Telemedicine Follow-Up for Intravitreal Bevacizumab Injection in the Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP) Cohort

Marco H Ji 1
Natalia F Callaway 1
Margaret A Greven 2
Daniel Vail 1
Darius M Moshfeghi 1

1 Byers Eye Institute, Horngren Family Vitreoretinal Center, Department of Ophthalmology, Stanford University School of Medicine, Palo Alto, California; 2 Department of Ophthalmology, Wake Forest University School of Medicine, Winston-Salem, North Carolina

Abstract: Telemedicine has emerged as a potential solution to face the disproportion between infants that need to be screened for retinopathy of prematurity (ROP) and the lack of ophthalmologists. We evaluated its utility in the follow-up after off-label intravitreal injection of bevacizumab. None of the treated infants ended up with bad anatomic outcome. Telemedicine is an alternative safe method to monitor patients after treatment.

Keywords: pediatric retina, retina, pediatric ophthalmology

Introduction
The discrepancy between the increasing screening population and the decreasing retinopathy of prematurity (ROP) workforce has raised concerns with the feasibility of binocular indirect ophthalmoscopy for every infant and telemedicine has emerged as a potential alternative to ensure all infants receive ROP screening efficiently while utilizing limited resources. Telemedicine applied to ROP screening has demonstrated feasibility, efficacy, and non-inferiority in pilot studies, medical outreach, and randomized clinical trials. It has been evaluated by the American Academy of Ophthalmology and found to be an useful adjunct. The Joint Statement screening guidelines for ROP validated its utility in the 2013 edition and reaffirmed it in the 2018 update. Historically, telemedicine has been used to screen at-risk infants for treatment intervention. Since telemedicine have been reported to be a reliable tool to screen infants for ROP, it is also a very promising technology for follow-ups after treatment with laser or injection of anti-VEGFs. Recently, we have demonstrated that telemedicine can be used to follow patients post-laser therapy to evaluate for progression to retinal detachment. With the recent shift to anti-VEGF therapy for ROP treatment, we reviewed our experience with telemedicine monitoring of post-anti-VEGF treated patients. In contrast to laser, injection of anti-VEGFs changes the natural history of ROP and requires continued surveillance for a longer interval to detect promptly recurrences or reactivations of disease that may occur even years after injection, with the highest risk between postmenstrual age 45 to 55 weeks. Reactivations or recurrences of ROP, if untreated, may progress to tractional retinal detachment despite early regression of the disease. The growing worldwide use of off-label anti-VEGF
medications in ROP is expected to increase the already heavy burden of ophthalmologists who provide ROP care.

**Patients and Methods**
The Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP) is a community outreach telemedicine screening program for ROP in six intensive care units in northern California. Among this cohort, we investigated the baseline characteristics and follow-up data for infants who received intravitreal injection of bevacizumab (IVB). The study was conducted in accordance with the Health Insurance Portability and Accountability Act (HIPAA) and the tenets of the Declaration of Helsinki. Institutional Board Review (IRB 8752) at Stanford University School Of Medicine, which granted a waiver of consent for retrospective data analysis of the efficacy and outcomes. At our institution, IVB has been offered as treatment option for Type 1 ROP or AP-ROP in the appropriate clinical context since 2013.

**Results**
Among a total of 959 screened for ROP from November 30, 2013, to December 1, 2018, 26 infants out of 28 who presented with treatment warranted ROP (TW-ROP) underwent treatment with IVB. Among them, 7 patients were followed in clinic following treatment and discharge from the neonatal intensive care unit (NICU), whereas the remaining 19 infants were monitored with telemedicine until discharge from their respective NICU for an average of 6.83 (range 2–14) exams. The first Retcam exams were performed at a mean of 6.63 (range 1–37) days after primary injection and the last ones averaged 6.06 (range 0.86–13.57) weeks after treatment (Figure 1). At the outpatient follow-up, none of the infants treated with IVB developed bad anatomic outcome, including retinal detachment, macular fold and retrolental mass.

**Conclusion**
The unpredictable course of the disease after anti-VEGFs urges strict and long-term follow-up in these infants. Telemedicine appears likely to be a safe method to monitor infants treated with anti-VEGF medications in the short term and has the potential to provide continued ROP care in resource limited settings.
Acknowledgments
This work was supported by the Heed Ophthalmic Foundation and Michels Fellowship Foundation awarded to Natalia F. Callaway, unrestricted grant from Research to Prevent Blindness, and NEI P30-EY026877.

Disclosure
DMM has the following disclosures: consultant for Akebia, Congruence, and Praxis UNS; Scientific Advisory Board: Allergan, Allegro, Clearside; Equity: dSentz, Grand Legend Technologies, Promisight, Versl, Visunex; Steering Committee/Data Monitoring Committee: Bayer, Genentech, Regeneron, Novartis, Iconic Therapeutics; Board of Director: 1800 Contacts, dSentz, Promisight, Versl, Line, and Pr3vent. He also reports personal fees from Akebia, Bayer Pharma AG, Genentech, Novartis, Regeneron, and Shapiro Law Group, outside the submitted work; and runs the Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP) telemedicine network. NFC has the following disclosure: consultant for Genentech. The authors report no other conflicts of interest in this work.

References