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Authors
Mathews, Marlon S
Su, Jianping
Heidari, Esmaeil
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Neuro-endovascular optical coherence tomography imaging: Clinical feasibility and applications

Marlon S. Mathews[1,2], Jianping Su[2,3] , Esmaeil Heidari[2,3], Mark E. Linskey[1], Zhongping Chen[2,3]

[1]*Department of Neurological Surgery, University of California Irvine, Orange, California 92868*

[2]*Beckman Laser Institute and Medical Clinic, University of California Irvine, Irvine, California 92612.*

[3]*Department of Biomedical Engineering, University of California Irvine, Irvine, California 92612.*

ABSTRACT

The authors report on the feasibility of clinical neuroendovascular optical coherence tomography (OCT) imaging as well as its efficacy and safety by comparing findings with histology in animal, cadaveric and clinical studies. Catheter-based *in vivo* endovascular OCT imaging was carried out intracranially in four patients, three in the anterior circulation and one in the posterior circulation (vertebral artery). The neuroendovascular OCT device was delivered to the desired location using groin access and standard endovascular procedures. *In vivo* findings were reproduced using *ex vivo* OCT imaging in corresponding animal and human (cadaveric) harvested tissue segments with findings matched by histology. OCT images correlated well with the images obtained after histologic sectioning, and visualized *in vivo* the laminar vascular structure. Satisfactory imaging findings were obtained with no complications. Neuroendovascular OCT imaging is thus feasible for clinical use and can detect with high resolution the structure of arterial segments. Understanding OCT imaging in non-diseased arteries is important in establishing baseline findings necessary for interpreting pathologic processes. This allows neuroendovascular optical biopsies of vascular tissue to be obtained without the need for excision and processing, and potentially allows prophylactic interventions against stroke and other cerebrovascular disease before they become symptomatic.

Key words: OCT, neuroendovascular, stroke, brain imaging, blood vessels, aneurysms, optical coherence tomography.

Send correspondence to: Marlon S. Mathews, MD.
101 The City Drive South, Building 56, Suite 400, Orange, CA 92868.
Fax# (714) 456-8284. Email: marlonmathews@yahoo.com.

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INTRODUCTION

Intravascular optical coherence tomography (OCT) is an optical imaging technique that provides high-resolution cross-sectional *in situ* images from intact tissue based on tissue reflectance of near-infrared or infrared light.[1, 2] Such tissue has been extensively used for the study of the coronary blood vessels to visualize pathology such as atherosclerotic plaques and dissections and to visualize interventions. OCT has the advantage of having a high resolution (~8 μm in tissue), which is a degree of magnitude higher than currently available clinical diagnostic imaging modalities.[3]

Experiments correlating a limited number of excised coronary and aortic specimens with histology have demonstrated that OCT is capable of resolving microstructural features of atherosclerotic plaques.[4-6] The capability of OCT to resolve micrometer-scale features of atherosclerosis makes it an attractive means for characterizing *in vivo* microstructural features of carotid plaques as well as those of intracranial vascular pathologic processes such as aneurysms, dissections, stenosis, and fibromuscular dysplasia. To date, there is scant literature on its feasibility for intracranial endovascular imaging in patients.

METHODS AND RESULTS

The neuroendovascular OCT device used in this study was specifically designed and developed for intracranial use. Specifics regarding its design and structure are previously described.[7] The study was approved by the Institutional Review Board (#2006-5031) and Institutional Animal Care and Use Committee (#2005-2616) at our institution. The OCT imaging was carried out using groin access and standard endovascular techniques in patients undergoing cerebral angiograms. The research was purely descriptive and no intervention was carried out based on OCT findings. Four patients underwent neuroendovascular OCT imaging in total. In three patients the intracranial internal carotid arteries were imaged (near its terminal bifurcation) while in a fourth the intracranial vertebral artery was imaged. Clinical procedures were carried out either under general anesthesia or conscious sedation each of which was determined based on the complexity of each case and was not influenced by the added research imaging procedure. All patients underwent preprocedure and postprocedure neurological examination. In patients that underwent postprocedure MRI scans of the brain there was no evidence of ischemic/embolic strokes on any sequence including Diffusion Weighted Imaging (DWI).

