Retinal Adherence and Fibrillary Surface Changes Correlate With Surgical Difficulty of Epiretinal Membrane Removal

JAE SUK KIM, JAY CHHABLANI, CANDY K. CHAN, LINGYUN CHENG, IGOR KOZAK, KATHRIN HARTMANN, AND WILLIAM R. FREEMAN

• PURPOSE: To correlate surgical difficulty of epiretinal membrane (ERM) removal with characteristics of ERM adherence seen by spectral-domain optical coherence tomography (SD-OCT).

• DESIGN: Prospective observational case series.

• METHODS: Surgical difficulty was correlated with extent of ERM adherence by SD-OCT using masked observers in consecutive eyes undergoing ERM removal (N = 31). Surgical videos were analyzed and difficulty of ERM removal (grade 1-3) was determined in 4 quadrants as well as the fovea by consensus of observers masked to SD-OCT findings. Extent of ERM adhesion was categorized (focal, broad, or complete) by masked observers using SD-OCT. The presence of fibrillary changes between the ERM and retinal nerve fiber layer (RNFL) was also evaluated. Surgical difficulty of ERM removal for each quadrant and fovea was compared to extent of ERM adherence and presence of fibrillary changes.

• RESULTS: Assessment of ERM adherence using SD-OCT between masked observers was highly concordant (kappa = 0.9178). Surgical difficulty of ERM removal was strongly associated with more extensive ERM adherence to the retina observed by SD-OCT. Complete ERM adherence correlated with an 8.6-fold increased surgical difficulty of ERM removal compared to focal adherence ($P < .0001$). The presence of fibrillary changes between the ERM and RNFL also correlated with a 25.5-fold increased difficulty of surgical removal compared to the absence of fibrillary changes ($P < .0001$).

• CONCLUSION: Extent of ERM-retinal adhesion and presence of fibrillary changes determined by SD-OCT provide reliable preoperative assessment of surgical difficulty. Furthermore, SD-OCT analysis may help localize surgically advantageous coordinates to initiate ERM removal. (Am J Ophthalmol 2012;153:692–697. Published by Elsevier Inc.)

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EPIRETINAL MEMBRANES (ERMS) CAUSE DISTORTION of the retina and vision loss.[1,2] Initial classifications of these membranes include the classic work by Gass.[2] Ophthalmoscopic grading includes early disease, also termed grade 0 or cellophane maculopathy, in which a sheen from the inner retinal surface is observed with no distortion. This is followed by grade 1 or crinkled cellophane maculopathy, when membrane contraction causes small irregular folding of the inner retina surface. Gass emphasized fine superficial radiating folds that can be seen extending from membrane epicenters. Grade 2 includes an opaque or semi-opaque membrane causing significant vessel dragging. More recently, optical coherence tomography (OCT) has allowed visualization of membranes and their relationship to the retinal surface.[3–6] However, the predictive value of OCT and clinical examination for surgical planning and for determining ease or difficulty of surgical removal remains unclear.[4,7]

Time-domain OCT studies have shown that primary epiretinal membranes are more often adherent "globally" to broad areas of the retina, as opposed to membranes that occur after retinal breaks or detachment, which are more often focally adherent.[8] More recently, spectral-domain optical coherence tomography (SD-OCT) analysis of epiretinal membranes has allowed determination of points of adhesion and relationships of the epiretinal membrane to the internal limiting membrane with a higher degree of detail.[9,10] Although SD-OCT allows better definition of the geometry of membrane adhesion to the retina and it is suggested that membranes may be globally or focally adherent, ERM structure may not correlate with vision.[11–14] Since the treatment of vision distortion from ERMs is surgical, correlation of ERM-retinal adherence with degree of surgical difficulty may aid in surgical planning.

In this study, we evaluated preoperative structural characteristics of epiretinal membranes including extent of retinal adhesion and presence of fibrillary changes using SD-OCT. These structural findings were correlated with

