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Early detection of cardiac allograft vasculopathy using highly automated 3-dimensional optical coherence tomography analysis

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intimal thickness;
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rapid progression

BACKGROUND: Optical coherence tomography (OCT)–based studies of cardiac allograft vasculopathy (CAV) published thus far have focused mainly on frame-based qualitative analysis of the vascular wall. Full capabilities of this inherently 3-dimensional (3D) imaging modality to quantify CAV have not been fully exploited.

METHODS: Coronary OCT imaging was performed at 1 month and 12 months after heart transplant (HTx) during routine surveillance cardiac catheterization. Both baseline and follow-up OCT examinations were analyzed using proprietary, highly automated 3D graph-based optimal segmentation software. Automatically identified borders were efficiently adjudicated using our "just-enough-interaction" graph-based segmentation approach that allows to efficiently correct local and regional segmentation errors without slice-by-slice retracing of borders.

RESULTS: A total of 50 patients with paired baseline and follow-up OCT studies were included. After registration of baseline and follow-up pullbacks, a total of 356 ± 89 frames were analyzed per patient. During the first post-transplant year, significant reduction in the mean luminal area ($p = 0.028$) and progression in mean intimal thickness ($p = 0.001$) were observed. Proximal parts of imaged coronary arteries were affected more than distal parts ($p < 0.001$). High levels of LDL cholesterol ($p = 0.02$) and total cholesterol ($p = 0.031$) in the first month after HTx were the main factors associated with early CAV development.

CONCLUSIONS: Our novel, highly automated 3D OCT image analysis method for analyzing intimal and medial thickness in HTx recipients provides fast, accurate, and highly detailed quantitative data on early CAV

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changes, which are characterized by significant luminal reduction and intimal thickness progression as early as within the first 12 months after HTx.
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Cardiac allograft vasculopathy (CAV) is a major cause of mortality in heart transplant (HTx) patients.[1,2] In its early stages the disease affects the intima but later manifests as typical atherosclerosis characterized by vulnerable plaques.[3] Optical coherence tomography (OCT) enables the thin intimal layer to be clearly differentiated from the tunica media, a crucial factor in determining early progression of CAV. OCT imaging can reveal rapid progression of CAV as early as during the first year after HTx.[4] Early diagnosis is of crucial importance as further progression of the disease can be managed using specific medical approaches.[5,6] Studies published thus far have yet to fully utilize the capabilities of 3-dimensional (3D) OCT for early quantitative analysis of CAV development, largely because manual coronary layer segmentation is a time-consuming process.[7–10] Our aim was to design a novel, highly automated image analysis method for assessing intimal and medial thickness (IT, MT) using OCT images from HTx patients.

Methods

Patients

Between October 2014 and December 2015, 50 subjects from the Heart Center at IKEM, Prague, Czech Republic, and from the Center of Cardiovascular and Transplantation Surgery, Brno, Czech Republic, were enrolled. The study (Clinical Trial NCT02503566) complied with the Declaration of Helsinki and was approved by the respective ethics committees. All HTx recipients ≥18 years of age were considered eligible for inclusion in the study provided they were able and willing to give their informed consent. Exclusion criteria were renal insufficiency Stage ≥IV (glomerular filtration 30 ml/min), unfavorable post-transplant clinical conditions such as episodes of severe rejection or nosocomial sepsis with prolonged antibiotic treatment during the first month, ongoing need for circulatory support using a ventricular assist device, and acute allograft failure.

OCT method

The reported method of OCT acquisition and analysis consists of the following main steps:

1. Image acquisition including vessel wiring (catheterization lab, 5 minutes).
2. Expert definition of excluded angular regions (computer-assisted, 1 hour per pullback).
3. One- to 12-month pullback registration (computer-assisted, 10 to 15 minutes).
4. Multilayer 3D segmentation (automated, 20 seconds).
5. "Just-enough-interaction" (JEI) adjustment (computer-assisted, 2 to 15 minutes).
6. Quantitative analysis (automated, immediate).

Image acquisition

Coronary OCT imaging was performed at 1 month (1M) and 12 months (12M) after HTx as part of routine surveillance cardiac catheterization with a commercial intracoronary OCT system (Ilumien/Dragonfly Optis; St. Jude Medical, St. Paul, MN). A 54-mm-long segment of each HTx patient's left anterior descending (LAD) artery, located within a proximal 100-mm segment, was imaged at 1M and 12M using automated pullback at 18 mm/s and 10 frames/mm. When the LAD exhibited unfavorable anatomic characteristics (small caliber, extreme tortuosity, muscle bridge), 100-mm proximal segments of the left circumflex (LCx) or the right coronary artery (RCA) were imaged. The baseline and follow-up OCT-imaged segments mutually overlapped.

Image interpretation

For each frame of all OCT pullbacks, luminal, intimal, and medial surfaces were automatically segmented using a fully 3D LOGISMOS graph-based approach developed at the University of Iowa (Figure 1).[11,12] Boundaries were identified as OCT brightness changes showing tissue interfaces between adjacent wall layers. Automatically identified borders were efficiently edited using our JEI method adapted for the OCT segmentation environment.[13,14] This technique allows segmentation errors to be corrected in a 3D fashion on a regional basis, as opposed to contour-by-contour/frame-by-frame manual retracing (Figure 2). This highly accurate multilayer model facilitated quantitative CAV analysis of every frame of the imaged vessel for both baseline and follow-up image pullbacks. After identifying corresponding vascular landmarks, baseline and follow-up pullback pairs were co-registered, facilitating location-specific and fully 3-dimensional comparisons of layer-based changes using quantitative indices.

Quantitative descriptors

Branches and ambiguous areas of the wall were excluded from the analysis according to the consensus of 2 expert cardiologists. Full frames were only excluded when appearing in 1 but not in the other of the 2 registered pullbacks. Branch locations were used to calculate distances from the nearest branch.

The luminal, intimal, and medial layers for each frame were segmented and analyzed to obtain average thickness and area. The intima-to-media (I/M) ratio was calculated by dividing the average intimal thickness (IT) by the average medial thickness (MT) for each frame of the analyzed pullbacks. Global intimal thickening, $\Delta IT = IT_{12M} - IT_{1M}$, was determined as the average difference between IT at 1M and 12M at all co-registered vessel wall locations. Maximal segmental intimal thickening, $\Delta SIT = \max\{SIT_{12M} - SIT_{1M}\}$, was determined by comparing all 3-mm-long, 90° wedges of the vessel wall, with SIT_{12M} and SIT_{1M} as the average intimal thicknesses in the respective registered wedge segments.