

# Contrast-enhanced intraoperative optical coherence tomography

Justis P Ehlers, Stephen A McNutt, Peter K Kaiser, Sunil K Srivastava

Vitreoretinal Service, Cole Eye Institute, Ophthalmic Imaging Center, Cleveland Clinic Foundation, Cleveland, Ohio, USA

## Correspondence to

Dr Justis P Ehlers, Vitreoretinal Service, Cole Eye Institute, Ophthalmic Imaging Center, Cleveland Clinic Foundation, 9500 Euclid Avenue/i32, Cleveland, OH 44195, USA; [ehlersj@ccf.org](mailto:ehlersj@ccf.org)

Received 28 December 2012

Revised 6 March 2013

Accepted 20 March 2013

Published Online First

23 April 2013

## 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.<sup>1</sup> The advent of spectral domain-optical coherence tomography (SD-OCT) improved the resolution and visualisation, while decreasing acquisition time.<sup>2</sup> 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.<sup>3</sup> In addition, we described perioperative contrast-enhanced OCT to provide functional assessment of corneal wound integrity in eyes undergoing cataract surgery.<sup>4</sup>

The enhanced visualisation achieved with contrast agents facilitates improved identification of tissue layers and allows for a more dynamic or functional OCT.<sup>3,4</sup> Intraoperative optical coherence tomography (*i*OCT) is an emerging field that uses the high-resolution cross-sectional information afforded by OCT to improve visualisation of surgical ophthalmic pathology. *i*OCT provides the surgeon with a rapid feedback on microarchitectural changes and reveals the underlying impact of surgical manoeuvres on ophthalmic tissues.<sup>5–10</sup> 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 *i*OCT into surgical practice include microscope integration, software advances, dynamic motion imaging, enhanced visualisation and development of surgical instruments.<sup>6–9</sup> Using contrast-enhanced *i*OCT may provide improved visualisation of tissue interfaces. In this report, we provide a novel description of

contrast-enhanced *i*OCT using preservative-free triamcinolone (Itrience, Alcon, Fort Worth, Texas, USA) as a contrast agent for posterior segment surgery.

## METHODS

A retrospective consecutive case series of four eyes with *i*OCT 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 *i*OCT.

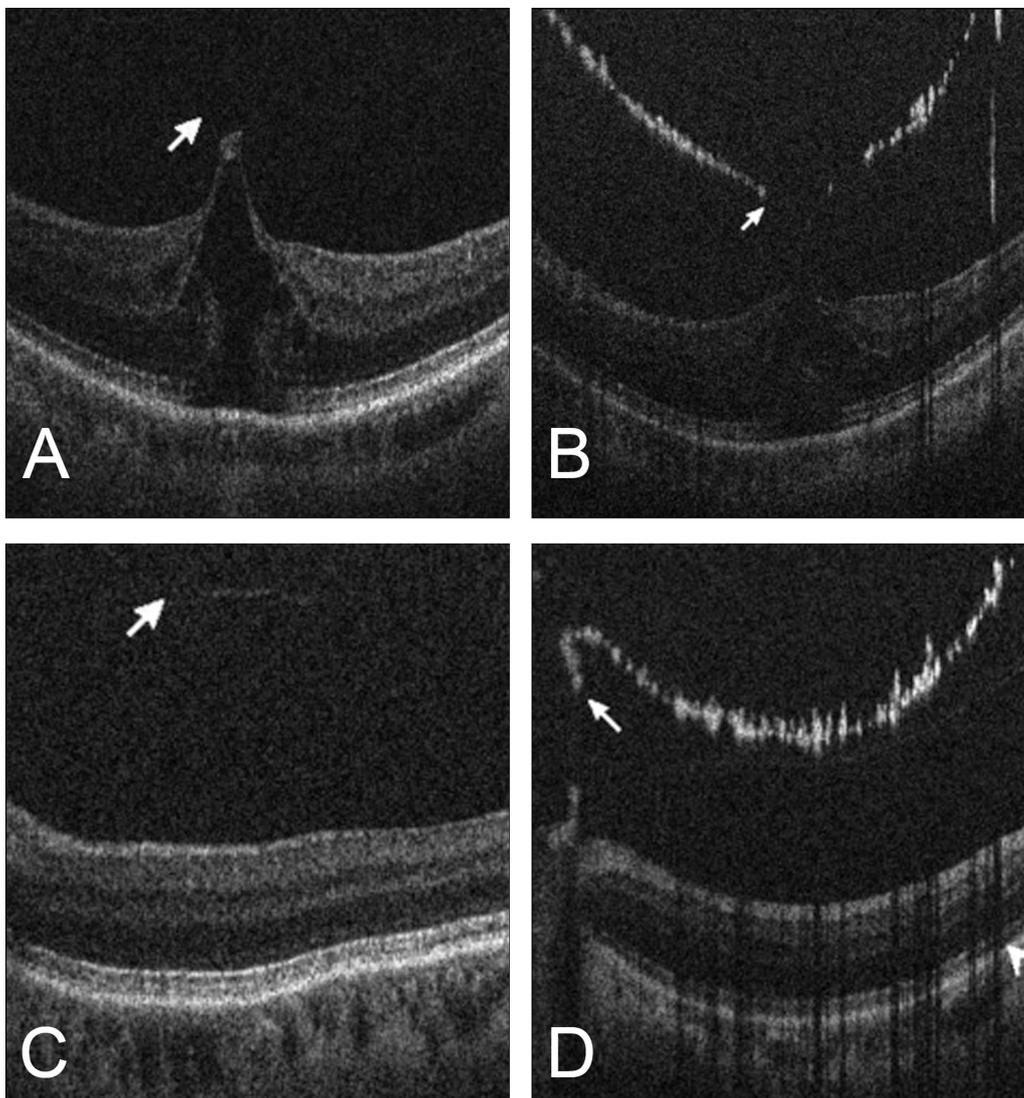
Intraoperative imaging was performed using a custom microscope-mounted *i*OCT system, using a portable SD-OCT probe (SDOIS; Bioptigen; Research Triangle Park, North Carolina, USA). A standardised imaging protocol was used with *i*OCT imaging performed at various surgical milestones as well as prior to the initial incision (eg, pre-incision). Volume scanning was performed with 10×10 mm area with 100 B-scans per area at both 0 and 90°. Pre-incision *i*OCT 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 (Itrience) was used to stain the posterior hyaloid. Following instillation of the triamcinolone, *i*OCT 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