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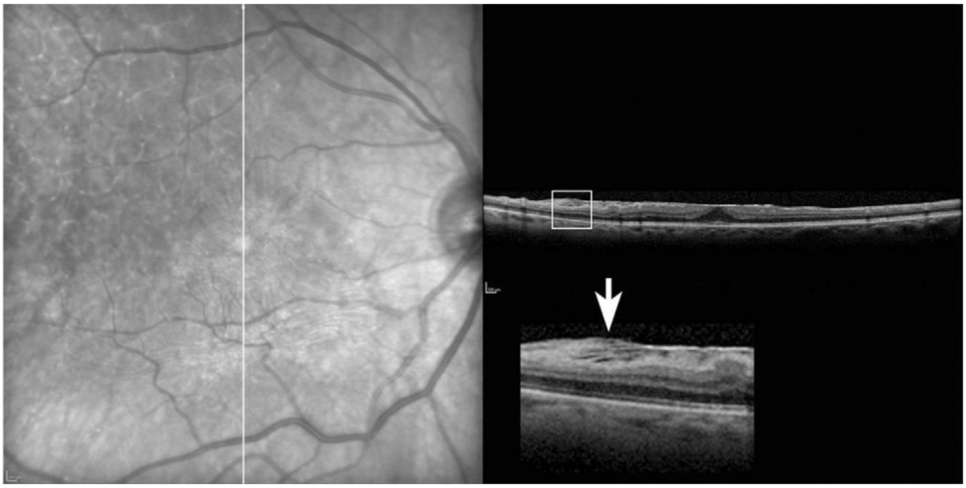

FIGURE 1. Representative grading of epiretinal membrane (ERM)-retinal adherence. Complete ERM-retinal adherence (Grade 3) along the posterior pole with exception inferiorly (broad ERM-retinal adherence, Grade 2). Fibrillary changes (arrow) are seen as alternating linear hyperreflective and hyporeflective signals between the ERM and retinal surface (inset).

TABLE. Spectral-Domain Optical Coherence Tomography Characteristics of Epiretinal Membranes in Each Area Evaluated

Characteristics	Fovea (N)	Nasal (N)	Temporal (N)	Superior (N)	Inferior (N)	Total (N)
Focal	2	3	1	6	12	24
Broad	2	13	9	8	7	39
Complete	26	13	20	15	12	86
Fibrillation (+)	2	4	2	6	8	22
Fibrillation (−)	28	25	28	23	23	127

Fibrillation (+) = presence of fibrillary change; Fibrillation (−) = absence of fibrillary change; N = number of quadrants.

ease or difficulty of surgical removal by reviewing surgical videography using masked observers.

METHODS

SURGICAL DIFFICULTY AND EXTENT OF ERM-RETINAL ADHESION was evaluated in a consecutive series of eyes (N = 31) undergoing idiopathic macular ERM removal. Inclusion criteria included visual acuity of 20/50 or worse or metamorphopsia. All patients underwent a 3-port 25-gauge pars plana vitrectomy with core vitrectomy and posterior hyaloid removal. Epiretinal membranes were removed with or without triamcinolone (TCA) dusting (400 mg/mL) or indocyanine green (1.25 mg/mL) as a negative stain during a period of 8 months performed by a single experienced retinal surgeon. Since the surgeon was masked to preoperative OCT findings, the quadrant to initiate ERM peeling was randomized and peeling was performed using an ILM forceps tip (Revolution; Grieshaber, Fort Worth, Texas, USA). The intended surgical plane was to remove the epiretinal membrane without removal of the internal limiting membrane. Epiretinal membranes with a known etiology of uveitis,

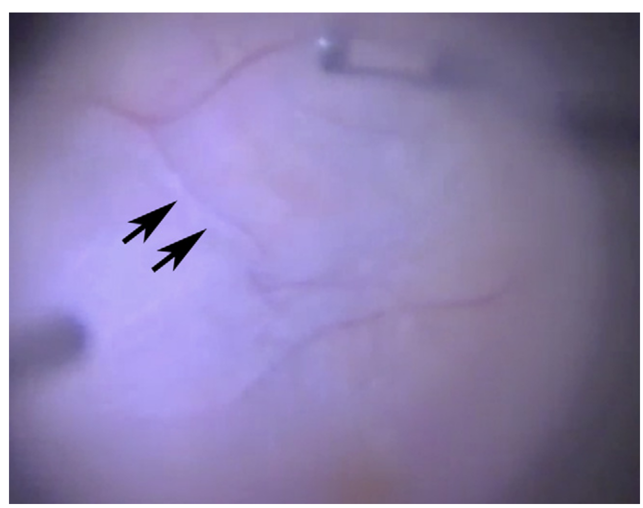

FIGURE 2. Representative example of difficult peeling of an epiretinal membrane in which vessel elevation is seen with perivascular white reflection (arrows) by forceps (upper frame) as the ERM is removed. This is a still frame from surgical videography (Supplemental Video 1).

