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Continuous Peripheral Nerve Blocks: An Update of the Published Evidence and Comparison with Novel, Alternative Analgesic Modalities

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A continuous peripheral nerve block (CPNB) consists of a percutaneously inserted catheter with its tip adjacent to a target nerve/plexus through which local anesthetic may be administered, providing a prolonged block that may be titrated to the desired effect. In the decades after its first report in 1946, a plethora of data relating to CPNB was published, much of which was examined in a 2011 *Anesthesia & Analgesia* article. The current update is an evidence-based review of the CPNB literature published in the interim. Novel insertion sites include the adductor canal, interpectoral, quadratus lumborum, lesser palatine, ulnar, superficial, and deep peroneal nerves. Noteworthy new indications include providing analgesia after traumatic rib/femur fracture, manipulation for adhesive capsulitis, and treating abdominal wall pain during pregnancy. The preponderance of recently published evidence suggests benefits nearly exclusively in favor of catheter insertion using ultrasound guidance compared with electrical stimulation, although little new data are available to help guide practitioners regarding the specifics of ultrasound-guided catheter insertion (eg, optimal needle–nerve orientation). After some previous suggestions that automated, repeated bolus doses could provide benefits over a basal infusion, there is a dearth of supporting data published in the past few years. An increasing number of disposable infusion pumps does now allow a similar ability to adjust basal rates, bolus volume, and lockout times compared with their electronic, programmable counterparts, and a promising area of research is communicating with and controlling pumps remotely via the Internet. Large, prospective studies now document the relatively few major complications during ambulatory CPNB, although randomized, controlled studies demonstrating an actual shortening of hospitalization duration are few. Recent evidence suggests that, compared with femoral infusion, adductor canal catheters both induce less quadriceps femoris weakness and improve mobilization/ambulation, although the relative analgesia afforded by each remains in dispute. Newly published data demonstrate that the incidence and/or severity of chronic, persistent postsurgical pain may, at times, be decreased with a short-term postoperative CPNB. Few new CPNB-related complications have been identified, although large, prospective trials provide additional data regarding the incidence of adverse events. Lastly, a number of novel, alternative analgesic modalities are under development/investigation. Four such techniques are described and contrasted with CPNB, including single-injection peripheral nerve blocks with newer adjuvants, liposome bupivacaine used in wound infiltration and peripheral nerve blocks, cryoanalgesia with cryoneurolysis, and percutaneous peripheral nerve stimulation. (*Anesth Analg* 2016;XXX:00–00)

A continuous peripheral nerve block (CPNB) consists of a percutaneously inserted catheter with its tip adjacent to a target nerve/plexus through which local anesthetic may be administered. Such a “perineural local anesthetic infusion” provides a prolonged peripheral nerve block that may be titrated to the desired effect.¹ In the decades after its first report in 1946,² a plethora of data

relating to CPNB was published, much of which was examined in a 2011 *Anesthesia & Analgesia* review.¹ The current update is an evidence-based review of the CPNB literature published in the interim. Because of publication limitations, the majority of information—including 364 citations— included in the previously published review is not repeated here.¹ Consequently, the current update is most likely best utilized in concert with the previous review article to provide a complete overview of CPNB. Because there are literally thousands of CPNB-related publications, only those that provide the highest quality data (eg, randomized controlled trials [RCTs]) and/or are the most influential (eg, unique case reports and observational studies) are included.

In addition, a variety of novel, alternative analgesic modalities are currently under development/testing. These techniques are also reviewed and compared/contrasted with CPNB.

INDICATIONS AND INSERTION LOCATIONS

The overwhelming majority of recently published CPNB data involves providing analgesia after surgical

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Parts of this report were previously presented annually since 2003 when I began giving presentations; this is a review article and therefore covers material that I have presented previously.

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procedures. Noteworthy exceptions include case reports/series using CPNB to treat chronic pain such as cancer-related pain,³⁻⁸ complex regional pain syndrome,⁹⁻¹² ischemia-induced pain,^{13,14} ulcer-derived pain,¹⁵ and phantom limb pain (Table 1).¹⁶⁻¹⁸ Regarding the latter, the only available randomized data come from a very small pilot study (n = 3) but does strongly suggest that further research is warranted.¹⁹ Another randomized, placebo-controlled pilot study (n = 4) provides evidence that a 3-day, continuous interscalene nerve block dramatically improves shoulder range of motion both during and up to 12 weeks after manipulation for adhesive capsulitis.²⁰ Also noteworthy, continuous paravertebral²¹⁻²³ and intercostal²⁴⁻²⁶ catheters have been used to treat pain after traumatic rib fracture; and a randomized pilot study (n = 30) detected no differences between this CPNB technique and a thoracic epidural infusion with the exception of a greater incidence and degree of hypotension using epidural analgesia.²⁷ Lastly, continuous transversus abdominis plane (TAP) and femoral blocks have been used to treat abdominal wall pain during pregnancy²⁸ and femur fracture pain,^{29,30} respectively.

