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Title: Adverse Events in Radiation Oncology: A Case Series from Wake Up Safe, the Pediatric Anesthesia Quality Improvement Initiative

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- **What is already known:** Radiation therapy in pediatric patients often requires anesthesia and, while generally safe, poses environmental challenges. Monitoring must be done remotely to limit radiation exposure to providers, patients are immobilized in masks or frames, and care is often delivered in distant locations.
- **What this article adds:** Based on the adverse events described, measures that may systematically reduce risks include: (1) double check of infusion pumps and use of cameras to visualize infusions; (2) continuous monitoring, including during transport; (3) consideration of

alternatives to succinylcholine when feasible; and (4) particular vigilance to maintain airway patency when radiation masks or frames are used.

Abstract

Background: Radiation therapy in pediatric patients often requires anesthesia and poses environmental challenges. Monitoring must be done remotely to limit radiation exposure to the provider. Airway access can be limited by masks or frames. Care is often delivered in relatively inaccessible locations in the hospital. While individual institutions have reported their outcomes, this case series aims to review a multicenter registry of significant adverse events (SAE) and make recommendations for improved care.
Methods: Wake Up Safe: The Pediatric Quality Improvement Initiative maintains a multi-site, voluntary registry of pediatric peri-anesthetic SAE. This was queried for reports from radiation oncology from January 1, 2010 to May 10, 2018. The database contained 3,379 SAE from approximately 3.3 million anesthetics. All 33 institutions submitted data on a standardized form (Supplemental Appendix 1) to a central data repository (Axio Research, Seattle Washington). Prior to each SAE case submission, three anesthesiologists who were not involved in the event analyzed the event using a standardized root cause analysis method to identify the causal or contributing factor(s).
Results: Six SAE were identified. In three, incorrect programming of a propofol infusion resulted in overdose. In case one, the 3 year old female became hypotensive, requiring vasopressors and volume resuscitation. In the second, the 2 year old female experienced airway obstruction and apnea resquiring chin lift. In case three, the child suffered no consequences despite a noted overdose of propofol infusion. In case four, a 2 year old female with recent respiratory infection suffered laryngospasm during an unmonitored transport to the recovery area. She developed profound oxygen desaturation with bradycardia treated with succinylcholine and chest compressions. In case five, a 6 year old former premature child suffered laryngospasm at the conclusion of mask creation under general anesthesia with a laryngeal mask airway. The radiation mask delayed recognition of copious secretions. Finally, in case six, a 6 year old undergoing stereotactic radiosurgery in a head halo suffered bronchospasm and unintended extubation during therapy which required multiple attempts at re-inbuation by multiple providers ultimately requiring cancellation of the treatment and transport to the intensive care unit.
Conclusions: There were few radiation oncology SAE, but analysis has led to the identification of several specific opportunities for improvement in pediatric anesthesia for radiation oncology.
Keywords: Radiation Oncology, Child, Anesthesia, Quality Improvement, Retrospective Studies, Medication Errors, Airway Obstruction

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Introduction:

Radiation therapy in pediatric patients may require anesthesia, which can provide unique challenges to the pediatric anesthesia provider. Care is often provided in isolated locations in the hospital, limiting availability of additional staff and resources. Furthermore, the recognition and treatment of a

patient's clinical status may be delayed due to remote monitoring and safety barriers to prevent radiation exposure to care team members.

Anesthetic practice has evolved for radiation oncology cases from ketamine based sedation[1] or inhalation techniques[2] to propofol based sedation.[3] Individual case reports[4] and institutions[1-3,5-13] have reported their outcomes, including rates of respiratory and other complications, to be similar to outcomes for other sedation cases performed out of an operating room.[14] No multi-institutional safety studies were found in our literature search.

In this case series, we reviewed all significant adverse events (SAE) reported to the Wake Up Safe database and found six cases occurring in radiation oncology. Wake Up Safe: The Pediatric Anesthesia Quality Improvement Initiative is a multi-site voluntary registry of pediatric peri-anesthetic SAE. In 2006, the Quality and Safety Committee of the Society for Pediatric Anesthesia initiated a quality improvement project for the specialty of pediatric anesthesiology that ultimately resulted in the development of Wake Up Safe, a patient safety organization that maintains a national registry of de-identified serious adverse events.[15,16] The ultimate goal of Wake Up Safe is to implement changes in processes of care that improve the quality and safety of anesthetic care provided to pediatric patients nationwide. Reporting of this case series is aimed to describe SAE that occurred during pediatric anesthetics provided in the unusual environment of radiation oncology and provide recommendations for improved care.

