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# **Reducing Intubations and Related Risks in Neonates with Retinopathy of Prematurity Undergoing Laser Photocoagulation**

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#### **Abstract**

Introduction: Although associated with respiratory morbidity, elective endotracheal intubation (ETI) for laser photocoagulation for retinopathy of prematurity (ROP) is the standard practice at our institution, with 100% of patients undergoing preoperation ETI. To mitigate this risk, we strove to reduce the percentage of infants intubated for laser photocoagulation by 30% by June 2022. Methods: We assembled a multidisciplinary team and implemented a deep sedation guideline utilizing dexmedetomidine, fentanyl, and midazolam with noninvasive ventilation support for laser photocoagulation in January 2020. Outcome, process, and balancing measures tracked the efficacy and safety of the quality improvement project. Results: We reduced the percentage of infants requiring intubation for laser photocoagulation from 100% (8/8) to 10% (1/10). We reduced the average time to return to baseline respiratory status from 224.1 to 33.8 hours (9.3d to 1.4 d). Cardiorespiratory index scores slightly increased (1 to 1.2), and pain scores remained unchanged after interventions. Conclusions: A multidisciplinary team approach using a deep sedation guideline and noninvasive ventilation can safely reduce the requirement for intubation during laser photocoagulation with a faster return to baseline respiratory status. (Pediatr Qual Saf 2025;10:e780; doi: 10.1097/pq9.000000000000000780; Published online December 24, 2024.)

**QUALITY & SAFETY** 

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Data were collected from charts and placed in a database, which can be pro-

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### INTRODUCTION

Retinopathy of prematurity (ROP), or the abnormal vascularization of the retina, is the leading cause of blindness in neonates and has an incidence of approximately 33%.1 Risk factors include gestational age, birth weight, supplemental oxygen, and mechanical ventilation.<sup>2</sup> Advancements in healthcare have led to increased survival rates of preterm infants. The factors contributing to ROP's development, such as retinal exposure to a hyperoxic environment from prolonged ventilation and low birth weight,

have increased its prevalence.<sup>1,3</sup> Laser photocoagulation is the current standard of care therapy for ROP. However, sedation practices for the procedure need to be standardized. The previous literature has argued that general anesthesia and intubation are necessary to avoid unwanted stress and pain in neonates.<sup>4</sup> Additionally, a survey of neonatologists and ophthalmologists affirmed that providers prefer general anesthesia and intubation during laser photocoagulation. 5 However, intubation and general anesthesia are not without risk, especially in preterm neonates at higher risk for chronic lung disease and apnea of prematurity. Often, these infants are on noninvasive ventilation, such as nasal cannula, continuous positive airway pressure, nasal intermittent positive pressure ventilation, or room air before

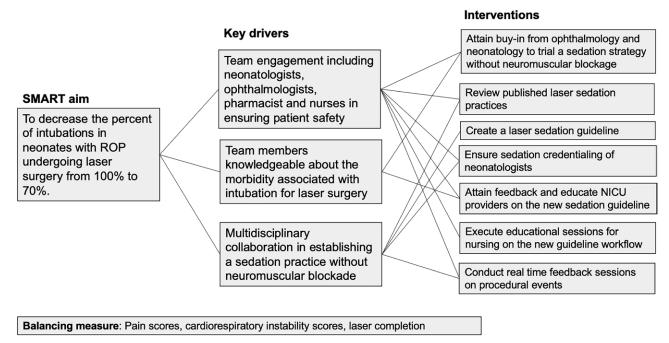


Fig. 1. Key driver diagram.