Recently, case reports and small series using CPNB to induce sympathectomy to improve transplantation success have been published.^{31,32} Similarly, a number of reports have been published, involving the use of continuous TAP blocks to treat postoperative pain after hernia repair,³³ renal transplantation,³⁴ and abdominal procedures.³⁵ Unfortunately, this catheter location remains unvalidated with the only (negative) randomized, placebo-controlled trial underpowered (n = 20),³³ and a different RCT comparing TAP and epidural catheters for upper abdominal surgery designed as a superiority trial yet detecting few differences between treatments (therefore, inconclusive).³⁶ Bilateral continuous paravertebral blocks have also been used for abdominal surgery in the presence of mild coagulopathy instead of an epidural because of concern of epidural hematoma formation.³⁷

Novel insertion sites include catheters adjacent to the lesser palatine,³⁸ ulnar,³⁹ superficial peroneal,^{40,41} and deep peroneal nerves.⁴⁰ New interfascial catheter sites have also been described: interpectoral^{42,43} and quadratus lumborum⁴⁴⁻⁴⁶ for breast and abdominal analgesia, respectively.

However, adductor canal catheters are by far the most examined and potentially influential anatomic site described recently (Table 1).⁴⁷ The adductor canal is an aponeurotic tunnel in the midthird of the thigh deep to the sartorius muscle that contains multiple afferent nerves innervating the knee, yet only a single efferent nerve innervating the medial part of the quadriceps femoris muscle.^{48,49} Therefore, local anesthetic administered in the canal induces dramatically less quadriceps weakness compared with deposition adjacent to the femoral nerve at the inguinal crease.⁵⁰ Reflecting the concern regarding the association between continuous femoral nerve blocks and both falls⁵¹⁻⁵⁶ and physical therapy limitations,^{57,58} adductor canal perineural infusion has garnered strong interest.^{59,60} Although this catheter site has been validated with a number of randomized, placebo-controlled trials,^{47,61-65} multiple issues remain in dispute⁶⁶⁻⁷¹ or are unclear/unknown^{72,73} such as

the relative analgesia afforded compared with a femoral infusion (see the following section on benefits).^{50,57-59,74}

Although RCTs involving surgical pediatric populations remain the exception,^{75,76} series of patients continue to be published.⁷⁷⁻⁸³

CATHETER INSERTION

Before the advent of ultrasound-guided regional anesthesia, CPNB-related clinical investigation focused on comparing nonstimulating and stimulating catheters inserted through an insulated needle used to localize a target nerve/plexus.^{84,85} With the subsequent widespread adoption of ultrasound to place a needle adjacent to a target nerve/plexus, the emphasis has shifted to comparing needle/catheter insertion using ultrasound versus electrical current.⁸⁶ Since publication of the previous CPNB review,¹ the preponderance of new evidence suggests benefits nearly exclusively in favor of catheter insertion using ultrasound guidance compared with electrical stimulation (passed via either the needle or the catheter). Catheter insertion success is higher using ultrasound guidance compared with nerve stimulation for most insertion sites, yet requires less time for placement, induces less procedure-related discomfort, and carries a lower risk of vascular penetration.⁸⁷

The data are somewhat conflicting on whether catheters inserted using ultrasound guidance provide superior analgesia during the perineural infusion itself.⁸⁷⁻⁹² Regarding this issue, the highest quality data are derived from an RCT involving over 450 subjects randomized to 3 different femoral catheter insertion techniques.⁹³ Using electrical current to guide the inserting needle and/or stimulating catheter failed to provide superior analgesia or decrease opioid requirements (and vice versa). In addition, using electric current with either the needle or the catheter required a longer insertion time and ultimately proved more costly. With the number of CPNB-related RCTs involving nerve stimulation appearing to fall precipitously within the past few years,^{14,94-99} it subjectively appears there is now some consensus emerging regarding the ultrasound-versus-stimulation debate.⁸⁶ Nonetheless, using electric current to supplement ultrasound guidance for difficult to visualize (eg, deep)¹⁰⁰ or ambiguous (eg, inexperienced practitioners) neural targets may prove beneficial in challenging cases.¹

Few RCTs have been published—recently or otherwise—to help guide practitioners regarding the specifics of ultrasound-guided catheter insertion.^{1,101,102} For example, imaging the target nerve in the short axis (a cross-section) is far easier¹⁰³ and decreases total insertion time compared with imaging the long axis^{103,104}, and nearly all publications report this transducer-to-nerve orientation. However, catheters may be inserted through a needle introduced either parallel or perpendicular to the target nerve.¹⁰⁵ Few RCTs compare these “in-” and “out-” of-plane techniques¹⁰⁶; and of those that do, results may agree (femoral)^{103,104} or conflict (interscalene).^{107,108} Although publication limitations of this review article preclude an in-depth discussion of these issues,¹⁰⁹ readers are referred elsewhere for related information.^{105,110}

Technologic innovations of the past few years offer possible improvements in CPNB application¹¹⁰ and include self-coiling catheters that curl immediately on exiting the

