Asleep or Awake
Rethinking "Safety"

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The article by Taenzer et al[1] in this issue of *Regional Anesthesia and Pain Medicine* provides important information concerning the management of pediatric patients undergoing regional anesthesia, prompting us to grapple with the critical question of safety in anesthesia. Although the study strongly supports the fact that performing a block in an anesthetized child is certainly not unsafe, it encourages us to consider these findings in a broader context: The word "safety" refers, of course, to "safety of the patient," but as human beings, we cannot deny that we constantly consider our own safety, too, especially from a medicolegal point of view. Even the term "patient safety" is ambiguous. All regional anesthetic procedures require the injection of a local anesthetic in the vicinity of sensory nerve fibers, either enclosed in a nerve trunk, a plexus, or near the spinal cord, and this needle puncture necessarily produces some degree of tissue damage and, for those fearing needle punctures, may elicit adverse reactions. Furthermore, concerns about safety apply not only to "histological" lesions but also to emotional lesions. Is the occurrence of long-lasting nightmares, phobias, or occasionally the development of psychiatric disorders resulting from the fear of needles, a minor issue if the technique does not result in any observable anatomical lesions? Neurological lesions, especially paraplegia, are unacceptable, and all possible precautions should be taken to avoid such consequences, but what exactly are "all possible precautions"?

Since the end of the 20th century, we have come to believe that evidence-based medicine is the way forward. The individual perception of sound decisions is no longer deemed appropriate, and good practice should be evaluated in large cohorts of patients who are treated in as much the same way as possible. Even with its limitations, evidence-based medicine undoubtedly represents a considerable improvement in evaluating our practice and promoting safety, but it is most fruitful for events occurring frequently, for which well-designed studies involving a rather limited number of patients allow definitive conclusions concerning safety of management. For rare and extremely rare events, definitive statements about the "safest technique" will never be possible due to the needed size of the study population. This is particularly true regarding the eternally asked question about the safety of block procedures performed in fully awake, sedated, or truly anesthetized patients, especially pediatric patients. Still, in 1996 Giaufré et al[2] published a multi-institutional prospective study on 85,412 pediatric anesthetics of which 24,409 involved a regional block, more than 90% of which were performed in fully anesthetized infants and children. This study reported an extremely low rate of complications, all minor and short-lasting. In 2003, Horlocker et al[3] reported epidural catheter placement in 4298 fully anesthetized patients undergoing thoracic surgery with no neurological complication. Of course, the population size of these studies is not sufficient to definitively exclude any potential harm, especially if we are examining neurological complications, due to techniques performed in unresponsive patients. Nevertheless, these numbers are reassuring given that the risk is less than 1 in more than 25,000 patients. The outstanding multicentric study of Taenzer et al[1] in this issue now suggests that the potential for such a risk, if any, is considerably less.

We cannot state that no harm will ever occur to a patient in this situation, but we can assert, looking at the scientific data currently available and given new evidence from Taenzer et al, that performing a block procedure in an anesthetized child is not unsafe. This point is very important. We must also ask if it is always safe to perform a regional block in an awake patient. The answer is clearly negative, given the number of published case reports of complications and the existence of a constant rate of minor or major neurological complications. Evidence-based medicine shows that, generally speaking, neither of the 2 strategies is either unsafe or totally safe; neither option can prevent a bad outcome with certainty in all circumstances.

Those who have argued in the past against the performance of a block technique in an anesthetized patient have focused on avoidance of the potential hazards and toxicity of general anesthesia. This is a strong argument when caring for a cooperative patient undergoing surgery in a tolerable position, but this scenario rarely applies to children, especially infants. Furthermore, most patients, including adults, are usually given strong sedatives during the block procedure, and it remains to be established that doing so is as safe as not giving any sedative. This does not seem likely and is not supported by the report of Taenzer et al[1] in children. A second argument is that without general anesthesia, a patient can inform the anesthesiologist that he might be damaging a neural structure due to perception of pain or paresthesia. This statement is true when peripheral nerve blocks are considered, but it is misleading when used to deny central block procedures in anesthetized patients. The brain and the spinal cord are not supplied with sensory innervation. In no case can a cooperative patient inform the anesthesiologist that the needle is progressing within the nervous tissue and, obviously, no infant or young children can be of any help even in the improbable case he was willing to help. Another flaw in this assumption is that the damage to neural structures produced by the cutting edge of the needle can be attenuated if it is noticed early: This may be true in case of a spinal hematoma (but remains to be established) that could be drained before compressive ischemia develops but in no case could a disrupted group of nerve fibers spontaneously reconnect if the needle were removed immediately after the dissection. Furthermore, as cleverly mentioned by Lang,[4] "Even if a patient reports procedural pain or paresthesia, it is not clear how we should proceed, as it is not an uncommon phenomenon, is rarely associated

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with clinical sequelae, and altering or abandoning the procedure may not affect outcome."