developing threshold ROP, resulting in elective intubation for laser surgery.6 This highlights the importance of balancing a safe, uninterrupted procedure with the ease of postprocedure extubation. Our group published a retrospective cohort study that evaluated the respiratory outcomes, cardiorespiratory index (CRI), and pain scores of infants treated with laser photocoagulation for ROP.6 We showed that 81.5% of infants underwent elective intubation for the procedure, with 36% requiring more than 1 intubation attempt and 18% failing extubation postoperatively.6 The average time of invasive mechanical ventilation postoperatively was  $2.46 \pm 7.13$  days, with some patients requiring steroids (40%) and racemic epinephrine (18%) to facilitate extubation. Although much progress has been made to reduce the need for intubation in preterm infants in the delivery room, 7,8 fewer studies have focused on avoiding intubation for ROP laser surgery. Medications such as ketamine, propofol, and fentanyl have demonstrated utility in avoiding general anesthesia during laser surgery, whereas nasal cannula is a suitable alternative method of respiratory support.9-11

Our quality improvement initiative aimed to reduce our level IV NICU's intubation rate for laser photocoagulation from 100% to 70% by June 2022.

#### **METHODS**

This quality improvement initiative was a pilot observational time series conducted from June 2018 to June 2022 in an academic, level IV neonatal intensive care unit (NICU). Our NICU is a 39-bed regional perinatal referral center in Philadelphia, Pa. All patients are out born, with approximately 250 admissions per year, including 40–50

patients per year with a birthweight <1000 g and 20–30 patients per year with ROP. During the study period, the electronic health record system transitioned from Cerner PowerChart to Epic. The institutional review board of Drexel University College of Medicine deemed this quality improvement study exempt. No authors had conflicts of interest.

A key driver diagram, depicted in Figure 1, was created to identify drivers and interventions for this quality initiative. Before this initiative, the standard for laser photocoagulation included endotracheal intubation (if not already on mechanical ventilation) utilizing rapid sequence intubation with atropine (0.02 mg/kg), fentanyl (2 μg/kg), and vecuronium (0.1 mg/kg). Those already intubated would receive fentanyl, midazolam, and vecuronium before the procedure. Additional doses of vecuronium, midazolam, and fentanyl were given as needed to ensure paralysis, sedation, and analgesia were maintained during the procedure. Laser surgery was performed in the NICU. Advanced practice providers, neonatal fellows, or neonatologists intubated the patient in the NICU, and neonatologists performed the sedation. Vital signs monitored during the surgery included pulse oximetry, heart rate, blood pressure, and respiratory rate. Postoperatively, patients were extubated once spontaneously breathing and were on minimum ventilator settings. Minimum ventilator settings were considered peak inspiratory pressure 15–20 cmH<sub>2</sub>0, positive end-expiratory pressure 5–6 cmH<sub>2</sub>0, rate between 20 and 30 breaths per minute, and FiO, 21%-25%.

To develop our sedation guideline, we assembled a quality improvement team that consisted of attending neonatologists, neonatology fellows,

# St Christopher's Hospital for Children NICU Retinopathy of Prematurity Laser Surgery Guideline

#### A day before laser surgery:

- o Obtain sedation consent
- o Orders (STC NICU Laser Surgery Order Set)
  - o NPO 6 hrs before the scheduled procedure
  - o Order medications as specified below to be at the bedside at least 3 hrs before the procedure
  - Order IVFs at TFL 120ml/kg/day to start 4 hrs before the procedure

#### Day of laser surgery

- o Nurse to obtain IV access 6 hrs before the procedure and start IVFs as ordered
- o 2 hrs before the procedure
  - o Initiate non-invasive respiratory support (i.e. NIPPV) —titrate to effect
  - Start sedation medications—titrate to effect (goal NPASS sedation scores -2 to -5) to ensure an adequate level of sedation prior to the procedure
  - If respiratory depression ensues, consider escalating non-invasive respiratory support or proceed with intubation