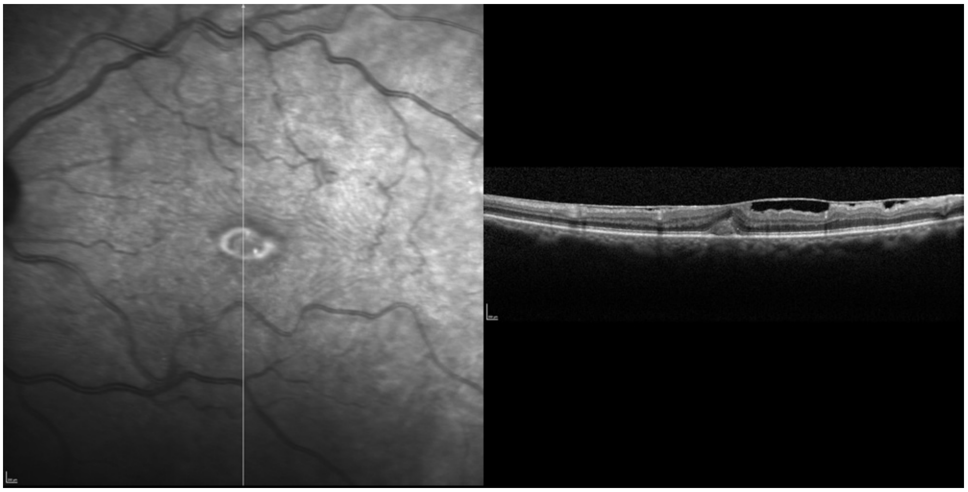

FIGURE 3. Focal ERM-retinal adherence is seen both superior and inferior to the fovea along the vertical axis using spectral-domain optical coherence tomography.

diabetic retinopathy, and previous retinal tears or detachments were excluded. Epiretinal membranes with lamellar macular holes were also excluded. Informed consent was obtained from all participants.

Surgical videography was recorded using an AVI adaptor mounted on a surgical microscope (Leica Microsystems, Wetzlar, Germany). Images were acquired using a 640 × 480 pixels digital video camera (Sony 3 CCD Exwave-HAD, Tokyo, Japan) mounted onto the surgical microscope. Digital feed was recorded directly onto a computer hard drive at DV resolution (Apple Macbook, Apple Computer, Cupertino, California, USA). Surgical videos were reviewed by 2 observers masked to preoperative SD-OCT imaging. Each masked observer was an experienced retinal surgeon and did not participate in ERM removal in this series of eyes. Degree of difficulty of membrane removal was determined for each quadrant of the macula and foveal area (total 5 areas per eye) following consensus by both reviewers. A grading scale (grade 1-3) was assigned according to surgical difficulty as follows: grade 1, peeling occurs easily with no evidence of retinal traction; grade 2, some evidence of retinal traction but retina retracts quickly following membrane removal; grade 3, appreciable retinal traction is observed with difficulty in ERM separation from the retina and retina remains elevated after ERM removal.

SD-OCT images (Spectralis OCT, Heidelberg Engineering, Vista, California, USA) of ERM structure along the vertical and horizontal meridians over the fovea (central 1000 μm) and macular quadrants (superior, inferior, nasal, and temporal) were also evaluated in a masked fashion by 2 observers. Thus, each eye was evaluated in a total of 5 areas (fovea, 4 quadrants). Both vertical and horizontal scanning meridians were obtained for each macular quadrant and foveal area was assessed for extent of ERM-retinal adhesion as well as for the presence of fibrillary changes along both vertical and horizontal scanning meridians. Calipers were used to measure the length of ERM-retinal adherence and divided by the total length of ERM to obtain ERM-retinal adhesion percentage. The extent of ERM-retinal adhesion was then categorized as focal, broad, or complete. Focal adhesion was defined as ERM-retinal adhesion <50%; broad adhesion between 50% and 90%; and complete adhesion >90%.

Fibrillary changes were defined as the presence of alternating linear hyperreflective and hyporeflective signals observed by SD-OCT extending between the ERM and retinal nerve fiber layer (RNFL) that were not parallel to the retinal surface (Figure 1). Fluorescein angiography was performed preoperatively in all eyes to exclude choroidal neovascularization or other non-ERM pathology.

All analyses used generalized estimating equations to account for intra-eye variations (the SAS system, Generalized Estimated Equations [GEE] analysis).