Those who argue for accepting the performance of a block procedure in a fully anesthetized child often note that children fear needle punctures and tolerate general anesthesia well. Although the first part of this assertion is readily evident, the second part is debatable, especially in premature babies and infants in whom neuroapoptosis might be a source of delayed neurological disorders. A second argument is that without general anesthesia, immobility and cooperation of the patient cannot be guaranteed throughout a potentially dangerous procedure such as a thoracic epidural.

Awake or asleep? The truth is that this is not a "never or always" decision. If we agree to take into consideration available data and accept to stop quibbling,[5] the decision can easily be sorted out. In the pediatric patient, if and when a regional block procedure is the best option, the following crucial questions should be answered:

–Is the indication appropriate?
–Is the technique fully explained to the patient and his representatives, with a consent form signed?
–Do I benefit from all the state-of-art equipment to perform the procedure in optimal conditions?
–Have I mastered the procedure adequately and am I comfortable with the indication?
–Is there a medical reason why I need to impose the performance of the technique in a way that is not in accordance with the desires of the patient?

In the end, when asking the question "Asleep vs awake: Does it matter," if the answer is certainly "yes" for the patient, it is mostly "no" for the anesthesiologist. Importantly, the report by Taenzer et al[1] strongly supports the fact that performing a block in an anesthetized child is certainly not unsafe. We must remain cognizant, however, that performing a block procedure conveys a risk of damage whether the patient is anesthetized or awake.

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Asleep Versus Awake: Does It Matter?

Pediatric Regional Block Complications by Patient State: A Report From the Pediatric Regional Anesthesia Network

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Background and Objectives: The impact of the patient state at time of placement of regional blocks on the risk of complications is unknown. Current opinion is based almost entirely on case reports, despite considerable interest in the question. Analyzing more than 50,000 pediatric regional anesthesia blocks from an observational prospective database, we determined the rate of adverse events in relation to the patient's state at the time of block placement. Primary outcomes considered were postoperative neurologic symptoms (PONSs) and local anesthetic systemic toxicity (LAST). Secondary outcome was extended hospital stay due to a block complication.

Methods: The Pediatric Regional Anesthesia Network is a multi-institutional research consortium that was created with an emphasis on rigorous, prospective, and complete data collection including a data validation and audit process. For the purpose of the analysis, blocks were divided in major groups by single injection versus continuous and by block location. Rates were determined in aggregate for these groups and classified further based on the patient's state (general anesthesia [GA] without neuromuscular blockade [NMB], GA with NMB, sedated, and awake) at the time of block placement.

Results: Postoperative neurological symptoms occurred at a rate of 0.93/1000 (confidence interval [CI], 0.7–1.2) under GA and 6.82/1000 (CI, 4.2–10.5) in sedated and awake patients. The only occurrence of PONSs lasting longer than 6 months (PONSs-L) was a small sensory deficit in a sedated patient (0.019/1000 [CI, 0–0.1] for all, 0.48/1000 [CI, 0.1–2.7] for sedated patients). There were no cases of paralysis. There were 5 cases of LAST or 0.09/1000 (CI, 0.03–0.21). The incidence of LAST in patients under GA (both with and without NMB) was 0.08/1000 (CI, 0.02–0.2) and 0.34/1000 (CI, 0–1.9) in awake/sedated patients. Extended hospital stays were described 18 times (0.33/1000 [CI, 0.2–0.53]). The rate for patients under GA without NMB was 0.29/1000 (CI, 0.13–0.48); GA with NMB, 0.29/1000 (CI, 0.06–0.84); sedated, 1.47/1000 (CI, 0.3–4.3); and awake, 1.15/1000 (CI, 0.02–6.4).