Table 1. Catheter Locations

Surgical Site	Major Approaches	Randomized and Controlled Study Design? (for Catheter Site)	Comments	Comparative CPNB Studies
Head and neck	Mandibular, maxillary, lesser palatine nerves, and cervical plexus	No ^{1,38,426}	Effectiveness of techniques unclear without RCT	
Shoulder and proximal humerus	Interscalene	Yes ^{20,98,99,108,116,119,130,131,145-147,153,163,164,173,176,195,427} No ^{4,5,8,16,77-81,159,162,168-172,175,428,429}	Recent RCT demonstrated a 2-d continuous interscalene block decreases pain 7 d after major shoulder surgery compared with a single-injection ropivacaine block ¹⁷⁶	A recent RCT demonstrated that a supraclavicular infusion is noninferior to an interscalene infusion and reduced the incidence of complete or partial hemidiaphragmatic paresis (analgesia was superior to the interscalene catheters in the recovery room) ⁴²⁷
	Cervical paravertebral	No ⁶	Little published since the widespread adoption of ultrasound-guided catheter insertion	
	Intersternocleidomastoid	No ¹	Little published since the widespread adoption of ultrasound-guided catheter insertion	
	Supraclavicular	Yes ⁴²⁷ No ^{77,165,430}	Relatively rare catheter site relative to the interscalene location for shoulder surgery ¹ ; however, the largest series to date was recently published (n = 498) ¹⁶⁵	
	Suprascapular	No ⁴³¹	Effectiveness of technique unclear without RCT	
Elbow, forearm, and hand	Supraclavicular	Yes ¹¹⁸ No ^{9,32,77,81,159,165}	Relatively rare catheter site relative to the infraclavicular and—historically—axillary locations ¹ ; however, the largest series to date was recently published (n = 271) ¹⁶⁵	Infraclavicular provides superior analgesia to both supraclavicular ⁴³² and axillary ⁴³³ catheters for hand, forearm, and elbow surgery; 1 new RCT detected few differences between supraclavicular and infraclavicular infusions benefits but was underpowered for these secondary endpoints, and there were trends in favor of the infraclavicular location ⁴³⁴
	Infraclavicular	Yes ^{173,434} No ^{19,77-80,102,127,173}	A recent RCT provided 60 h of infraclavicular infusion to all participants and randomized subjects to remain hospitalized for 1 vs 3 nights ¹⁷³ ; total hospital cost of care was 15% lower in the early discharge group and no other differences between treatment groups including elbow range of motion	
	Axillary	Yes ⁴³³ No ^{31,77,79-81,127,128,435}	Dramatic decrease in publications since the widespread adoption of ultrasound-guided catheter insertion	
	Median, ulnar nerves	No ^{39,436}	Effectiveness of techniques unclear without RCT	
Thorax and breast	Thoracic paravertebral	Yes ^{27,135,158,167,177,204,221,437} No ^{21-23,77,83,109,438}	For mastectomy, mixed evidence ^{439,440} with RCTs demonstrating no infusion benefits over placebo ²²¹ and single-injection, ⁴⁴¹ yet others demonstrating benefits both during ^{167,437} and after (up to 1 y) perineural infusion ^{177,221}	There are no studies comparing these CPNB techniques
	Intercostal	No ²⁴⁻²⁶	Effectiveness of this technique unclear without RCT	
	Interpectoral	No ^{42,43}	Effectiveness of this relatively novel technique unclear without RCT	
Abdomen and inguinal region	Paravertebral	No ^{37,77,83,442,443}	New published data include pediatric patients ^{77,83,442}	
	Transversus abdominis plane	Yes ^{33,36} No ^{28,34,35,77,256,444}	Remains unvalidated with an RCT: one RCT was negative compared with placebo but was underpowered, ³³ and a second RCT detected few differences between a continuous subcostal TAP and epidural infusion but was designed as a superiority study and the negative results should therefore be considered inconclusive and not equivalent ³⁶	
	Quadratus lumborum	No ⁴⁴⁻⁴⁶	Effectiveness of this relatively novel technique unclear without RCT	

(Continued)