*i*OCT 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 *i*OCT 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 *i*OCT scan was suboptimal with limited resolution of the retinal architecture. However, with the presence of the contrast agent, this subclinical abnormality

**To cite:** Ehlers JP, McNutt SA, Kaiser PK, *et al.* *Br J Ophthalmol* 2013;**97**:1384–1386.



**Figure 1** (A) Pre-contrast intraoperative optical coherence tomography (*iOCT*) B-scan showing a faintly visible hyaloid and its insertion (arrow) at the macular hole shown above. (B) Post-contrast *iOCT* B-scan showing contrast enhancement of hyaloid insertion at a macular hole (arrow). (C) Pre-contrast *iOCT* B-scan showing a faint posterior hyaloid (arrow). (D) Post-contrast *iOCT* B-scan showing the hyaloidal insertion at the optic nerve (arrow) and shadowing posterior to IVT 'granules' (arrowhead).

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).

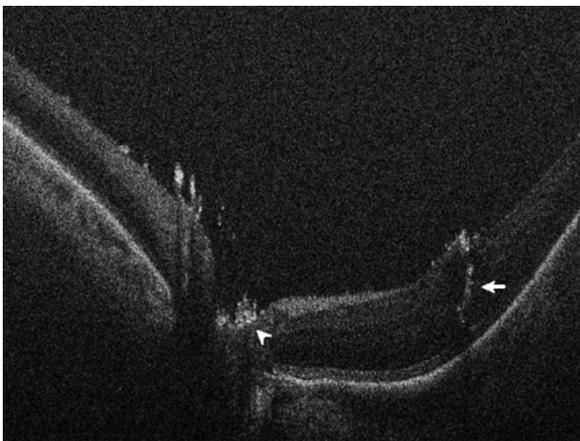
## DISCUSSION

The *in vivo* use of contrast-enhanced OCT has been limited.<sup>3 4</sup> 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 findings, 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



**Figure 2** Intraoperative optical coherence tomography B-scan following hyaloid removal revealing contrast enhancement within the retinal substance (arrow) secondary to triamcinolone. Scan is of limited quality and was unable to be improved at the time of imaging, making the resolution of retinal architecture difficult. Increased contrast and hyper-reflectivity within the retina allows the surgeon to identify the abnormality and strongly suggests the presence of an inner retinal defect with partial or full-thickness retinal hole. Note triamcinolone granules located at the optic nerve (arrowhead).

utility, resulting in a more dynamic or functional assessment tool.<sup>3 4 11</sup>

The definitive role for contrast agents in OCT remains unknown and further research is needed to better understand the role for contrast agents in *i*OCT. 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 *i*OCT is important. We have initiated a prospective study on the utility of *i*OCT 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.

**Acknowledgements** The authors thank Amit Vasani, PhD of ImagenQ for his assistance with three-dimensional reconstruction.

**Competing interests** The following competing interests may be relevant to this publication: JPE-Bioptigen (P); PKK-Carl Zeiss Meditec (C); Alcon (C); SKS-Bausch and Lomb (C); Bioptigen (P).