Methods:

Member institutions of Wake Up Safe submit quarterly data regarding the types and numbers of anesthetics performed, including ASA physical status, surgical billing codes, age and gender for all cases at their institution. They also submit more detailed, though deidentified, case information pertaining to specific SAE as defined by Wake Up Safe guidelines.[17] Supplemental appendix 1 lists the specific questions for each type of event and possible responses. The original anesthetic records are not submitted. In designing the forms, Wake Up Safe sought to balance data capture with data entry burden for practicing anesthsiologists.

Prior to each case submission, 3 anesthesiologists from the reporting institution who were not involved in the event analyze the event using a standardized root cause analysis method to identify the causal or contributing factor(s).[18] Representatives from each member institution received education on root cause analysis methodology prior to participation in an effort to standardize case evaluation across sites.

For the purpose of this case series, the database was queried for all events reported between January 1, 2010 and May 10, 2018 to identify all SAE that occurred in children (≤18 years of age) in the radiation oncology setting or during transport to the post anesthesia care unit (PACU) from radiation oncology. All reported data were extracted, including: demographics, comorbid conditions, reported

contributors to the significant adverse events (primary and secondary), management details and outcomes, including survival and extent of harm. Narrative data were edited for typographical errors, brevity and clarity.

While quarterly data regarding the number and types of anesthetics performed at each institution are reported, the use of a generic "anesthesia for other radiologic procedures" billing code for services provided in radiation oncology made it impossible to consistently separate these anesthetics. We have reported the numbers of anesthetics that had a clearly identifiable radiation oncology billing code, but expect this to be a signficant underestimate.

Results:

The Wake Up Safe database contained 3,379 adverse events from 3.35 million anesthetics at 33 institutions as of May 10, 2018. The data query yielded six SAE on six different patients, described in table 1. A total of 48,578 cases included a radiation oncology billing code for an incidence of approximately 1/8000. This may be an overestimate as generic billing codes such as "Anesthesia for other radiologic procedure" were present in place of radiation oncology codes for some of the reported SAE. For each of the SAE, while there are many details available (see Supplemental Appendix 1), the standardized forms does not capture all the granular details present in an anesthetic record. We do not have access to the vital signs, specific timing of interventions, et cetera.

Consistent with the outpatient nature of most radiation therapy, all events occurred on weekdays during normal hours. There were no handovers associated with these events. Harm in all cases was limited to no harm or additional treatment, with no reported permanent consequences. All cases reported anesthesia as the primary cause of the event.

In the first case, unrecognized incorrect programming by a trainee of a propofol infusion resulted in overdose. This was recognized when the infusion pump alarmed audibly that the syringe was almost empty. The 3 year old female became hypotensive, requiring ephedrine and fluid bolus.

In the second case, the propofol infusion was entered by a trainee in milligrams per kilogram per minute instead of micrograms per kilogram per minute, resulting in overdose. This error was recognized when the 2 year old patient became apneic. The airway obstruction responded to chin lift and nasal cannula oxygen while a fluid bolus was also administered.

In the third case, an anesthesiologist providing care directly programmed the infusion pump for micrograms per kilogram per hour instead of the intended micrograms per kilogram per minute. This was not recognized until the case was complete, but did not result in any harm to the patient.

In case four, a 2 year old female with recent respiratory infection suffered laryngospasm during an unmonitored transport. This was recognized when the patient appeared "dusky." Succinylcholine and positive pressure ventilation were administered during transport, but this progressed to profound

desaturation. Upon application of monitors in the post anesthesia care unit, she was bradycardic. Approximately 30 seconds of chest compressions were performed. She was intubated and rapidly recovered. She was extubated in the recovery area and admitted to intensive care for observation. While in the ICU, she had mild stridor treated with dexamethasone.