Table 1. Continued

Surgical Site	Major Approaches	Randomized and Controlled Study Design? (for Catheter Site)	Comments	Comparative CPNB Studies
Hip, thigh, and leg	Posterior lumbar plexus	Yes ^{133,206}	Published RCTs dramatically diminished in numbers within the past few years, possibly indicating a general preference for other catheter locations	For hip arthroplasty, patients with femoral (vs posterior lumbar plexus) catheters: no difference in resting pain scores, but ambulation suffered; dynamic pain scores either higher or no difference; and increased opioid-related side effects and satisfaction ¹
	Femoral	No ^{3,6,77-80,178} Yes ^{29,203} No ^{3,7,9,18,19,30,77-81,150,159,162}		
	Fascia iliaca	Yes ⁴⁴⁵		
	Parasacral	No ¹		
Knee (femoral nerve)	Posterior lumbar plexus	Yes ¹ No ^{77-80,96}	Published RCTs dramatically diminished in numbers within the past few years, possibly indicating a general preference for other catheter locations	Compared with femoral infusion, adductor canal CPNB induces less quadriceps femoris muscle weakness ⁵⁰ and ambulatory disability ^{57,58,74} ; however, the evidence is mixed regarding comparable analgesia, ^{50,57,58,74} and further research is required to draw definitive conclusions
	Femoral	Yes ^{50,57-59,74,85,91,93,95,101,104,121,132,138,198,216,446,447} No ^{77-80,97,100,201,205,448-451}	Until recently, the most commonly published catheter location for knee surgery, but concerns regarding associated falls have raised interest in alternative catheter locations such as the adductor canal	
	Adductor canal	Yes ^{47,50,57-59,61-65,73,74,144} No ^{156,263,279,452-456}	Relatively recently validated with randomized, placebo-controlled trials, ^{47,61-65} but multiple issues remain in dispute ⁶⁶⁻⁷¹ or unclear/unknown ^{72,73} such as relative analgesia afforded compared with a femoral infusion ^{50,57,58,74}	
	Fascia iliaca	Yes ¹ No ⁷⁷	Dramatic decrease in publications since the widespread adoption of ultrasound-guided catheter insertion	
	Subgluteal/parasacral	Yes ^{94,96,97,126,201} No ^{77,78,82,128,159}	Three recent RCTs have investigated the effects of adding a continuous sciatic nerve block to a continuous femoral or posterior lumbar plexus (psoas compartment) block after total knee arthroplasty ^{96,97,201} ; all demonstrated lower pain scores and decreased supplemental analgesic consumption, ^{96,97,201} and one detected a lower incidence of nausea and vomiting as well as improved knee flexion and ambulation ²⁰¹	
Knee (sciatic nerve), leg, ankle, and foot	Popliteal	Yes ^{88,92,134,194,200} No ^{9,12-15,18,19,77-81,100,128,162,165,174,457,458}	A recent RCT provided 3 d of popliteal sciatic infusion to all participants (n = 120) and randomized subjects to remain hospitalized for 0 vs 2 nights after major orthopedic foot surgery ¹⁹⁴ ; total costs of care were decreased 79% in the early discharge group, and no other differences between treatments were detected, including pain scores, complications, and readmission rates	No major analgesic differences found between subgluteal and popliteal ¹
	Tibial, superficial peroneal and deep peroneal nerves	No ^{11,40,41}	Effectiveness of these techniques unclear without RCT	
	Femoral/saphenous	Yes ¹	Femoral infusion in addition to—and not in place of—popliteal infusion for major ankle surgery	

Due to publication limitations, includes selected reports published subsequent to a previously published review article (Ilfeld¹) and is not intended as an exhaustive list.

CPNB, continuous peripheral nerve block; RCT, randomized controlled trial.

needle, theoretically decreasing the catheter tip-to-nerve distance^{111–113}; a catheter attached to a needle that is passed adjacent to the target nerve and then exited out of the body on the other side of the transducer (remaining in plane the entire trajectory)^{114,115}; a 6-hole catheter to theoretically improve local anesthetic spread (failed in 1 RCT)¹¹⁶; a perineural catheter that is introduced over an insertion needle to theoretically decrease the incidence of leakage (similar to an intravenous catheter)^{30,117–120}; and a novel needle-over-cannula set to also decrease leakage (successful in 1 RCT).¹²¹

Because flexible perineural catheters usually deviate from the ultrasound plane of view after exiting a rigid in-plane needle, evaluating the crucial catheter tip-to-nerve distance can be difficult.⁸⁷ Various investigators have injected—under real-time ultrasound visualization—fluid, an agitated air/fluid admixture, or a small volume of air, although the relative benefits of each were previously uninvestigated.¹ The “air test” was recently evaluated within a porcine-bovine model, but unfortunately there was no benefit over simply visualizing the catheter without air injection.^{122,123} Attempts to improve the echogenicity of perineural catheters have been somewhat equivocal^{124,125} with 1 RCT detecting no differences in visibility between the experimental echogenic and the standard stimulating catheters.¹²⁶ Although visualizing catheter tip location using 3-dimensional ultrasound^{127,128} and catheter stylet “pumping” combined with color Doppler are promising techniques,¹²⁹ neither has been validated.¹¹⁰

INFUSATES

Long-acting local anesthetic remains the primary analgesic infused during CPNB,¹ and there is minimal new information to help guide clinical practice: data suggest that ropivacaine, bupivacaine, and levobupivacaine provide similar analgesia¹³⁰ with the main differences being ropivacaine’s shorter duration of action—presumably allowing easier titration yet added expense (at least within the United States).¹ New data do support previously available evidence¹ that total dose and not concentration/volume is the primary determinant of clinical effects for continuous interscalene,¹³¹ femoral,¹³² posterior lumbar plexus (psoas compartment),¹³³ and popliteal sciatic nerve blocks¹³⁴; although it remains unclear whether this relationship is valid for other brachial plexus,¹ adductor canal,^{57,58} TAP, and paravertebral perineural infusions.¹³⁵