In order to identify and confirm the findings with clinical OCT imaging in patients, cadaveric intracranial ICA segments were obtained that were subjected to OCT imaging as well as histologic examination. The OCT findings in cadaveric ICA segments matched the findings in clinical imaging and were identifiable on

histology (FIGURE 1). Similarly endovascular OCT imaging was carried out in farm pigs under general anesthesia and nondiseased segments of the common carotid arteries were imaged. These segments were then examined histologically to identify and confirm findings with *in vivo* OCT imaging. OCT findings were readily identifiable on histologic evaluation (FIGURE 2). Thus it was demonstrated from these preliminary findings that neuroendovascular OCT imaging for clinical intracranial use is feasible, efficacious and potentially safe. The overall increase in duration of the clinical procedure varied from 5 to 15 minutes but is expected to decrease with increased experience.

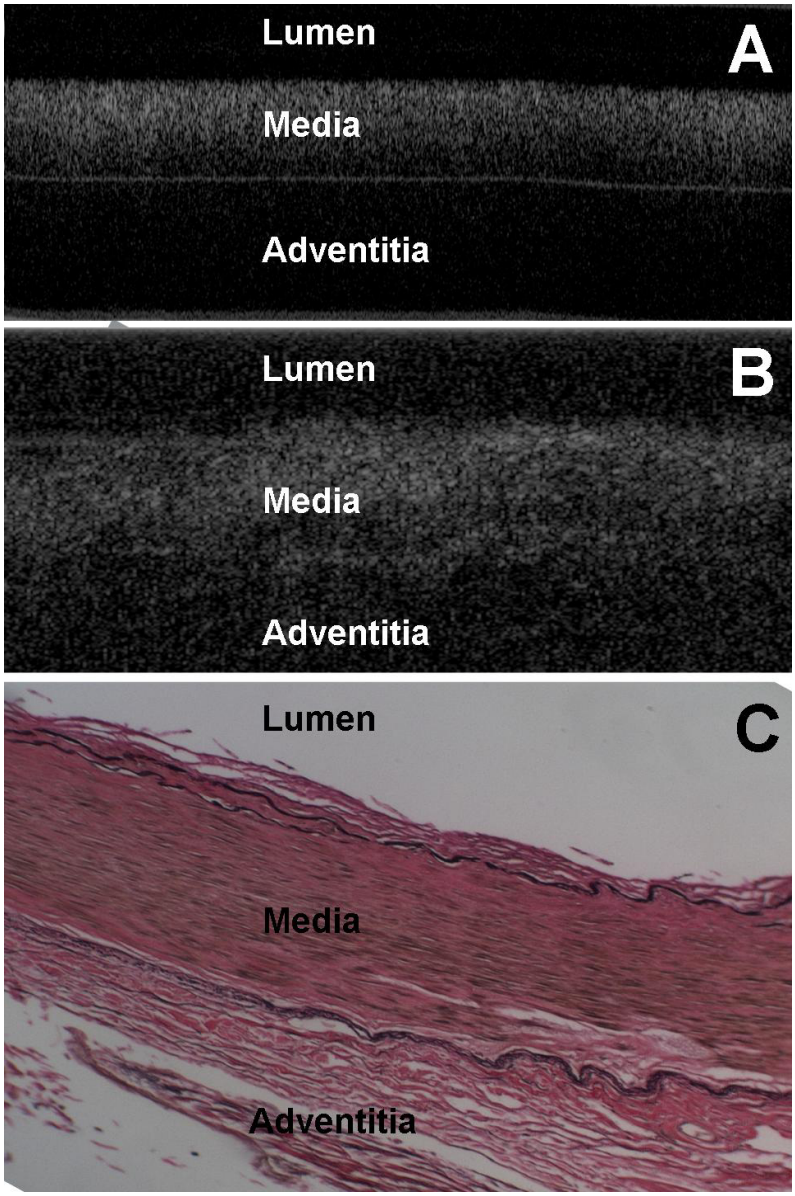

FIGURE 1: OCT image (using linear scanning) of the intracranial internal carotid artery (ICA) obtained *in vivo* in a patient (A), ex vivo from the corresponding location in a human cadaveric specimen (B), with corresponding histology

