INTRODUCTION

The cerebrovascular endothelium is known to play a pivotal role in regulating inflammatory pathways, permeability of the blood-brain barrier, and thrombosis. During endovascular thrombectomy (EVT) with second-generation stent retrievers, considerable outward radial force can be delivered to the vessel wall via the stent struts or thrombus. Studies evaluating for iatrogenic endothelial injury during EVT have been done by means of retrieved human thrombus, post-mortem histopathologic analysis, magnetic resonance vessel-wall (MRVW) imaging, and animal histopathologic studies. Furthermore, damage to the endothelium may not strictly be due to the mechanical thrombectomy device alone. Prolonged vessel wall exposure to luminal thrombus can also cause endothelial damage. Reil et al. showed that ligated arteries with thrombus had increased endothelial damage compared to arteries with interrupted flow in the absence of thrombus. Various components of the thrombus can affect endothelial function and morphology.

Endovascular optical coherence tomography (OCT) imaging is the highest-resolution intravascular imaging modality currently available. This technology has traditionally been utilized in interventional cardiology, and more recently applied in neurointerventional surgery. OCT utilizes near-infrared light with a wavelength of approximately 1.3µm and excellent intraluminal spatial resolution of 10-20 µm is achievable.

Although studies have shown that some degree of iatrogenic endothelial injury likely occurs during EVT, whether this is clinically significant remains unknown. Before attempting to correlate vessel injury with clinical outcome, the degree of vessel wall injury should be adequately quantified, as it is likely endothelial denudation, intimal dissection, and edema of the tunica media will have varying clinical implications. Current techniques such as MRVW imaging have insufficient spatial resolution to directly visualize endothelial injury, and histopathologic examinations are ex-vivo, prone to processing artifacts, and unable to provide real-time patterns of injury.

The purpose of this project is to assess the feasibility of endovascular OCT in quantifying vessel injury in real-time after EVT, correlate the OCT findings of vessel injury with histology, and lastly imaging after EVT at varying time intervals to assess the impact of prolonged direct vessel exposure to thrombus. The pre-clinical animal model and preliminary human model and results are described.

METHODS

Animal Model: All experiments were conducted in accordance with policies established by our institutional research ethics board committee. Nine vessels in three Yorkshire swine weighing 35-40kg were selected for the animal model, as they have well-developed superficial cervical
arteries (SCA) similar in caliber to human middle cerebral arteries. All procedures were carried out under general anesthetic with continuous hemodynamic monitoring. Autologous venous whole blood was drawn 48 hours before the procedure and subsequently used as thrombus.

An 8 French sheath was inserted into the right common femoral artery. Thrombi were deposited into three arteries sequentially: 1) right SCA, 2) right internal thoracic artery (ITA), and 3) left SCA. EVT was then performed at one, three, and six hour after vessel occlusion. A FlowGate guide catheter was positioned in the subclavian artery. A Trevo-18 microcatheter (Stryker, Fremont, California) was advanced over a microwire 3mm beyond the thrombus. A Trevo 4mm X 20mm stent retriever (Stryker, Fremont, California) was deployed for 5 minutes before retrieval. The thrombectomy devices were slowly withdrawn under proximal balloon occlusion and continued aspiration through a 60cc syringe. The goal was complete revascularization defined as thrombolysis in cerebral infarction (TICI) reperfusion grade 3 and arterial occlusive lesion (AOL) recanalization score of 3. If incomplete angiographic revascularization was observed, the procedure was repeated again up to a maximum of three attempts.

Immediately after thrombectomy OCT images were immediately obtained. The Dragonfly™ OCT catheter (Abbott Vascular, Chicago, IL) was used. All cross-sectional OCT images were analyzed. The percentage of surface area was used to quantify endothelial injury, and the inner media circumference percentage was used for media layer edema/separation. After OCT imaging and the sacrifice of the animal, an approximately 5 cm segment of each affected artery was harvested.

The resected arterial segments were fixed in 10% neutral buffered formalin. After formalin fixation, the arteries were cross-sectioned into 5mm segments and embedded in paraffin. Three different levels through each of these tissue blocks were created, and 5 micrometer thick tissue sections were mounted on glass slides and stained with hematoxylin and eosin (H&E). H&E stained slides from each level of the sampled arteries were examined at 4X, 10X and 20 X magnification. Bland-Altman plots were generated using the mean difference between histology and OCT scores and a 1.96 standard deviation (SD) with respect to the various vessel wall injury characteristics.

**Human Stroke Imaging:** After showing that OCT was feasible in pre-clinical studies, with the aim of investigating for endothelial injury and residual thrombus in stroke patients undergoing EVT, institutional research ethics board approval was obtained for endovascular OCT after EVT. Patients with acute basilar artery occlusions (BAO) undergoing EVT were imaged with OCT after clot retrieval (Figure 1). Patients with BAO were first selected for technical purposes, as the posterior circulation is less tortuous and hence navigating the OCT catheter is more straightforward. Four consecutive patients with BAO underwent OCT imaging immediately after EVT. Two patients had stent-retriever thrombectomy, and two patients had direct aspiration thrombectomy.