Although there is recently published preclinical evidence involving perineural pregabalin infusion¹³⁶ as well as the addition of clonidine, dexamethasone, and buprenorphine to perineural bupivacaine in a rat model,¹³⁷ these data are preliminary and there remains no medication other than local anesthetic approved for continuous perineural administration by the US Food and Drug Administration (FDA).¹ Randomized, controlled clinical trials have failed to detect benefits of adding clonidine or epinephrine to perineural infusions.¹ There are sporadic RCTs reporting benefits of various opioids in a perineural infusion^{14,138–141}; however, all but 1¹⁴⁰ lacked an active systemic control group, precluding any determination on the importance of perineural (vs intravenous) administration. Unsurprisingly, the addition of opioids often resulted in an increased incidence of

opioid-related side effects.^{14,139} Regardless, considering the absence of safety data,¹⁴² a dearth of evidence of perineural efficacy, reports of unacceptable side effects,^{14,139} and lack of Federal regulatory approval,¹⁴³ no adjuvants can be recommended at this time; and CPNB with solely local anesthetic remains the infusate by general consensus as judged by published reports of the past 2 decades.¹

LOCAL ANESTHETIC DELIVERY REGIMENS

The RCTs published in the past few years have done little to clarify the optimal mode of delivering perineural local anesthetic: as exclusively a basal infusion, solely repeated bolus doses, or a combination of the 2.¹ A large body of relatively older evidence suggests that providing a basal infusion improves baseline analgesia, decreases the incidence and severity of breakthrough pain, and decreases sleep disturbances and supplemental analgesic requirements for interscalene, infraclavicular, subgluteal, and popliteal sciatic infusions.¹ In contrast, recently published data indicate that few benefits—if any—are afforded with a basal infusion, as opposed to repeated boluses for catheters in these anatomic locations (Table 2).^{94,144–147} Contrary new data also exist for femoral CPNB: although previous data suggested that the delivery mode is irrelevant for femoral infusions,¹ a recent RCT suggests that including a basal infusion improves analgesia for this catheter site.⁹⁵

The conflicting results are most likely due to the heterogeneity of catheter designs (eg, nonstimulating vs stimulating), catheter insertion techniques (eg, ultrasound vs stimulating vs a combination), local anesthetic type (eg, ropivacaine vs bupivacaine) and concentration, basal infusion rates, bolus volumes, lockout times, surgical procedures, outcome measures evaluated, measurement sensitivity, and a multitude of other factors. Consequently, there is no evidence-based “ideal” delivery regimen,¹⁴⁸ although investigators have provided clinical recommendations.^{143,149} Nevertheless, there are some clinical situations in which including bolus doses are theoretically beneficial such as to enable block reinforcement before potentially painful dressing changes¹⁵⁰ or physical therapy.²⁰ Virtually all RCTs providing patient-controlled boluses to 1 treatment group report a lower local anesthetic requirement, suggesting 3 possible benefits: (1) theoretically decreasing motor block by decreasing the required basal infusion rate (inadequately investigated to date)^{51,151,152}; (2) decreasing the incidence of an insensate extremity¹⁵³; and (3) increasing infusion/analgesia duration for outpatients discharged with a fixed local anesthetic reservoir volume.^{154,155}

One technique variation has recently garnered increased interest: the use of mandatory/automatic bolus doses based on the theory that increasing the volume of local anesthetic introduced at a single time point might improve perineural spread compared with an equivalent volume/dose provided as a basal infusion.¹³ Continuous adductor canal blocks appear to require a higher basal rate of local anesthetic than their femoral counterparts; and a recent study demonstrated that even with a relatively high rate of 8 mL/h, local anesthetic spread remains somewhat limited.¹⁵⁶ A subsequent investigation involving healthy volunteers found sensory perception and quadriceps femoris

Table 2. Local Anesthetic Delivery Regimens for Continuous Peripheral Nerve Blocks

Catheter Location	Infusate(s)	n	Treatment Groups			Primary Findings
			Basal (mL/h)	Bolus (mL)	Lockout (min)	
Interscalene¹⁴⁷ • Arthroscopic rotator cuff repair • Ultrasound in-plane • Nonstimulating needle • Nonstimulating catheter	Ropivacaine 0.2%	33	4	0	—	Two groups receiving ropivacaine had lower pain scores and consumed less supplemental analgesics than the control group No differences between the basal and bolus treatment groups
	Control (no catheter)	33	—	—	60	
Interscalene¹⁴⁶ • Arthroscopic rotator cuff repair • Ultrasound in-plane • Stimulating needle • Stimulating catheter	Ropivacaine 0.2%	32	4	4	60	Bolus group used a lower total volume of local anesthetic and experienced less motor block No other differences between the basal and the bolus treatment groups noted
		32	0	4	30	
Interscalene¹⁵³ • Arthroscopic or open rotator cuff repair • Ultrasound out-of-plane • Nonstimulating needle • Nonstimulating catheter	Ropivacaine 0.2%	38	2	5	60	No differences detected between treatments with one exception: higher basal rate group required a temporary infusion cessation because of side effects (predominantly hand numbness)
		43	5	5	60	
Interscalene¹⁴⁵ • Major shoulder surgery • Ultrasound, out-of-plane • Stimulating needle • Nonstimulating catheter	Ropivacaine 0.2%	50	4	3	30	No differences detected between treatments
		51	0	3	30	
Paravertebral¹⁵⁸ • Thoracotomy • Nonstimulating catheter • Inserted by surgeon under direct vision	Bupivacaine 0.5%	40	0	15 mL every 6 h ^a	—	Pain scores lower in bolus group, although statistically significant only at 48 and 72 h Higher total volume of local anesthetic consumed by the basal group
	Bupivacaine 0.25%	40	5	0	—	
Adductor canal¹⁴⁴ • Healthy volunteers • Ultrasound, in plane • Nonstimulating needle • Nonstimulating catheter	Ropivacaine 0.2%	24	8	0	—	Equivalence between treatments to tolerance to cutaneous electrical current and quadriceps femoris maximum voluntary isometric contraction strength
		24	0	8 mL every 1 h ^a	—	
Femoral⁹⁵ • Anterior cruciate ligament repair • Stimulating needle • Nonstimulating catheter	Bupivacaine 0.1%	16	5	5	30	Analgesia superior in basal + bolus group at rest and during mobilization
		19	0	5	15	
Sciatic⁹⁴ • Total knee arthroplasty • Anterior approach • Stimulating needle • Nonstimulating catheter • Femoral catheter and continuous infusion also used for both groups	Ropivacaine 0.2%	56	6	10	<30 min	Few differences between groups, other than the basal + bolus group consumed a higher total volume of local anesthetic
		52	0	10	<30 min	