Medications *∞	Dosing
Atropine 1% ophthalmic solution*	1 drop to each eye every 12 hours for 2 doses
Cyclopentolate-phenylephrine (Cyclomydril) 0.2-1% ophthalmic solution	1 drop each eye every 5 minutes x 3 starting 30 min prior to procedure
Tetracaine 0.5% ophthalmic solution	1 drop each eye just prior to procedure
Dexmedetomidine	Bolus: 0.5 mcg/kg $\times$ 1 administered over 20 min 2 hrs before the procedure Maintenance Dosing: 0.5 – 1.5 mcg/kg/hr
	To be initiated after completion of first bolus
	Begin at 0.5 mcg/kg/hr and titrate up per MD order until desired level of sedation is achieved.
	May repeat bolus of 0.5 mcg/kg x 1 if sedation is not adequate Discontinue at end of procedure
Fentanyl	Bolus: 2 mcg/kg x 1 administered over 10 min 2 hrs before the procedure Maintenance Dosing: 2 mcg/kg/hr
	To be initiated after completion of first bolus
	May repeat bolus of 2 mcg/kg $\times$ 1 if sedation is not adequate.
	Discontinue at end of procedure
Acetaminophen	10-15mg/kg q6hrs PRN post-procedural pain
Emergency Medications (order to bedside)	
Atropine	0.2mg/kg/dose IV every 5 mins PRN for bradycardia, RSI
Vecuronium	0.1mg/kg/dose IV PRN for rigid chest, RSI
Midazolam	0.1mg/kg/dose IV PRN for sedation
Normal saline	20ml/kg bolus x1 IV PRN hypotension

<sup>\*</sup> Addition of atropine eye drops for patients with a previous history of difficult dilation RSI: rapid sequence intubation

Fig. 2. Retinopathy of prematurity laser surgery guideline. Comprehensive guideline for sedation for laser surgery in a level IV NICU.

ophthalmologists, pharmacists, nurses, and a medical student. We designed a deep sedation guideline, described in Figure 2, to prevent the need for paralysis and intubation while providing respiratory support, sedation, and pain management. This guideline was introduced via education sessions and implemented in January 2020. Dexmedetomidine (off-label use), chosen for its sedative and analgesic properties without causing respiratory depression, and fentanyl,

chosen for its analgesic and short half-life properties, were titrated for goal NPASS sedation scores of -2 to -5 while supported on noninvasive ventilation. Other medications, such as midazolam for additional sedation, vecuronium, and atropine for rapid sequence intubation, were available at the bedside as needed. Once the surgery was completed, dexmedetomidine and fentanyl infusions were discontinued. Education sessions were held again in October 2022 to disseminate modifications

to the guideline (Fig. 2) to streamline dexmedetomidine dose escalation and ensure compliance among team members.

This pilot quality initiative included infants admitted to the NICU requiring laser photocoagulation and receiving noninvasive respiratory support or in-room air. Patients already receiving invasive mechanical ventilation at the time of laser photocoagulation were excluded. Descriptive characteristics collected from the patient's EHR included demographics, maternal characteristics, gestational age, birth weight, ROP examination, and prior bevacizumab therapy. Outcome measures included the percentage of infants requiring intubation, successful completion of laser surgery, time to return to baseline respiratory status, and need for repeat lasers during hospitalization. Baseline respiratory status was defined as the prelaser respiratory support requirement (ie, none, nasal cannula, continuous positive airway pressure, or nasal intermittent positive pressure ventilation settings). Process measures included adherence to guidelines and percent with sedation consent. The balancing measures—pain scores (0-10) and CRI scores (see Supplemental Material 1, http://links.lww. com/PQ9/A616) were tracked. Outcome and balancing measures were tracked utilizing QI Macros 2021 statistical process control charts. The center line was adjusted with eight or more consecutive points above or below the

mean. Pre- and postintervention data were analyzed utilizing SPSS version 26.

#### RESULTS

Twenty-three infants required laser photocoagulation during this initiative. After excluding infants already intubated (n = 5), the pilot program evaluated 8 patients in the preintervention group and 10 in the postintervention group. The pre- and postintervention groups were similar in gestation age, birthweight, gender, history of placental chorioamnionitis, and ROP severity (Table 1). More patients in the preintervention group received antenatal steroids compared with the postintervention group (100% versus 60%, P = 0.015).