In case five, a 6 year old former premature child suffered laryngospasm at the conclusion of computed tomography simulation in radiation oncology under general anesthesia with a laryngeal mask airway. When the radiation mask was removed at the end of the procedure, copious secretions were seen and thought to have triggered his airway reflexes. The laryngeal mask airway was removed, succinylcholine was given, the patient was intubated and transported to intensive care.

In case six, a 6 year old undergoing stereotactic radiosurgery in radiation oncology in a head halo suffered bronchospasm and unintended extubation during therapy. Initially, wheezing was heard and the tape securing the endotracheal tube was noted to be peeling. The “usual device” for securing the endotracheal tube was missing that day. Multiple direct laryngoscopies by the nurse anesthetist and anesthesiologist appeared to show the endotracheal tube in position, but the halo frame was impeding visualization. This proceeded to loss of end tidal carbon dioxide and bradycardic cardiac arrest. Epinephrine was administered both intravenously and via endotracheal tube. Repeat direct laryngoscopy by another anesthesiologist with the frame removed showed that the tube was in the esophagus. The patient was reintubated and rapidly recovered. The case was cancelled, and the patient transported to intensive care, waking there without apparent deficits.

Discussion:

There were few radiation oncology SAE in the Wake Up Safe database, but these allowed recognition of possible preventive measures. While the nature of these events (3 respiratory SAE and 3 medication errors) are consistent with the overall WUS data,[19] the unique environment associated with administering pediatric anesthetics for radiation oncology contributed to all events in this series.

In the first three cases, remote monitoring of the patient and equipment via camera with poor lighting may have impaired prompt recognition of drug administration errors. In case four, the prolonged transport from the treatment room to recovery area of an unmonitored patient affected prompt detection and treatment of laryngospasm. Though hypoxemia is the most likely cause of bradycardia in this patient, it is possible the patient developed hyperkalemia from administration of succinylcholine. Radiation therapy as a risk factor for hyperkalemic response to succinylcholine has been previously described in a human case report[20] and animal data,[21] but no electrolyte or electrocardiographic information were reported to confirm this. In the fifth case, the process of making a facial mask to prevent head movement during treatment made airway management more challenging. In similar manner, the halo used for stereotactic radiosurgery impaired airway management in the last case.

This case series highlights potential safety concerns for providing anesthesia services in radiation oncology. To prevent the medication errors, previously published recommendations regarding medication infusions,[19] such as two provider checks, intelligent pumps and bar coding should be implemented. Particular to the radiation oncology environment, remote monitoring cameras should also adequately visualize the infusion pumps. Continuous monitoring of oxygenation and/or ventilation throughout anesthetic care including during transport with portable monitors, as well as the availability of a nearby recovery area may mitigate the risk of transporting an anesthetized patient. Finally, airway patency and access may be impeded in the presence of radiation halos and masks. Consideration should be given to having additional help and airway equipment such as fiberoptic or video laryngoscopes available. Removal of the halo or mask should also be implemented early as this will require some time to accomplish.

The voluntary, multi-center nature of the database used in this study posed the potential for selection and reporting biases. In particular, the literature reported a significant incidence (>3%) of line sepsis,[10] but none were reported here. The data reported were limited such that important information such as laboratory results, timing of vasoactives, nadir oxygen saturation, et cetera were unobtainable. Erroneous data entry is also a concern. The use of a generic billing code may have resulted in undercounting of the number of anesthetics in radiation oncology. This likely resulted in an overestimate of the incidence of SAE and precluded a comprehensive analysis of factors systematically associated with significant adverse events. Furthermore, despite centralized training, specific guidelines and definitions, root cause analyses methodology may have differed between institutions. These data must therefore be interpreted with caution.

In conclusion, there were few radiation oncology SAE identified in the Wake Up Safe database, but these exposed opportunities for quality improvement particular to this environment. In particular, routine use of remote camera monitoring of infusion pumps during therapy would detect problems. Monitoring during transport to recovery and avoidance of succinylcholine should also be considered. Lastly, airway patency and access may be impaired by radiation masks and halos, so early removal of these devices in the event of airway compromise should be planned.

Ethical Approval: Although each institution received individual institutional review board approval prior to data submission to Wake Up Safe, this study of the de-identified data was deemed not regulated by the institutional review board at the University of Michigan and the requirement for informed consent was waived.