RESULTS

ERM-RETINAL ADHERENCE PATTERN RESULTED IN COMplete concordance (kappa = 1) in each quadrant between the horizontal and vertical meridians for each observer. In addition, assessment of ERM-retinal adherence resulted in an extremely high concordance between masked observers (kappa = 0.9178). Therefore, categorization of ERM-retinal adherence by 1 observer was used for statistical analysis.

Among 31 consecutive eyes, ERM-retinal adherence pattern was evaluated preoperatively in a total of 149 areas since no evidence of an ERM was seen in 6 areas. The mean age of our patients in this study (female =14, male = 17) was 67.8 ± 11.4 years. Complete ERM-retinal adherence was observed in the majority of areas (86/149) evaluated

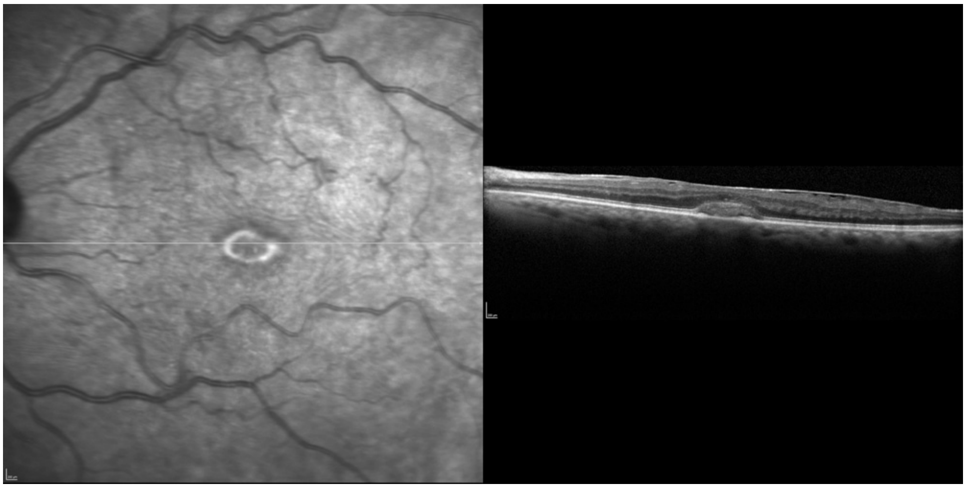

FIGURE 4. Broad ERM-retinal adhesion (50%–90%) is seen nasally and temporally across the horizontal axis by SD-OCT. Complete ERM-retinal adherence (>90%) is seen at the fovea.

(Table). The presence of fibrillary changes was similarly distributed among all quadrants in 13 patients.

Surgical difficulty of ERM removal was also evaluated in the same 149 areas. ERM tissue was easily removed over 59 areas with no evidence of retinal traction (grade 1) (Figure 2 and Supplemental Video 1 [available at AJO.com]). Difficult ERM removal (grade 3) (Figure 3 and Supplemental Video 2 [available at AJO.com]) was observed in 46 areas with appreciable retinal traction and retinal elevation. Intermediate difficulty in surgical removal (grade 2) of ERM tissue was observed in 44 areas. A partial-thickness retinal defect occurred during ERM removal in 1 case over a single quadrant in which the presence of fibrillary changes was noted preoperatively. No other complications occurred.

Complete ERM-retinal adhesion correlated with a 3.7-fold and 8.6-fold increase in surgical removal difficulty compared to broad ($P < .02$) and focal ERM-retinal adhesion ($P < .0001$), respectively, using generalized estimating equation modeling.

Additionally, irrespective of ERM-retinal adhesion type, the presence of fibrillary changes between the ERM and RNFL observed by SD-OCT correlated with a 25.5-fold increase in difficulty of surgical removal ($P < .0001$) compared to the absence of fibrillary changes.

• **CASE 1: REPRESENTATIVE DIFFICULT EPPIRETINAL MEMBRANE PEEL (GRADE 3):** A 53-year-old man with complete ERM-retinal adherence along the entire posterior pole with exception inferiorly (broad ERM-retinal adherence) and low-density ERM-RNFL fibrillation by SD-OCT along the vertical meridian (Figure 1; arrow indicates fibrillation) underwent a difficult ERM peel (grade 3) (Figure 3 and Supplemental Video 2 [available at AJO.com]). An elevated vessel (arrows) is seen during peeling of the membrane held by forceps in the upper frame (Figure 3). Supplemental Video 2 (available at AJO.com) shows difficulty of membrane removal over the area of ERM-RNFL fibrillation.