(C) obtained on the specimen imaged in B. OCT images are alike in clinical and cadaveric specimen and show histologically identifiable layers- lumen, media and adventitia. Histology is obtained using a trichrome stain (Sigma-Aldrich, NJ) under a light microsope, where collagen stains pink, elastin stains black, and muscle stains brown).

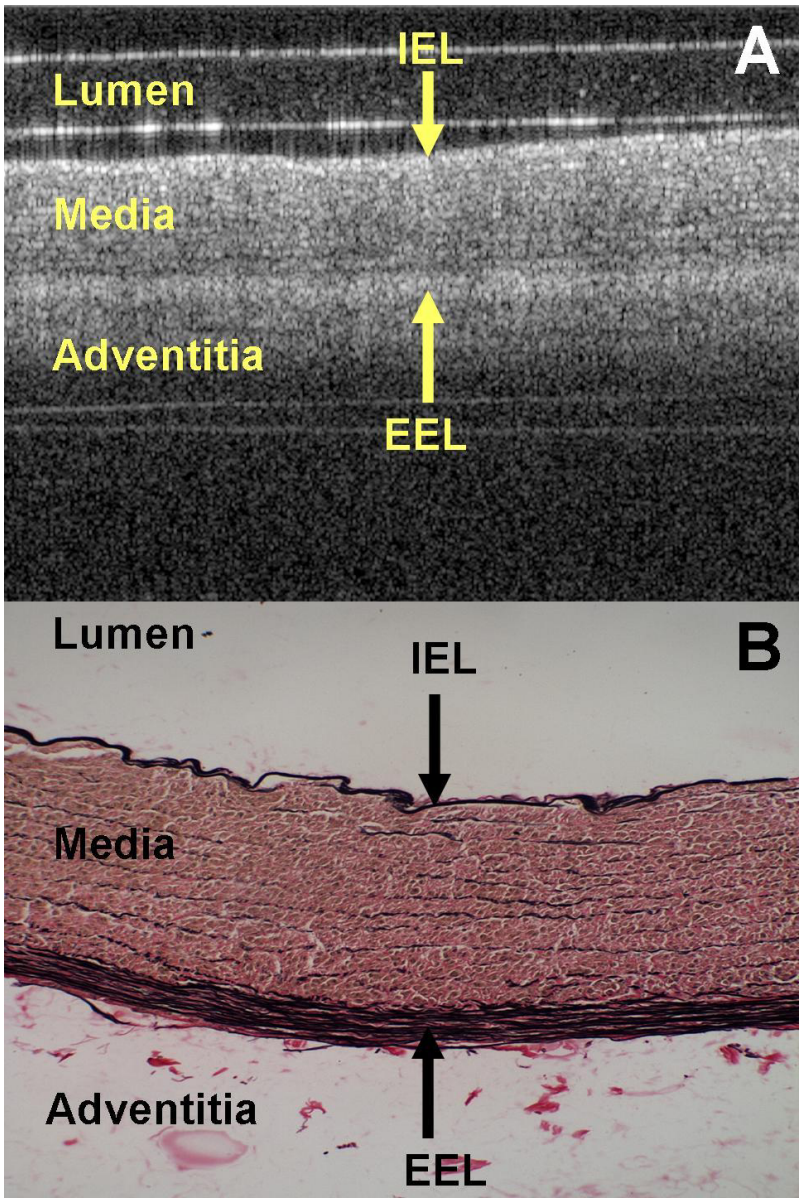

FIGURE 2: OCT image obtain *in vivo* from the segment of a swine common carotid artery (A) with corresponding histology from the same specimen (trichrome stain). The laminar structure of the vessel wall is visible including the internal elastic lamina (IEL), media, external elastic lamina (EEL), and adventitia. Elastic tissue shows up as regions of high reflectance on OCT images.