Financial Disclosures: This research was carried out without funding.

Conflicts of Interest: None

References:

1. Lo JN, Buckley JJ, Kim TH, Lopez R. Anesthesia for high-dose total body irradiation in children. Anesthesiology 1984;61:101-3.
2. Casey WF, Price V, Smith HS. Anaesthesia and Monitoring for Paediatric Radiotherapy. J R Soc Med 1986;79:454-6.
3. Anghelescu DL, Burgoyne LL, Liu W, et al. Safe anesthesia for radiotherapy in pediatric oncology: St. Jude Children's Research Hospital Experience, 2004-2006. Int J Radiat Oncol Biol Phys 2008;71:491-7.
4. Davies DJ. Anesthesia and monitoring for pediatric radiation therapy. Anesthesiology 1986;64:406-7.
5. Weiss M, Frei M, Buehrer S, Feurer R, Goitein G, Timmermann B. Deep propofol sedation for vacuum-assisted bite-block immobilization in children undergoing proton radiation therapy of cranial tumors. Paediatr Anaesth 2007;17:867-73.
6. Stokes MA, Soriano SG, Tarbell NJ, et al. Anesthesia for Stereotactic Radiosurgery in Children. J Neurosurg Anesthesiol 1995;7:100-8.
7. Fortney JT, Halperin EC, Hertz CM, Schulman SR. Anesthesia for pediatric external beam radiation therapy. Int J Radiat Oncol Biol Phys 1999;44:587-91.
8. Seiler G, De Vol E, Khafaga Y, et al. Evaluation of the safety and efficacy of repeated sedations for the radiotherapy of young children with cancer: a prospective study of 1033 consecutive sedations. Int J Radiat Oncol Biol Phys 2001;49:771-83.
9. Buchsbaum JC, McMullen KP, Douglas JG, et al. Repetitive pediatric anesthesia in a non-hospital setting. Int J Radiat Oncol Biol Phys 2013;85:1296-300.
10. Bratton J, Johnstone PAS, McMullen KP. Outpatient management of vascular access devices in children receiving radiotherapy: Complications and morbidity. Pediatr Blood Cancer 2014;61:499-501.
11. Owusu-Agyemang P, Grosshans D, Arunkumar R, et al. Non-invasive anesthesia for children undergoing proton radiation therapy. Radiother Oncol 2014;111:30-4.
12. Anghelescu DL, Rakes LC, Shearer JR, Bikhazi GB. Prevention of emergence agitation in seven children receiving low-dose ketamine and propofol total intravenous anesthesia. AANA J 2011;79:238-42.
13. Khurmi N, Patel P, Koushik S, Daniels T, Kraus M. Anesthesia Practice in Pediatric Radiation Oncology: Mayo Clinic Arizona's Experience 2014–2016. Paediatr Drugs 2018;20(1):89-95.
14. Cravero JP, Beach ML, Blike GT, Gallagher SM, Hertzog JH. The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium. Anesth Analg 2009;108:795-804.
15. Buck D, Kreeger R, Spaeth J. Case Discussion and Root Cause Analysis: Bupivacaine Overdose in an Infant Leading to Ventricular Tachycardia. Anesth Analg 2014;119:137-40.
16. Rampersad S, Rossi MG, Yarnell C, Uejima T. Wrong Site Frenulectomy in a Child: A Serious Safety Event. Anesth Analg 2014;119:141-4.

17. Williams GD, Muffly MK, Mendoza JM, Wixson N, Leong K, Claure RE. Reporting of Perioperative Adverse Events by Pediatric Anesthesiologists at a Tertiary Children's Hospital: Targeted Interventions to Increase the Rate of Reporting. Anesth Analg 2017;125(5):1515-1523.
18. Tjia I, Rampersad S, Varughese A, et al. Wake Up Safe and root cause analysis: quality improvement in pediatric anesthesia. Anesth Analg 2014;119:122-36.
19. Lobaugh LMY, Martin LD, Schleelein LE, Tyler DC, Litman RS. Medication Errors in Pediatric Anesthesia: A Report From the Wake Up Safe Quality Improvement Initiative. Anesth Analg 2017;125:936-42.
20. Holak EJ, Connelly JF, Pagel PS. Suxamethonium-induced hyperkalaemia 6 weeks after chemoradiotherapy in a patient with rectal carcinoma. Br J Anaesth 2007;98:766-8.
21. Cairoli VJ, Ivankovich AD, Vucicevic D, Patel K. Succinylcholine-induced hyperkalemia in the rat following radiation injury to muscle. Anesth Analg 1982;61:83-6.