Conclusions: The placement of regional anesthetic blocks in pediatric patients under GA is as safe as placement in sedated and awake children. Our results provide the first prospective evidence for the pediatric anesthesia community that the practice of placing blocks in anesthetized patients should be considered safe and should remain the prevailing standard of care. Prohibitive recommendations based on anecdote and case reports cannot be supported.

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More than 10 years ago, Bromage and Benumof[1] asserted that placement of epidural catheters under general anesthesia (GA) is contraindicated. They based their statement on a single closed-claim case report of a spinal cord injury from a thoracic epidural placed in an adult with spine pathology under GA. Since this publication, there has been considerable debate on the topic, with a notable lack of evidence on either side of the debate. Krane et al[2] responded to the case report in an editorial representing the view of the international pediatric anesthesia community, supporting the safety of placement of regional blocks in anesthetized children. A regional anesthesia practice advisory published in this journal in 2008, largely based on expert opinion, case reports, and closed-claim cases, rather than empirical data, supported placing blocks under GA in pediatric patients, with the exception of interscalene blocks.[3]

In children, as in adults, local anesthetic systemic toxicity (LAST) and postoperative neurologic symptoms (PONSs) are 2 serious adverse events associated with regional anesthesia. Ecoffey et al,[4] in a summary of almost 30,000 voluntarily practitioner-reported pediatric regional anesthesia blocks with no structured follow-up, found 5 cases (0.17/1000) of transient PONSs, of which only 1 lasted longer than 5 days. In adults receiving neuraxial and peripheral nerve blocks, Auroy and colleagues[5] report a rate of 0.19/1000. Sites et al[6] report a PONSs incidence of 1.8/1000 lasting longer than 5 days and 0.9/1000 longer than 6 months for adults receiving peripheral nerve blocks.

For this report, we queried the database of the Pediatric Regional Anesthesia Network (PRAN). Pediatric Regional Anesthesia Network is a collaborative effort of pediatric anesthesiologists from participating children's hospitals established to define prevailing practice patterns in order to increase patient safety and quality of care.[7] The collaborative collects data prospectively on every regional anesthetic performed by anesthesiologists in participating institutions, with an emphasis on data completeness and audit verification.

The objective of this report was to define the incidence of PONSs, LAST, and other adverse events related to regional anesthesia depending on the patient's conscious state: awake, sedated, anesthetized, or anesthetized with neuromuscular blockade (NMB) at the time of block placement. We report data based on a multi-institutional clinical registry with mandatory reporting and a rigorous data verification process. In addition to the incidence of PONSs and LAST as they relate to patient state at the time of block, we describe as secondary outcomes causes of

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TABLE 1. Summary of all Blocks and Corresponding Patient State

	GA No NMB	GA With NMB	GA Total	Sedated	Awake	Missing	Total
Single-shot blocks							
Neuraxial	15,867	3261	19,128	186	282	0	19,596
Upper extremity	2571	205	2776	350	111	45	3282
Lower extremity	8210	892	9102	563	116	0	9781
Head and neck	1324	511	1835	62	54	0	1951
Other	7102	2349	9451	132	50	0	9633
Catheter blocks							
Neuraxial	3748	3033	6781	608	228	0	7617
Upper extremity	105	11	116	33	5	0	154
Lower extremity	1302	99	1401	126	23	0	1550
Total	40,229	10,361	50,590	2060	869	45	53,564

prolonged hospital stay related to the block as a proxy metric for adverse events.

METHODS

With institutional review board approval of all participating centers (see Appendix), data submitted from April 2007 through December 2012 were analyzed. Each PRAN study center collected data on every regional anesthetic performed by an anesthesiologist in patients younger than 18 years. Regional nerve blocks performed by other practitioners (surgeons, emergency medicine physicians, etc) were excluded. Details regarding the PRAN collaboration, the data collection, and the verification and validation process are described in previous publications.[7,8]

Each patient's clinical status during the block placement was recorded in the database. This "patient state" was categorized as GA without NMB, GA with NMB, sedated, and awake.

