Contrast-enhanced intraoperative optical coherence tomography

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ABSTRACT
Optical coherence tomography (OCT) has revolutionised clinical ophthalmology. The translation of OCT into the operating room is a natural next step given its high-resolution anatomic information. Contrast agents and enhancement have significantly improved the diagnostic capabilities of numerous imaging modalities (such as CT and MRI). The use of OCT contrast agents in ophthalmology has been generally lacking. In this report, we describe the novel application of triamcinolone as an OCT contrast agent for intraoperative OCT to improve visibility of tissue interfaces and planes (eg, posterior hyaloid insertion points). The application of this technology may have wide-ranging implications for enhanced image-guided surgery, intraoperative OCT and dynamic or functional applications of OCT technology.

INTRODUCTION
Since the initial descriptions of optical coherence tomography (OCT), the ability to visualise anatomic features and pathology in the eye has improved tremendously.1 The advent of spectral domain-optical coherence tomography (SD-OCT) improved the resolution and visualisation, while decreasing acquisition time.2 Although the quality of in vivo imaging has improved, widespread development of contrast-enhanced OCT has been limited. We have previously described the ex vivo use of prednisolone, lipid-based artificial tears and triamcinolone for contrast-enhanced OCT in the anterior segment.3 In addition, we described perioperative contrast-enhanced OCT to provide functional assessment of corneal wound integrity in eyes undergoing cataract surgery.4

The enhanced visualisation achieved with contrast agents facilitates improved identification of tissue layers and allows for a more dynamic or functional OCT.1 4 Intraoperative optical coherence tomography (iOCT) is an emerging field that uses the high-resolution cross-sectional information afforded by OCT to improve visualisation of surgical ophthalmic pathology. iOCT provides the surgeon with a rapid feedback on microarchitectural changes and reveals the underlying impact of surgical manoeuvres on ophthalmic tissues.5–10 Transparent and translucent tissues are visualised en face in real time during a surgical procedure with a standard operating microscope. Efforts at seamless integration of iOCT into surgical practice include microscope integration, software advances, dynamic motion imaging, enhanced visualisation and development of surgical instruments.5 7 9 Using contrast-enhanced iOCT may provide improved visualisation of tissue interfaces. In this report, we provide a novel description of contrast-enhanced iOCT using preservative-free triamcinolone (Triavance, Alcon, Fort Worth, Texas, USA) as a contrast agent for posterior segment surgery.

METHODS
A retrospective consecutive case series of four eyes with iOCT imaging following placement of preservative-free triamcinolone was performed. Institutional review board approval was obtained and the study adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants for surgical intervention and iOCT.

Intraoperative imaging was performed using a custom microscope-mounted iOCT system, using a portable SD-OCT probe (SDOIs; Biopigen; Research Triangle Park, North Carolina, USA). A standardised imaging protocol was used with iOCT imaging performed at various surgical milestones as well as prior to the initial incision (eg, pre-incision). Volume scanning was performed with 10×10 m area with 100 B-scans per area at both 0 and 90°. Pre-incision iOCT scans were performed once the patient was positioned and prepped for surgery. All patients underwent core pars plana vitrectomy. Prior to elevating the posterior hyaloid, intravitreal triamcinolone (Triavance) was used to stain the posterior hyaloid. Following instillation of the triamcinolone, iOCT scanning was repeated.

Qualitative analysis of the changes in reflectivity in the pre-injection and post-injection scans was performed with particular attention to the posterior hyaloid as well as at the level of the retina. Three-dimensional reconstruction was performed to evaluate the contrast enhancement of the posterior hyaloid anatomy.

RESULTS
iOCT image analysis following instillation of triamcinolone revealed increased hyper-reflectivity at the posterior hyaloid. This provided improved visualisation of the posterior hyaloid anatomy and its focal insertion points (eg, fovea and optic nerve) and pre-macular bursa (figure 1A–D). Contrast enhancement was noted to have a granular hyper-reflectivity with increased shadowing noted posterior to the triamcinolone 'granules' (figure 1B,D). Triamcinolone contrast-enhanced iOCT also provided evidence for the presence of a subclinical, inner retinal defect and possible full-thickness hole in a vitreomacular traction case. Following removal of the hyaloid, the signal strength of the iOCT scan was suboptimal with limited resolution of the retinal architecture. However, with the presence of the contrast agent, this subclinical abnormality
could be visualised, as there appeared to be triamcinolone particles within the retinal substance suggesting a retinal defect (figure 2).

Given these iOCT findings, the surgeon was able to address the abnormality (eg, gas tamponade, positioning) appropriately with an optimal surgical result. Three-dimensional reconstruction of contrast-enhanced iOCT scans highlighted the increased reflectivity of the stained hyaloid intraoperatively and provided an outstanding view of the hyaloidal anatomy (figure 3).

**DISCUSSION**

The in vivo use of contrast-enhanced OCT has been limited. In this report, we highlight the translation of this method to the operating room through the use of contrast-enhanced iOCT. The increased reflectivity profile of triamcinolone, as visualised during iOCT, allowed for improved visualisation of posterior structures during vitreoretinal surgery, particularly related to posterior hyaloidal anatomy. The improved visualisation of posterior tissues has many implications for vitreoretinal surgery and iOCT. In one case of vitreomacular traction syndrome, iOCT following hyaloid removal was of limited quality. However, contrast enhancement within the retinal substance at the fovea provided evidence of an inner retinal defect allowing the surgeon to make appropriate changes in surgical management. Due to the limited scan quality, the enhanced contrast provided improved visibility of the area of interest. Based on these finding, contrast-enhanced iOCT may facilitate the identification of surgical planes and optimise surgical manoeuvres given the improvement in anatomic visualisation. This is an area of active research that we are pursuing.

The limitations of this study include the small sample size and retrospective nature. The qualitative analysis limits statistical testing of the data. However, the image differences are striking and clearly represent changes in the reflectivity profile of the scans due to the presence of the agent. The novel nature of the use of contrast enhancement for iOCT provides strength for this study.

The advent of contrast agents has greatly improved the diagnostic and therapeutic capacity of imaging modalities throughout medicine, such as CT and MRI. The development of contrast enhancement for OCT may expand its application and
utility, resulting in a more dynamic or functional assessment tool. The definitive role for contrast agents in OCT remains unknown and further research is needed to better understand the role for contrast agents in iOCT. Additional testing of various agents is also warranted to identify those agents with optimal properties (eg, increased reflectivity with minimal shadowing). Targeted contrast is also important, such as for the internal limiting membrane or posterior hyaloid. Additionally, applications for anterior segment surgery need to be explored. Prospective analysis of the utility of contrast agents for iOCT is important. We have initiated a prospective study on the utility of iOCT that includes analysis of the reflectivity properties of adjuvant dyes (eg, indocyanine green) and other agents (eg, triamcinolone). Along with the microscope integration of OCT systems and OCT-compatible microsurgical tools, OCT contrast agents may help to change the approach to ophthalmic surgery.

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