Due to publication limitations, includes selected randomized, controlled trials specifically investigating varying local anesthetic delivery method completed subsequent to a previously-published review article (Ilfeld¹), and is not intended as an exhaustive list.

—, not included for this treatment group.

^aMandatory bolus doses administered (not as needed).

strength equivalent when administering ropivacaine 0.2% at 8 mL/h as either a continuous basal or hourly bolus doses.¹⁴⁴ Similar results were reported for interscalene,¹⁴⁵ femoral,¹⁵² and popliteal catheters.¹⁵⁷ It would therefore be understandable to discount the concept of repeated bolus doses, except a new RCT did find analgesic benefit after thoracotomy in

administering a relatively large volume of levobupivacaine (15 mL) via paravertebral catheters once every 6 hours compared with a continuous infusion.¹⁵⁸ Although this study was somewhat confounded by the use of 2 different concentrations of levobupivacaine, it does raise the possibility that the strategy previously used—a repeated hourly bolus

equivalent to the volume from 1 hour of a basal infusion comparator—could be improved by scheduling larger bolus volumes over a longer period of time. Additional investigation at other catheter sites and administering a higher volume of local anesthetic is required (ClinicalTrials.gov, NCT02662023 and NCT02539628).

Lastly, evidence accumulates that prolonged ropivacaine infusions—even at relatively high doses >40 mg/h—have an extraordinarily low incidence of inducing toxicity signs, symptoms, or plasma levels.¹⁵⁹

PORTABLE INFUSION PUMPS

Little has changed regarding portable infusion pumps since they were last reviewed^{1,149,160} with 3 exceptions. First, more disposable pumps now allow a similar ability to adjust basal rates, bolus volume, and lockout times compared with their electronic, programmable counterparts.¹⁶¹ Second, a number of portable pumps now have the capability of delivering repeated bolus doses at intervals set by the provider.¹⁴⁴ How useful this capability will prove to be remains under investigation (see the previous section).¹³ However, the development with potentially the most influence on clinical care is the new ability of health care providers to remotely communicate directly with electronic infusion pumps via the Internet.¹⁶² In a prospective cohort study of 59 hospitalized subjects undergoing CPNB over approximately 3 days, investigators were alerted by text message when the need for pump changes arose because of an insensate extremity, muscle weakness, or difficulty during physical therapy. The infusion pumps would query subjects and, based on the responses, then communicate directly with health care providers who could remotely control the device. The mean (standard deviation) time for pump setting adjustment from the initial alert was 15 (2) minutes with no associated adverse events, demonstrating at least the feasibility of this technique.

AMBULATORY PERINEURAL INFUSION

In contrast to the topic of portable infusion pumps, research involving ambulatory CPNB has been relatively prolific in recent years.^{4,6,7,19,23,33,78,79,116,153,163–175} Originally, the objective of ambulatory perineural infusion was to simply improve analgesia for patients who were never intended to be hospitalized overnight.^{149,155} Because enhanced pain control and its many derived benefits have been well documented in earlier RCTs (reviewed previously),¹ nearly^{20,33,167,173,176,177} all recent investigation has centered on describing new applications or complications,^{4,6–8,19,23,171,174,175} optimizing perineural techniques (few major revelations),^{14,116,160} and reporting large series of cases (including over 1600 pediatric patients).^{78,79,165,168,169,178} Although most series were retrospective in design, 1 large multicenter effort prospectively enrolled over 1500 patients receiving ambulatory continuous interscalene nerve blocks at home.¹⁶⁸ This study documented relatively few CPNB-related complications after discharge with a 1.5% catheter dislodgement rate and no catastrophic incidents. Whereas major problems outside the hospital are very rare,¹⁷⁴ they can prove more challenging to treat than in hospitalized patients.^{171,174,179,180}