After the implementation of the sedation guideline, we reduced the proportion of patients requiring intubation for laser from 100% to 10% (P < 0.001), median extubation attempts (1 [1, 1.75] to 0 [0, 0], P < 0.001), and median duration of intubation after laser (22.5 h [16.3, 60.3] to 0 h [0, 0], P = 0.002, Table 2). There was no statistically significant difference in length of stay between groups.

Regarding our outcome measures, we demonstrated special cause variation with a reduction in the average time to return to baseline respiratory status from 224.1 to 33.8 h

Table 1. Group Characteristics

	Preintervention (n = 8)	Postintervention (n = 10)	P
Gestation age (median [IQR], wk)	25.1 [23.8, 27]	24.6 [24.1, 24.6]	0.31
Birth weight (median [IQR], g)	682 [595, 885]	578 [463, 707]	0.083
Postnatal age at laser (median [IQR], wk)	38.8 [35.1, 42.6]	39.1 [38.4, 43.3]	0.620
Postnatal weight at laser (median [IQR], g)	2428 [2300, 2922]	2348 [2308, 2767]	0.902
Gender (female, %)	5 (62.5)	4 (40)	0.637
Hispanic (%)	Ò (O)	4 (40)	0.092
Small for gestational age (%)	1 (12.5)	3 (30)	0.588
Delivery room intubation (%)	5 (62.5)	8 (10Ó)	0.069
Pregnancy-induced hypertension (%)	1 (12.5)	5 (50)	0.152
Placental chorioamnionitis (%)	2 (25)	0 (0)	0.183
Maternal antibiotics (%)	5 (62.5)	4 (40)	0.637
Antenatal steroid (%)	8 (100)	6 (60)	0.015*
C-section (%)	5 (62.5)	7 (70)	1.0
Most severe ROP Examination			0.352
Stage 1	1 (12.5)	0 (0)	
Stage 2	5 (62.5)	5 (50)	
Stage 3	2 (25)	5 (50)	
Bevacuzimab (%)	4 (50)	2 (20)	0.321

<sup>\*</sup>P value < 0.05 is statistically significant.

IQR, interquartile range.

Table 2. Respiratory Outcomes between Groups

	Preintervention (n = 8)	Postintervention (n = 10)	P value
Prelaser respiratory status			0.120
Room air, n (%)	5 (62.5)	3 (30)	
Nasal cannula, n (%)	1 (12.5)	6 (60)	
CPAP/NIPPV, n (%)	2 (25)	1 (10)	
Intubated for laser, n (%)	8 (100)	1 (10)	<0.001*
Prelaser intubation attempts, median [IQR]	1 [1, 3]	0 [0, 0]	<0.001*
Postlaser extubation attempts, median [IQR]	1 [1, 1.75]	0 [0, 0] 0 [0, 0]	<0.001*
Total duration of intubation after laser (median [IQR], h)	22.5 [16.3, 60.3]	0 [0,0]	0.002*
Laser completed	8 (100)	10 (100)	1.0
Length of stay (median [IQR], d)	153 [99, 163]	106 [81, 128]	0.122

<sup>\*</sup>P value < 0.05 is statistically significant.

CPAP, continuous positive pressure ventilation; IQR, interquartile range; NIPPV, noninvasive positive pressure ventilation.

(9.3 to 1.4 d, Fig. 3). Only one patient in the postintervention group required intubation. A review of this case revealed nonadherence to the pilot sedation guideline due to delay in sedation and analgesia infusions and the inability to achieve goal sedation by the time of the procedure. Subsequent fentanyl and dexmedetomidine boluses to achieve the desired sedation led to bradycardia, resulting in elective intubation. With all (100%) laser procedures completed, all patients postguideline had sedation consent, 90% (9/10) of the cases adhered to the sedation guideline, and 1 (10%) case needed repeat laser during hospitalization.

