rich, distinct region within the intima (white arrow) which exceeds the intensity of the background speckle noise (consistent with possible macrophage infiltration); D. (KD-04) Signal poor OCT region with poorly defined diffuse border (consistent with lipid pool).

**Figure 3.** Qualitative OCT findings in KD patients.

**Figure 4.** A. (KD-01) Selective right coronary artery angiogram in a child with a history of coronary aneurysms in the setting of Kawasaki disease demonstrates mild irregularity of the proximal RCA. The white lines denote the areas of co-localization of the OCT findings shown in panels B-D. B. (KD-01) Eccentric intimal thickening with non-obstructive luminal narrowing (white arrow) with preservation of the normal layered structure of the vessel wall; C. (KD-01) Eccentric intimal thickening with non-obstructive luminal narrowing and loss of the normal layered structure of the vessel wall (white arrow); D. (KD-01) Concentric intimal thickening
with loss of the normal layered structure of the vessel wall and localized calcification (white arrow).

**Figure 5.** A. (TX-01) Normal selective right coronary artery angiogram in a child who has undergone remote cardiac transplantation. The white line (b) denotes the areas of co-localization of the OCT findings shown in panel B. B. (TX-01) Concentric intimal thickening with preservation of the normal layered structure of the vessel wall. The I/M ratio is 2.4.
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Feasibility of Optical Coherence Tomography in Children with Kawasaki Disease and Pediatric Heart Transplant Recipients

Kevin C. Harris, Anas Manouzi, Anthony Fung, Astrid De Souza, Hiram G. Bezerra, James E. Potts and Martin C.K. Hosking

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SUPPLEMENTAL MATERIAL

Supplementary Video #1
OCT pull-back in a child with Kawasaki disease demonstrating marked intimal thickening, loss of the normal layered structure of the vessel wall, neovascularization, calcification, and white thrombus.

Supplementary Video #2
OCT pull-back in a child who had undergone cardiac transplantation demonstrating intimal thickening.