However, with the collective experience and thousands of published cases in the past 15 years, the main arguments

against ambulatory CPNB has shifted from a lack of validation and the risks of complications¹⁸¹ to instead the challenges of setting up and running an effective ambulatory service (“perineural catheter analgesia as a routine method after ambulatory surgery: effective but unrealistic”).^{182,183} This view is countered by others who contend that “rather than dismissing these techniques as too difficult, and settling for an unsubstantiated (but probably ineffective) alternative [wound infusion], future research should focus on facilitating the uptake of perineural infusions....”¹⁸⁴ Indeed, there are published accounts specifically addressing practitioners’ successes¹⁸⁵ and challenges¹⁸⁶ in developing and implementing ambulatory infusion programs.^{172,187}

A second goal of ambulatory infusion eventually developed: using improved pain control to allow patients—who would be expected to remain in the hospital—to be instead discharged earlier than otherwise possible.^{188,20,175} Theoretical benefits include improved patient satisfaction, decreased risk of nosocomial infection and health care provider error, and decreasing health care-related costs.^{170,189,190} Although multiple RCTs demonstrate that ambulatory CPNB reduces the time until discharge readiness,¹ only 2 have demonstrated a shortening of actual hospitalization duration.^{191,192}

Nevertheless, with interest growing in the “perioperative surgical home,” ambulatory CPNB is being viewed as a possible enabling intervention.¹⁹³ One recent example is an investigation that randomized subjects (n = 38) undergoing complex arthroscopic elbow surgery accompanied by a 60-hour continuous infraclavicular (brachial plexus) nerve block to either remain hospitalized for the 3-day standard of care or be allowed discharge as early as the morning after surgery (Table 3).¹⁷³ Both groups underwent continuous passive motion of the elbow for 14 days, and subjects discharged early had similar elbow range of motion after 2 weeks and 3 months compared with patients remaining hospitalized for at least 3 days. Furthermore, there were no statistically significant differences in pain scores, opioid requirements, patient satisfaction, and function-related questionnaires. Importantly, the cost of care for subjects remaining hospitalized was greater than for those allowed early discharge. Although there remains debate as to the significance of the degree of savings (15%),¹⁹³ these data are supported by an additional clinical trial that permitted a total avoidance of hospital admission.¹⁹⁴ This second investigation randomized subjects (n = 120) with a continuous popliteal nerve block having major orthopedic foot surgery to be discharged either after surgery or remain hospitalized for 2 nights (Table 3).¹⁹⁴ Total costs of care were decreased 79% in the early discharge group, and no other differences between treatments were detected, including pain scores, complications, and readmission rates. These savings are not applicable to practices within the United States because the surgical procedures under investigation—osteotomies and hallux valgus corrections—are already nearly exclusively performed as outpatients procedures, regardless of the presence of CPNB. However, the strong interest in these investigations may be an indication of the direction ambulatory infusion research—and practice worldwide—will take over the coming decade.

Table 3. Randomized, Controlled Clinical Trials Involving At Least 1 Treatment Group With a Continuous Peripheral Nerve Block

First Author, Year	Surgical Procedure	Treatment Group	Control Group(s) During Catheter Utilization	Primary Positive Findings During Catheter Use (Treatment Group Superior Unless Otherwise Noted)
Interscalene catheters				
Fredrickson et al ¹⁶³ (2010)	Minor arthroscopic shoulder	Ropivacaine 0.2% (n = 31) 2 mL/h + 5 mL PCB [60]	Catheters removed in recovery room (n = 30)	Lower resting and dynamic pain scores; less supplemental analgesic requirements
Malhotra et al ²⁰ (2013)	Adhesive capsulitis manipulation	Ropivacaine 0.2% (n = 2) 8 mL/h + 4 mL PCB [30]	Normal saline (n = 2) 8 mL/h + 4 mL PCB [30]	Lower average and dynamic pain scores; lower opioid analgesics; fewer awakenings because of pain; greater shoulder range of motion on day 1 as well as weeks 6 and 12 (preliminary data from a pilot study—underpowered for definitive conclusions)
Salviz et al ¹⁷⁶ (2013)	Arthroscopic rotator cuff repair	Ropivacaine 0.2% (n = 20) 5 mL/h + 5 mL PCB [60]	• Single injection only (n = 23) • No block or catheter (n = 20)	Catheter group with less pain, opioid requirements, and sleep disturbances; at 7 d (2-d infusion) only 26% of catheter group reported NRS ≥4 compared with 83% and 58% of single-injection and no block groups, respectively
Infraclavicular catheters				
Eng et al ¹⁷³ (2015)	Complex arthroscopic elbow	Ropivacaine 0.2% 7 mL/h + 5 mL PCB [30] Discharge as early as postoperative day 1 (n = 19)	Required to remain hospitalized 72 h (n = 19)	Total hospital cost of care was 15% lower in the early discharge group; no other differences between treatment groups including elbow range of motion
Paravertebral catheters				
Ilfeld et al ^{167,177} (2014) and (2015)	Mastectomy	Ropivacaine 0.4% (n = 30) 5 mL/h basal only	Normal saline (n = 30) 5 mL/h basal only	Lower resting and breakthrough pain scores; less pain-induced physical and emotional dysfunction during infusion; less chronic pain at 1 y
Karmakar et al ²²¹ (2014)	Modified radical mastectomy	Ropivacaine 0.25% (n = 60) 0.1 mL/kg/h basal only	• Single injection only (n = 57) • No block or catheter (n = 60)	No differences among groups during infusion period nor chronic pain incidence at 3 or 6 mo, but at 3 and 6 mo, both infusion and single-injection group had less severe pain, exhibited fewer symptoms and signs of chronic pain, and experienced better physical and mental health-related quality of life
Pintaric et al ²⁰⁴ (2011)	Thoracotomy (open lung surgery)	Levobupivacaine 0.125% and morphine 30 µg/mL (n = 16) 0.1 mL/kg/h + 0.1 mL/kg PCB [60]	Epidural levobupivacaine and morphine at same concentration and rate/bolus as paravertebral catheters	Similar analgesia but greater hemodynamic stability than epidural analgesia with less required colloid volume and vasopressors to maintain target oxygen delivery index
Transversus abdominis plane (TAP) catheters				
Heil et al ³³ (2014)	Abdominal or inguinal hernia repair	Ropivacaine 0.2% (n = 10) 10 mL/h basal only	Normal saline (n = 10) 10 mL/h basal only	No statistically significant difference in pain scores or supplemental analgesics (underpowered study because of curtailment of enrollment)
Niraj et al ³⁶ (2011)	Open renal or hepatobiliary	Bupivacaine 0.375% (n = 29) 1 mg/kg each of bilateral catheters every 8 h	Epidural bupivacaine 0.125% with fentanyl 2 µg/mL (n = 33) 6–12 mL/h + 2 mL PCB [30]	No statistically significant differences in any outcomes between treatments except that the TAP group required a higher dose of rescue analgesics
Adductor canal catheters (placebo controlled)				
Andersen et al ⁶⁴ (2013)	Total knee arthroplasty	Ropivacaine 0.75% (n = 20) 15 mL “twice daily”	Normal saline (n = 20) 15 mL “twice daily”	Lower average resting and breakthrough (maximum) pain scores and fewer sleep disturbances; ambulation possible in 100% vs 65% of subjects in the ropivacaine vs saline groups, respectively
Grevstad et al ⁶⁵ (2015)	Severe pain on flexion after total knee arthroplasty	Ropivacaine 0.75% (n = 24) 30 mL single injection	Normal saline (n = 25) 30 mL single injection	Reduced pain during active flexion of the knee, but a large proportion (78%) still had at least moderate pain on flexion