DISCUSSION

Cerebrovascular disease/stroke is the leading causes of disability within our population and among the leading causes of death in the USA. Strokes occur when blood vessels supplying the brain are occluded, starving the brain cells supplied by the vessel of oxygen and glucose. The majority of strokes arise from a clot originating from a proximal source (embolic) mostly from arteries with pre-existing pathology such as atherosclerotic plaques, dissections, etc.

The OCT imaging findings in our study correlate well with structural information obtained in corresponding vessel segments using histologic examination. This was confirmed in the intracranial and carotid arterial segments each with its unique structural anatomy. Imaging of intra-arterial vascular pathology thus provides information of both diagnostic and potentially therapeutic value. Current diagnostic imaging modalities such as catheter angiography, ultrasonography, computed tomographic (CT), magnetic resonance imaging (MRI) etc provide luminal macrostructural and flow-related information with typical imaging resolutions in the millimeter range. These modalities provide limited information on vessel wall structural pathology outside of luminal alterations. Recently, high-frequency intravascular ultrasound (IVUS) devices have become available that provide better resolution imaging on the order of 100 to 150 microns. Studies have shown IVUS to be superior to angiography with respect to plaque characterization, stent deployment,[8-9] and correlation between plaque features and acute coronary syndrome.[10] Images of the coronary arteries comparing endovascular OCT to IVUS imaging for vascular pathology demonstrate better resolution and clearer images using OCT.[6] Neuroendovascular OCT imaging thus holds the potential of identifying vascular structural pathology before they become symptomatic, allowing for prophylactic treatment or interventions to prevent stroke occurenence or occurrence of other cerebrovascular events.

Intracranial saccular aneurysms arise as abnormal outpouchings of arterial walls seen most commonly at arterial branch points at the circle of Willis at the base of the brain. Etiologically, they are may be related to congenital or acquired structural defects at these branch points with contribution from flow induced hemodynamic stresses. These defects commonly involve the absence of a tunica media and are known as medial cushion defects.[11-12] Characterizing OCT signals arising from vascular elastin and tunica media has particular applicability in the imaging of intracranial aneurysms. Arteries at the base of the brain also lack the structural protection of the external elastic lamina (EEL) seen in the more proximal extracranial portions of these arteries. These aneurysms rupture in some patients with the risk of rupture only crudely correlating with the aneurysm diameter.[13] Clearly an objective assessment of aneurysm wall structure could lead to more sensitive and useful modeling of aneurysm rupture risk. In addition OCT can internally visualized the status of healing of treated (particularly) coiled or stented aneurysms and determine the adequacy of treatment and/or need for further intervention.[14]

CONCLUSIONS

Neuroendovascular OCT imaging can be safely carried out in patients with appropriately engineered endovascular OCT devices. The signal obtained from is of sufficient quality to resolve the circumferential cross-sectional structural composition of extracranial and intracranial arteries. Imaging information gathered from the *in vivo* application of the device closely correlates with histologic information. Endovascular OCT may be particularly effective and attractive for detecting and analyzing special features of complex vascular pathology, such as arterial plaques and aneurysms. Further studies are necessary for more detailed assessment of safety and efficacy. Potentially more useful and relevant means for modeling stroke and intracranial aneurysm pathology based on lesion-specific cross-sectional structural information are on the horizon.

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DISCLOSURES

Dr. Chen is a co-founder and director of OCT Medical Imaging. He has ownership interests in and is a consultant for OCT Medical Imaging. Dr. Mathews has significant ownership interest in Universal Coherence Imaging, LLC.

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