Regarding our balancing measures, special cause variation in CRI scores slightly increased after the pilot sedation intervention from 1 to 1.2 (Fig. 4A). It is important to note that such an increase is not clinically significant as one represents no change from baseline and two mild instability. The most common reason for an increase in CRI score was the increase in FiO<sub>2</sub> during the procedure and the one patient described above who had bradycardia requiring intubation. Pain scores did not change throughout the initiative (Fig. 4B). The specific duration of the laser procedure was not documented in the electronic medical record.

#### **DISCUSSION**

This pilot quality improvement initiative utilizing a sedation guideline with noninvasive respiratory support safely reduced intubation frequency during ROP laser photocoagulation in a level IV NICU by 90%. This initiative promoted a faster return to baseline respiratory status than

prior practice without compromising the completion of laser photocoagulation.

Decreasing the need for intubation and excessive sedation is essential in avoiding the complications reported from general anesthesia with ETI during laser photocoagulation, such as intraoperative hypotension, postextubation apnea, and prolonged postprocedure mechanical ventilation. <sup>6,12</sup> Thus, by avoiding neuromuscular blockade and intubation, our sedation guideline mitigates unnecessary respiratory morbidity infants may experience related to this surgery. To our knowledge, this quality improvement initiative is one of the first to report an efficacious intravenous sedation and analgesia technique that provides noninvasive respiratory support with quantitative evidence of pain control and minimal cardiorespiratory instability during ROP surgery.

The available literature on sedation strategies for laser photocoagulation is limited. Most recently, Yang et al<sup>13</sup> conducted a 12-year retrospective case series where infants received phenobarbitone 10 mg/kg and diazepam 0.25–0.49 mg/kg for sedation and proparacaine eye drops for topical anesthesia. This series reported a large cohort of 364 infants managed with intravenous sedation and solely topical (ocular) analgesia for laser photocoagulation without intubation. Of note, this study excluded pain scores, and 11.8% of patients had intraoperative bradycardia, which required positive pressure ventilation. Although some research investigated topical anesthesia as an alternative to intravenous analgesia and sedation, <sup>14</sup> it is associated with more extended procedure length (approximately

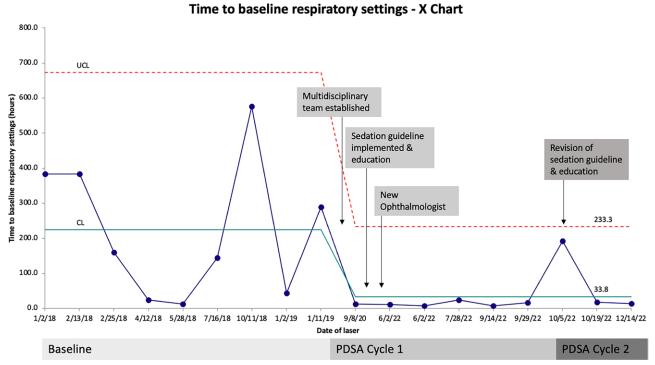
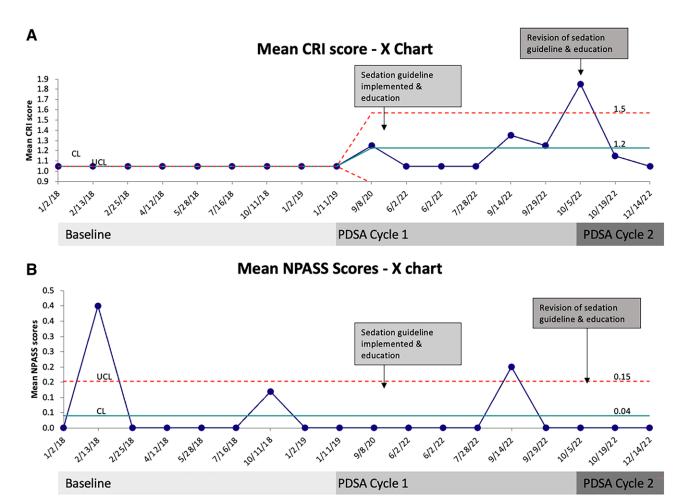


Fig. 3. X-chart time to return to baseline respiratory status after laser surgery. After interventions, there was a special cause variation in time to return to baseline respiratory status. Data point October 5, 2022, was the only infant requiring intubation in the sedation group. CL, center line; LCL, lower control limit; PDSA, plan-do-study-act; UCL, upper control limit.