Three primary outcomes were used for this analysis: PONSs of any duration, PONSs lasting longer than 6 months (PONSs-L), and local anesthetic toxicity (LAST), either in the form of cardiovascular symptoms or seizures. In addition to complication entries in those categories, notes and comments in the database were reviewed for each complication. For example, pharmacologic intervention in the form of intravenous fluids or inotropic support for hypotension was not coded as a cardiovascular complication secondary to LAST, but cardiac arrest or arrhythmia with or without chest compressions, or the administration of a rescue lipid emulsion was coded as LAST.

Secondary outcome was extended hospital stay due to a block complication. Pediatric Regional Anesthesia Network uses a data field for prolonged hospital stay secondary to regional anesthetics, and reasons for those extended stays were categorized and summarized.

Outcomes are reported as number of occurrences and rates per 1000 blocks with corresponding 95% confidence intervals (CIs). The latter were calculated using R (v3.0.2; http://r-project.org).

RESULTS

A total of 53,564 regional nerve blocks were analyzed: 40,229 (75%) blocks performed under GA without NMB, 10,361 (19.5%) under GA with NMB, 2060 (4%) sedated, and 869 (1.5%) awake (Table 1).

About one-third (34.6%) of the blocks were placed in children between 10 and 18 years, 21.8% in children between 3 and 10 years, 14.9% between 1 and 3 years, 15.3% between 6 and 12 months, 10.7% in younger than 6 months, and 2.7% in younger than 1 month (Table 2). Relatively more neuraxial blocks were performed in younger children, whereas peripheral nerve blocks were more frequent in older children. For example, 57% of blocks in children younger than 1 month and 4.2% in children older than 10 years were single-injection neuraxial blocks, whereas lower-extremity perineural catheters made up 0.07% of blocks in children younger than 1 month and 7.2% in children older than 10 years.

In children younger than 1 month, 91% of blocks were placed under GA, a lower rate than that in the older children, with the exception of children older than 10 years (Table 3).

TABLE 2. Summary of all Blocks and Corresponding Patient Age

	<1 mo	1 to <6 mo	6 to <12 mo	1 to <3 y	3 to <10 y	10–18 y
Single-shot blocks						
Neuraxial	764	3729	6042	3347	1205	722
Upper extremity	37	93	128	523	945	1550
Lower extremity	12	48	105	496	1967	7133
Head and neck	16	226	185	281	530	712
Other	185	608	629	1434	3841	2923
Catheter blocks						
Neuraxial	314	587	514	1284	2076	2823
Upper extremity	0	0	5	10	30	107
Lower extremity	1	4	18	42	246	1236
Total	1329	5295	7626	7417	10,840	17,206

TABLE 3. Patient State at Time of Block and Corresponding Age Bracket

Age	GA No NMB	GA With NMB	GA total	Sedated	Awake	Under GA [%]
<1 mo	643	568	1211	18	100	91.1
1 to <6 mo	3842	1215	5057	47	190	95.5
6 to <12 mo	5025	919	5944	47	11	99.0
1 to <3 y	8806	1616	10,422	128	33	98.4
3 to <10 y	10,050	2744	12,794	222	15	98.2
10–18 y	11,808	3275	15,083	1590	515	87.7

Primary Outcomes

The overall rate of complications and adverse events was 11.9/1000 (CI, 11.0–12.8); postoperative neurological complications were 1.3/1000 (CI, 1.02–1.65, total of 70 in 53,564 blocks), and local anesthetic toxicity was 0.09/1000 (CI, 0.03–0.21, total of 5 in 53,564 blocks) (Table 4). There was 1 case of PONSs-L and no reports of paralysis.

Postoperative neurologic symptoms occurred at a rate of 0.93/1000 (CI, 0.7–1.2) under GA and 6.82/1000 (CI, 4.2–10.5) in sedated and awake patients. Subgroup analysis revealed an incidence of 0.62/1000 (CI, 0.4–0.92) in patients under GA without NMB, 2.4/1000 (CI, 1.6–3.6) in patients under GA with NMB, 8.3/1000 (CI, 4.9–13.3) in sedated, and 3.4/1000 (CI, 0.7–10.0) in awake patients. The 1 case of PONSs-L occurred in a teenager who was sedated for a popliteal fossa block and has permanent numbness in the fourth toe. All other PONSs resolved.