Case	Adverse Event(s)	Narrative	Providers	Primary Cause	Contributing Cause(s)
1	Propofol overdose	3 year old ASA[1] 3 female undergoing radiation therapy for adrenal cancer with natural airway and propofol infusion received 150mg of propofol in 3 minutes from a pump programmed incorrectly by student nurse anesthetist. Recognized when pump alarmed almost empty. Hypotension treated with ephedrine and fluid bolus.	Anesthesiologist covering 2 sites and student nurse anesthetist	Technical error	Equipment misuse
2	Propofol overdose	2 year old ASA[1] 2 female undergoing radiation therapy for adrenal cancer with natural airway and propofol infusion received a propofol overdose from a pump programmed for mg/kg/min instead of mcg/kg/min. Recognized when patient became apneic. Treated with chin lift, nasal cannula oxygen and fluid bolus.	Anesthesiologist covering 2 sites and anesthesiology resident	Haste and Inattention	Lighting too low, equipment misuse
3	Propofol underdose	2 year old ASA[1] 2 male undergoing radiation therapy for unclear indication[2] with natural airway and propofol infusion received an underdose of propofol as pump was programmed for mcg/kg/hr instead of mcg/kg/min. No apparent harm.	Anesthesiologist alone	Clinical equipment or Tool Related Factors: Misuse by provider (technical)	None reported.
4	Laryngospasm	2 year old ASA[1] 4 female undergoing radiation	Anesthesiologist	Failure to	None reported

[1] ASA=American Society of Anesthesiologists Physical Status
[2] Reported billing code was dual role transvestism, a likely data entry error.

	to cardiac arrest	therapy for anaplastic ependymoma with natural airway and propofol infusion. En route to recovery, started to look dusky and was found to be in laryngospasm. Was given positive pressure ventilation and succinylcholine. When placed back on the monitor she was bradycardic and received chest compressions for about 30 seconds. She was intubated and given albuterol. She was eventually extubated and sent to intensive care. She had mild stridor and was given dexamethasone.	covering 1 site and nurse anesthetist	obtain or act on available information	
5	Laryngospasm and bronchospasm	6 year old ASA[1] 3 female for computed tomography simulation for brain tumor with LMA.[3] At the end, simulation mask removed and patient had copious clear secretions. Patient coughed and ventilation was difficult, LMA[2] removed. Oral airway placed and 2 person mask ventilation started. Succinylcholine given. Decision made to intubate. ETT[4] placed. Albuterol given and tube suctioned. Admitted to intensive care.	Anesthesiologist alone with rapid response team called for help.	Patient Disease	None reported
6	Bronchospasm, unintended extubation to cardiac arrest	6 year old ASA[1] 3 male for radiosurgery of brain tumor in head frame. Nurse noted pulling on circuit and tape peeling off face. Team went in after radiation powered down. Wheezing heard, albuterol given chest rise noted. Direct laryngoscopy by nurse	Anesthesiologist covering 1 site and nurse anesthetist with additional	Failure to obtain or act on available information	Interpersonal conflict, Crowding (Lack of space)

[3] LMA=Laryngeal Mask Airway
[4] ETT=Endotracheal tube

		anesthetist noted ETT[3] through cords. End tidal carbon dioxide lost. Laryngoscopy by attending showed ETT[3] through cords but head frame hindering view. Help called, frame removed, bradycardia arrest. Epinephrine through ETT[3] and intravenous, other anesthesiologist laryngoscopy with frame off, ETT[3] in esophagus. Reintubated with rapid improvement in saturation and return of pulse. 1.5 minutes chest compressions. Admitted to intensive care.Woke up hour later with no deficits. Noted that usual device to secure ett to prevent pulling was missing that day.	anesthesiologist called for help.		