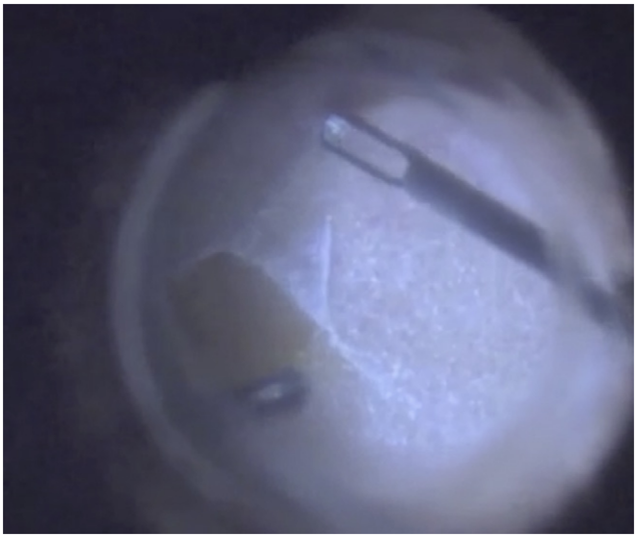

FIGURE 5. Easy removal of ERM from the temporal area with no retinal traction seen in a still frame from surgical videography (Supplemental Video 2).

• **CASE 2: EASY EPIRETINAL MEMBRANE PEEL (PREDOMINANTLY GRADE 1):** In Case 2, an 85-year-old man with focal ERM-retinal adherence superior and inferior to the fovea; broad adherence nasal and temporal to fovea; and complete adherence at the fovea area using SD-OCT (Figures 4 and 5) underwent an easy ERM peel (predominantly grade 1) (Figure 2 and Supplemental Video 1 [available at AJO.com]). A video still frame (Figure 2) illustrates the temporal area of the TCA-dusted membrane, which was easy to remove, with no retinal traction seen.

DISCUSSION

SPECTRAL-DOMAIN OPTICAL COHERENCE TOMOGRAPHY provides higher-resolution imaging of macular disease and, in particular, retinal surface pathology.[5,9–11,13] Our study is the first to characterize ERM-retinal surface details regarding extent of ERM-retinal adhesion and presence of fibrillary changes by SD-OCT. Furthermore, ERM surface characteristics were correlated with difficulty of surgical removal of these membranes.

Although a smaller study suggested that idiopathic epiretinal membrane structure could predict ease of surgical removal, surgical ease of removal was based on operative dictation by the surgeon who was not masked to SD-OCT findings.[4] Additionally, surgical ease was determined based on the number of attempts made to remove the ERM, which is more dependent on surgical technique rather than ERM adherence to the retinal surface.

Complete ERM-retinal adhesion resulted in a 3.7-fold and 8.6-fold increase in surgical difficulty of membrane removal compared to broad ($P < .02$) and focal ($P < .0001$) adhesion, respectively. It is not surprising that increased ERM-retinal adherence would increase surgical difficulty of membrane peeling. As the extent of ERM-retinal adhesion increases, the extent of ERM with non-adjacent retinal tissue directly abutting the membrane also decreases. This lamellar space between the ERM and retinal surface likely represents a true tissue-free space between the ERM and retinal surface. Although the presence of fluid cannot be excluded, this tissue-free space may provide a cleavage plane between ERM and retina to facilitate membrane peeling during vitrectomy surgery.

Notably, the presence of fibrillary changes (alternating hyperreflective and hyporeflective signals between ERM and retinal surface not parallel to the retinal surface) resulted in a 25.5-fold increase in surgical removal difficulty compared to its absence ($P < .0001$). These fibrillary changes are likely glial in nature and may produce strong adhesional forces between the ERM and the retinal surface that may increase the strength of ERM-retinal adhesion and subsequently increase difficulty in surgical removal (sticky peel). These fibrillary changes are likely a distinct entity from fibrocellular proliferation observed along the posterior surface of the posterior hyaloid in vitreomacular traction described in prior studies, given the differences in localization.[11,13] Additionally, ERM-associated fibrillary changes described in this study likely contribute adhesion as opposed to tractional forces. In this study, the intended surgical plane was between the ERM and the retinal surface. Future studies with the intended surgical plane at the level of the internal limiting membrane correlating fibrillary changes in ERMs with surgical difficulty of removal may help elucidate the localization of fibrillary ERMs.