There were 5 cases of LAST or 0.9/1000 (CI, 0.3–2.1) (Table 5). The incidence of LAST in patients under GA (both with and without NMB) was 0.08/1000 (CI, 0.02–0.2) and 0.34/1000 (CI, 0–1.9) in awake/sedated patients. Cardiovascular complications were found in 3 (0.05/1000 [CI, 0.01–0.16]) patients; 2 occurred in patients with blocks performed under GA with NMB (0.04/1000 [CI, 0.01–0.1]), and 1 in an awake patient (1.1/1000 [CI, 0.02–6.4]). Seizures were reported in 2 patients (0.04/1000 [CI, 0–1.4]), both with blocks performed under GA without NMB.

Secondary Outcomes

Hospital stays were extended 18 times (0.33/1000 [CI, 0.2–0.53]), 15 times for 1 to 2 days, 2 times between 3 and 5 days, and once for more than 5 days. Reasons for prolonged stays were PONSs (n = 7: excessive motor block, 4, dysesthesia 3), infection (n = 4), postdural puncture headaches (n = 2), LAST (n = 1: cardiovascular), and pruritus, adverse drug, or dressing reaction (n = 1 each). The rate for patients under GA without NMB was 0.29/1000 (CI, 0.13–0.48); GA with NMB, 0.29/1000 (CI, 0.06 –0.84); sedated, 1.47/1000 (CI, 0.3–4.3); and awake, 1.15/1000 (CI, 0.02–6.4) (Fig. 1).

DISCUSSION

This report is a summary of complications of regional anesthetics in children based on patient state at the time of block placement. Major complications such as PONSs (1.3/1000), PONSs-L (0.02/1000), and LAST (0.09/1000) are rare, and our findings are consistent with previously reported data in children[9] and adults.[5,6] Indeed, the incidence of PONSs-L (duration >6 months) associated with peripheral nerve blocks is lower than data reported in adults.[6] While LAST complications were more common in young children, PONSs were more common in older children. This difference may be due to the fact that weight-based local anesthetic dosing approaches common "adult" doses at approximately 30 to 40 kg. Therefore, dosing for blocks in older children has a relatively larger therapeutic index than that for smaller children. In addition, older children are more capable of reporting mild neurological problems such as persistent numbness or paresthesia, which would make the reported incidence of PONSs higher in this group, especially considering that the majority of the neurologic complications resolved without sequelae.

Summarizing blocks in broad categories and patient states in 4 categories, we found complication rates that do not indicate that blocks placed under anesthesia with or without NMB carry more risk than blocks placed in children awake or sedated—on the contrary, the rate of PONSs in awake and sedated patients was more than 7 times higher than that in patients under GA. Our data could be interpreted as showing that placing regional blocks under GA is in fact safer, because every primary adverse outcome had a lower incidence rate with patients under GA than if sedated or awake.

TABLE 4. Summary of Complications

Complication	GA No NMB	GA With NMB	GA Total	Sedated	Awake	Total
PONSs	25	25	50	17	3	70
PONSs-L	0	0	0	1	0	1
Cardiovascular	0	2	2	0	1	3
Seizure	2	0	2	0	0	2
Dural puncture	49	32	73	5	1	87
Positive test dose	35	15	50	3	3	56
Vascular puncture	184	56	240	7	8	419
Total	295	130	417	33	16	638
All complications (%)	0.73	1.25	0.82	1.60	1.84	1.19
LAST (per 1000)	0.05	0.193	0.04		1.15	0.093
PONSs (per 1000)	0.62	2.41	0.99	8.25	3.45	1.31
PONSs-L (per 1000)				0.485		0.019

TABLE 5. Reported Local Anesthesia Toxicity Complications, Intervention, Patient State During Block Placement, Block, and Age

Complication	Intervention	Patient State	Block	Age
Cardiac arrest	Epinephrine, calcium, lipids, bicarbonate	GA with NMB	Thoracic catheter	2 mo
Hypotension, ST changes	Epinephrine, lipids	Awake	Spinal	2 mo
Cardiac arrest	Chest compressions	GA with NMB	Single shot caudal	3 y
Seizure	Anticonvulsants	GA no NMB	Single shot caudal	1 mo
Seizure	Hypotension, intubation, anticonvulsants	GA no NMB	Caudal to lumbar catheter	3 mo

We purposely did not provide more detailed data for specific blocks, because of the relatively small numbers in some subcategories. We caution against overinterpretation of these data, as serious complications from regional anesthesia have been documented in pediatrics, including blocks placed under GA.[10] Nevertheless, we provide the largest overview of regional block complications based on patient state, lending credence to the belief that placement of regional anesthetics in children and adolescents under GA does not increase the risk of PONSs and LAST, and therefore prohibitive recommendations based on anecdote and case reports cannot be supported. Furthermore, the data provide impetus to study the question of whether placement of regional blocks in children is in fact safer if done under GA and should prompt research comparing the risks of regional nerve blocks in anesthetized versus awake adults.