**Fig. 4.** Balancing measures. A, The x-chart shows a special cause variation in the mean CRI scores, with a slight increase after interventions. Data point October 5, 2022 reflects an infant requiring intubation. B, X-charts show mean NPASS scores that did not change other than two patients in the baseline period and one after interventions. CL, center line; LCL, lower control limit; PDSA, plan-do-study-act; UCL, upper control limit.

12-16 min) and greater postoperative cardiorespiratory instability requiring resuscitation.<sup>15</sup> Our initiative included intravenous sedation and analgesia with off-label use of dexmedetomidine and fentanyl infusions to maximize the short-acting properties of these medications, and ocular analgesia with tetracaine. Although we did not obtain data on surgery duration, the combination of sedation and analgesia in our guideline was effective in minimizing pain scores without resulting in clinically significant cardiorespiratory instability. It is important to note that the Food and Drug Administration has approved dexmedetomidine for sedation of nonintubated adult patients before and during surgical or other procedures; however, at the time of this report, there are no approved pediatric indications for use. Piersigilli et al9 reduced intubation for laser surgery with the use of propofol and fentanyl. Their respiratory support consisted of a laryngeal mask and flow-inflating resuscitation bag.9 Our initiative used a nasal cannula to deliver consistent, noninvasive positive pressure ventilation without an advanced airway device.

The most important strength of this initiative was the avoidance of intubation in 90% of the patients in the postintervention period. Additionally, this bedside guideline facilitated the ability to maintain patients in the NICU for the bedside procedure, which can benefit institutions that otherwise perform laser surgery in the operating room.

Significant limitations to this study include its applicability to other NICUs, as our institution's NICU is a tertiary care center with specialized services such as dedicated NICU pharmacists, nurse educators, and team members who facilitated the implementation of our new sedation guideline. Additionally, this guideline requires additional care, time, and preparation, as medication administration starts several hours before the procedure. The feasibility and efficiency of this workflow relied on a coordinated, multidisciplinary team. Such consideration is essential for the project's scalability, as larger cohorts or expansive studies require more time and coordination between care members.

Another limitation is the sample size. Although there were no differences between groups, the sample size was limited by the incidence of ROP requiring transfer for laser therapy to our institution. Additionally, as a small pilot study, it is limited by its generalizability and would benefit from a more extensive, randomized study to appropriately demonstrate superiority to other means of sedation. A small sample size also raises the concern that providers may need to be well-practiced or exposed to the procedure and guidelines, which may introduce bias and practice variability. To address this concern, neonatologists attended educational sessions and didactics on the sedation guidelines and strategies for troubleshooting with nursing. This fact does highlight the need for continued in-service training and the importance of key stakeholders in promoting guideline compliance. This initiative did not address the cost nor savings attained with this change in practice; however, it demonstrated a decrease in morbidity in infants requiring laser photocoagulation. Other possible applications of this sedation guideline include complex or lengthy imaging studies requiring minimal motion artifacts rather than resorting to intubation.

In conclusion, our pilot quality improvement initiative showed a sedation guideline with noninvasive respiratory support reduced intubations in infants requiring ROP laser photocoagulation. With regularly scheduled education and multidisciplinary collaboration, this sedation guideline has the potential to be sustainable and integrated into other tertiary care NICUs. This initiative catalyzes the need to refine our sedation strategies to prevent intubation and promote safety during ROP surgery while minimizing sedative and analgesia procedural exposure and postoperative complications.

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