Thus, ERM-retinal surface findings by SD-OCT may allow surgeons to anticipate difficulty of surgical removal and facilitate surgical planning. Initiating ERM peeling over an area of focal or broad ERM-retinal adhesion in contrast to areas of complete ERM-retinal adhesion or over areas of fibrillary changes may provide a large enough flap or even peeling momentum to maximize facilitation of complete ERM removal. Focal or broad ERM retinal adhesion patterns may allow the underlying retinal tissue to become more plicated. In contrast, complete ERM-retinal adhesion may prohibit the formation of retinal tissue plication. Patients with ERMs of predominantly complete ERM-retinal adherence or fibrillary changes seen by SD-OCT could be advised that surgical removal could potentially be more difficult. Additionally, it would be interesting to assess long-term visual outcomes or rates of complication after removing ERMs with differing SD-OCT characteristics in future studies.

Our results note that any particular eye may contain multiple adhesion patterns and varying areas of difficulty for ERM removal. Although characterization of SD-OCT findings in each quadrant along the vertical and horizontal scanning meridians correlated completely, further studies using 3-dimensional SD-OCT may provide more extensive topographic understanding of ERM-retinal surface adhesion and may further facilitate surgical approaches to ERM peeling. Additionally, correlating these lamellar spacing and fibrillary surface changes found on SD-OCT with electron microscopy may provide a cellular basis to our understanding of the constituents of ERM-retinal surface adhesion.

In summary, we have shown that SD-OCT may help determine surgical difficulty and thus be an important adjunct for planning ERM surgery. We found that the presence of fibrillary changes may have a stronger association with difficulty in ERM peeling than extent of ERM adhesion to the retinal surface, given that the odds ratio was 25.5 compared to complete adhesion with an odds ratio of 8.6. SD-OCT analysis of ERMs provides valuable detailed ERM-retinal surface information to facilitate surgical planning for removal of membranes.

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Biosketch

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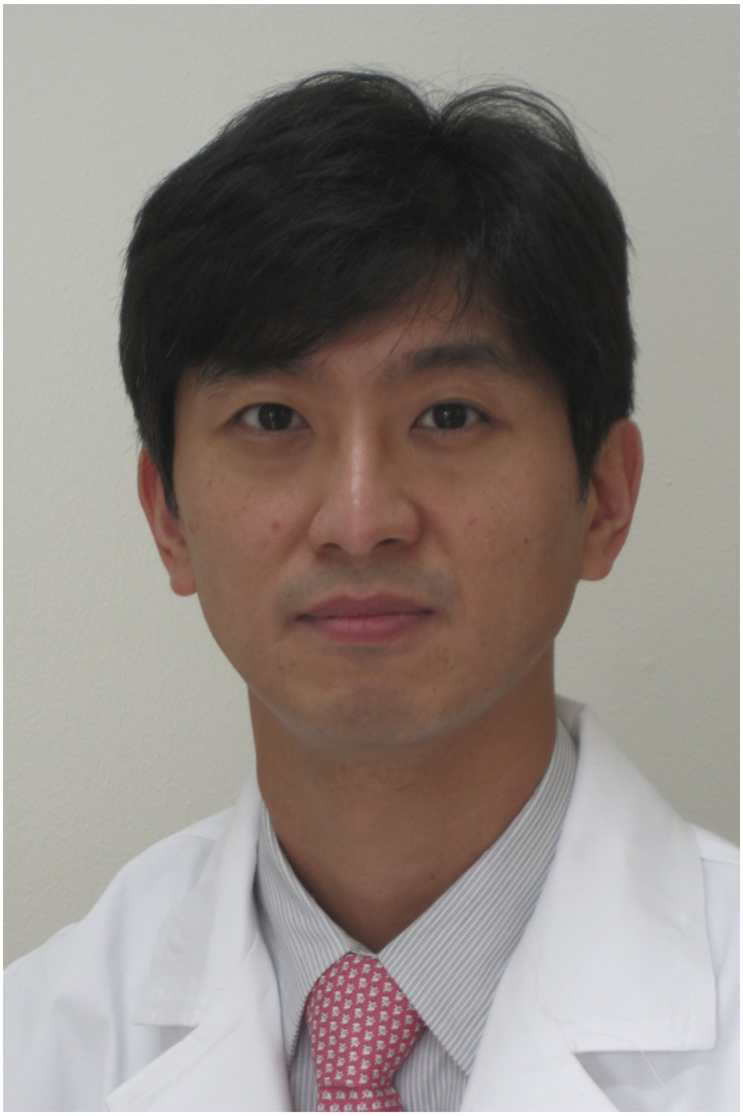

Biosketch

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