This study is limited by several factors and should not be taken to be more than what it is: a report of complication rates based on patient state across many ages and between centers, with a diversity of practices and an uneven distribution of blocks and patient states across ages. The data collected are prospective and observational with patients accrued from 20 academic teaching hospitals with their corresponding patient populations; hence, they are not a representative sample of all children receiving regional blocks, nor do the data speak to causality. Complication data are subject to population bias, design effect, and other confounding variables that may affect reported incidence rates. The different sizes of the subgroup denominators also affect reported incidence data, as the majority of patients were in the GA groups, with much smaller groups being awake or sedated.

Furthermore, there was a binary distribution of patients who received awake or sedated blocks, being either very young (eg, neonates receiving spinals as a primary anesthetic) or in their teen years. Of course, neonates or children with severe neurodevelopmental disorders would not be able to report mild sensory or motor PONSs, but more severe motor deficits would likely have been detected. While some block types are more evenly distributed across the all ages (eg, epidurals), others (eg, subarachnoid blocks, caudal blocks, and peripheral nerve blocks) are not.[7]

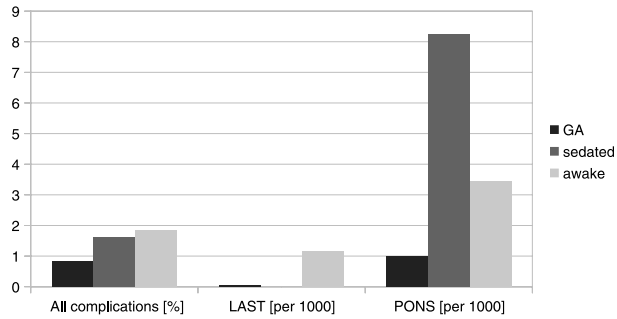

FIGURE 1. Rates of complications based on patient state at time of block placement.

Reporting bias may alter results as well. As is the case with newborns, nonverbal children are less likely to be detected to have PONSs, and because of the uneven distribution of patient states across ages, this could have changed the observed incidence. Because PRAN does not collect patient-specific diagnostic or demographic information beyond age, gender, weight, and regional anesthesia, we have no method to address that question. Finally, the fact that there was no paralysis in over 50,000 blocks does not exclude an incidence of 3/50,000 or 0.06/1000 blocks.[11]

CONCLUSIONS

The placement of regional anesthetic blocks in pediatric patients under GA is as safe as placement in sedated and awake children. Our results provide the first prospective evidence for the pediatric anesthesia community that the practice of placing blocks in anesthetized patients should be considered both safe and should remain the prevailing standard of care.

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APPENDIX

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8	University of Texas-Houston, Houston, Texas	Ranu Jain Maria Matuszczak
9	Children's Hospital, Boston, Massachusetts	Navil Sethna
10	University of New Mexico Children's Hospital, Albuquerque, New Mexico	Tim Petersen Nicholas Lam Jennifer Dillow
11	Texas Children's Hospital, Houston, Texas	Robert Power Kim Nguyen Nancy Glass
12	Oregon Health and Science University, Portland, Oregon	Jorge Pineda
13	Nationwide Children's Hospital, Columbus, Ohio	Tarun Bhalla
14	Hospital Municipal Jesus–Rio de Janeiro, Brazil	Pedro Paulo Vanzillotta
15	University of Wisconsin–American Family Children's Hospital, Madison, Wisconsin	Ben Walker
16	University of Minnesota Amplatz Children's Hospital, Minneapolis, Minnesota	Chandra Castro
17	Columbia University,* New York, New York	Susumu Ohkawa
18	University Hospital Rijeka, Croatia*	Helga Usljebrka

*No longer a PRAN member, but data are included in this analysis.