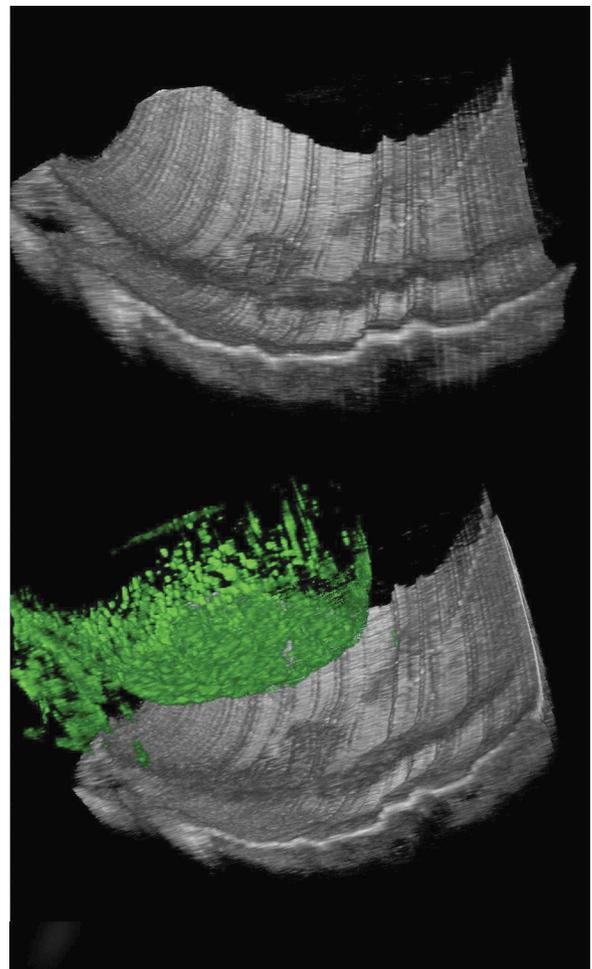
**Ethics approval** Cleveland Clinic's IRB.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** Additional images of contrast-enhanced OCT images from the eyes included in this study are available if needed.

## REFERENCES

- Huang D, Swanson EA, Lin CP, *et al.* Optical coherence tomography. *Science* 1991;254:1178–81.
- Wojtkowski M, Leitgeb R, Kowalczyk A, *et al.* In vivo human retinal imaging by Fourier domain optical coherence tomography. *J Biomed Opt* 2002;7:457–63.
- Ehlers JP, Gupta PK, Farsiu S, *et al.* Evaluation of contrast agents for enhanced visualization in optical coherence tomography. *Invest Ophthalmol Vis Sci* 2010;51:6614–19.



**Figure 3** Three-dimensional reconstruction showing pre-contrast and post-contrast-enhanced images improving visibility of the posterior hyaloid and the hyaloidal anatomy. Prior to contrast application, the posterior hyaloid is minimally visible on optical coherence tomography (upper). Following instillation of contrast agent (triamcinolone), the hyaloid is visualised clearly (lower).

- Gupta PK, Ehlers JP, Kim T. Evaluation of clear corneal wound dynamics with contrast-enhanced spectral-domain optical coherence tomography. *Ophthalmic Surg Lasers Imaging* 2012;43:222–8.
- Ehlers JP, Kernstine K, Farsiu S, *et al.* Analysis of pars plana vitrectomy for optic pit-related maculopathy with intraoperative optical coherence tomography: a possible connection with the vitreous cavity. *Arch Ophthalmol* 2011;129:1483–6.
- Ehlers JP, Tao YK, Farsiu S, *et al.* Integration of a spectral domain optical coherence tomography system into a surgical microscope for intraoperative imaging. *Invest Ophthalmol Vis Sci* 2011;52:3153–9.
- Ehlers JP, Tao YK, Farsiu S, *et al.* Visualization of real-time intraoperative maneuvers with a microscope-mounted spectral domain optical coherence tomography system. *Retina* 2013;33:232–6.
- Ray R, Baranano DE, Fortun JA, *et al.* Intraoperative microscope-mounted spectral domain optical coherence tomography for evaluation of retinal anatomy during macular surgery. *Ophthalmology* 2011;118:2212–17.
- Binder S, Falkner-Radler CI, Hauger C, *et al.* Feasibility of intrasurgical spectral-domain optical coherence tomography. *Retina* 2011;31:1332–6.
- Dayani PN, Maldonado R, Farsiu S, *et al.* Intraoperative use of handheld spectral domain optical coherence tomography imaging in macular surgery. *Retina* 2009;29:1457–68.
- Agrawal A, Huang S, Wei Haw Lin A, *et al.* Quantitative evaluation of optical coherence tomography signal enhancement with gold nanoshells. *J Biomed Opt* 2006;11:041121.



## Contrast-enhanced intraoperative optical coherence tomography

Justis P Ehlers, Stephen A McNutt, Peter K Kaiser, et al.

*Br J Ophthalmol* 2013 97: 1384-1386 originally published online April 23, 2013

doi: 10.1136/bjophthalmol-2012-303048

---

Updated information and services can be found at:

<http://bjo.bmj.com/content/97/11/1384.full.html>

---

*These include:*

### References

This article cites 11 articles, 3 of which can be accessed free at:

<http://bjo.bmj.com/content/97/11/1384.full.html#ref-list-1>

### Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

---

### Notes

---

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>