**RESULTS**

**Animal Model:** OCT image acquisition was technically successful in all 9 vessels. Endothelial denudation was present in 65 ±16%, 87 ±8%, and 93 ±7% of the vessel surface 1, 3, and 6 hours after thrombus deposition and subsequent EVT, respectively (Figure 2). Residual intraluminal thrombus was present in vessels at all time intervals despite complete angiographic revascularization. Bland-Altman plots showed good agreement between OCT and histologic analysis with respect to the degree of endothelial denudation and elevation, separation of the media, and hemorrhage within the media. OCT appears to be more specific in detecting endothelial elevation.
Human Imaging: Technically successful images were obtained for 4 consecutive patients. There were no immediate or delayed complications. Anatomic features of the vessel wall were discernible for all patients, including intima, media, adventitia and internal/external elastic lamina. Basilar artery thick concentric plaque fibrosis was present causing outward remodelling and loss of the internal/external lamina in certain regions in 3/4 patients. Evidence of significant residual thrombus was also visible in 2/4 of patients, with mostly red thrombus present despite complete angiographic revascularization (Figure 3). The residual thrombus was not visible on CT, MR, or cerebral angiography. There was also thrombosis of basilar perforators next to patent perforators in 2/4 patients.

DISCUSSION

To our knowledge, we describe for the first time endovascular OCT imaging after acute stroke treatment. Our pre-clinical animal experiment findings include: 1) Endothelial injury is present and can be observed in real-time after EVT using OCT, 2) Residual luminal thrombus can be present despite complete angiographic revascularization (TICI/AOL Grade 3), and 3) It is possible that the longer occlusive thrombus is present, the more endothelial injury will occur during EVT.

Although histologic analysis remains the gold standard in the characterization of vascular injury, with spatial resolution of 10µm OCT is able to clearly define the different layers of the arterial wall and provide an assessment of the luminal environment without tissue preparation. This novel technique could address the deficiencies of prior models utilized to evaluate thrombectomy devices. Currently most devices are tested in silicon and glass phantom models to allow for direct visualization, and these models lack a biologically representative environment. OCT can specifically address this, and allow for observation of the interaction between the device and vessel wall in vivo.

We also interestingly observed in 2/4 basilar stroke patients imaged that significant residual thrombus can exist at the thrombectomy site despite patients having TICI grade/AOL grade of 3. Distal emboli released downstream during thrombectomy have certainly been described, but to our knowledge there are no reports in the literature of residual thrombus at the site of the target lesion in the presence of complete recanalization and reperfusion. Furthermore, the residual thrombus was also not visible on CT angiography or MRVW imaging done within 24 hours of EVT. The two possible reasons for this are that the thrombus either migrated or dissolved at the time of CT/MRVW imaging, or endovascular OCT is better at detecting small thrombi given the superior spatial resolution.

The utility of OCT imaging after EVT has great promise. We demonstrate that the micron-scale spatial resolution of OCT enables detection of residual luminal thrombus and ongoing thrombosis of basilar perforators. The current standard of reporting reperfusion after EVT using the TICI scale may not adequately capture the luminal environment after EVT. OCT could theoretically provide clinicians with added information and possibly guide antithrombotic management after EVT.

In summary, we describe a novel application of endovascular OCT in basilar stroke patients after EVT. OCT may be safe and capable of producing cross-sectional images displaying evidence of endothelial injury, atherosclerosis, and residual thrombus. Furthermore, we observed that significant residual thrombus may exist after EVT and this residual thrombus could certainly cause ongoing function-limiting strokes with occlusion of vital basilar perforators after EVT.
REFERENCES
Figure 1: OCT Imaging of the Basilar Artery. The OCT catheter is positioned such that the optical lens marker is beyond the arterial region of interest. Each pullback images 54mm of artery. OCT is able to define endothelial anatomy, atherosclerosis, and residual thrombus. A cross section is shown depicting residual thrombus (light blue arrow), patent perforator (orange arrow), and thrombosed perforator (dark blue arrow). **Abbreviations:** OCT=Optical Coherence Tomography.
Figure 2: OCT imaging of normal and damaged swine endothelium. A) Normal swine vessel anatomy with thick tunica media occupying most of the vessel wall (blue arrow), with a thin layer of endothelial cells (red arrow). B) Damaged endothelial layer (green arrows) elevated from the tunica media with intraluminal thrombus (pink arrow). C) Elevated endothelium (green arrow) and denuded endothelium (yellow arrow). D) Floating intima/media within the vessel lumen (green arrow). **Abbreviations:** OCT= optical coherence tomography. *OCT catheter. White bar length=1mm.
Figure 3: Patient one angiographic and OCT imaging.  
A) Angiogram demonstrating complete basilar occlusion (yellow arrow) and TICI 3 reperfusion after thrombectomy.  
B) Thick plaque fibrosis was present (red arrows) causing concentric outward remodelling and loss of normal vessel architecture, and no internal and external lamina.  
C-D) Significant intraluminal red thrombus (light blue arrows) causing signal attenuation (green arrows) beyond the clot. Concentric fibrous plaque throughout the vessel wall (red arrows).  
Abbreviations: OCT=optical coherence tomography, TICI=thrombosis in cerebral infarction. White asterisk (*) denotes the guidewire and the shadow produced from the wire. White bar length=1mm.