(Continued)

Table 3. Continued

First Author, Year	Surgical Procedure	Treatment Group	Control Group(s) During Catheter Utilization	Primary Positive Findings During Catheter Use (Treatment Group Superior Unless Otherwise Noted)
Hanson et al ⁶¹ (2014)	Total knee arthroplasty	Ropivacaine 0.2% (n = 36) 8 mL/h basal only	Sham catheter (n = 40)	Decreased resting and dynamic pain scores, lower required supplemental analgesics, greater quadriceps strength, greater ambulation distance, and higher satisfaction
Jaeger et al ⁴⁷ (2012)	Total knee arthroplasty	Ropivacaine 0.75% (n = 21) 30 mL single injection	Normal saline (n = 20) 30 mL single injection	Decreased pain during hours 1–6 and less nausea
Jæger et al ⁶³ (2014)	Revision total knee arthroplasty	Ropivacaine 0.75% (n = 14) 30 mL bolus; 6 h later 0.2% 15 mL bolus; then ropivacaine 0.2% 8 mL/h	Normal saline (n = 13) administered at the same time points and volumes as the ropivacaine group	Lower pain on knee flexion at 4 h (underpowered study for remainder of endpoints)
Jenstrup et al ⁶² (2012)	Total knee arthroplasty	Ropivacaine 0.75% (n = 34) 30 mL bolus; then 15 mL bolus at 6, 12, 18, and 24 h	Normal saline (n = 37) administered at the same time points and volumes as the ropivacaine group	Lower dynamic pain on flexion and supplemental analgesic requirements, superior ambulation, and mobilization at 24 h
Fisker et al ⁴⁵⁹ (2015)	Major ankle surgery	Continuous popliteal sciatic blocks for all subjects Ropivacaine 0.2% (n = 20) 5 mL/h basal only	Normal saline (n = 24) 5 mL/h basal only	No differences between treatment groups detected
Adductor canal catheters (versus femoral catheters)				
Elkassabany et al ⁵⁹ (2016)	Total knee arthroplasty	Adductor ropivacaine 0.2% (n = 31) 8 mL/h basal only	Femoral ropivacaine 0.2% (n = 31) 8 mL/h basal only	Greater quadriceps femoris strength ^a
Jæger et al ⁵⁰ (2013)	Total knee arthroplasty	Adductor ropivacaine 0.2% (n = 22) 8 mL/h basal only	Femoral ropivacaine 0.2% (n = 26) 8 mL/h basal only	Greater quadriceps femoris strength (52% vs 18% of baseline)
Machi et al ⁵⁸ (2015)	Total knee arthroplasty	Adductor ropivacaine 0.2% (n = 39) 6–8 mL/h + 4 mL PCB [30]	Femoral ropivacaine 0.2% (n = 39) 4–8 mL/h + 4 mL PCB [30]	Improved ability to stand, sit, and ambulate, but higher dynamic pain scores than femoral infusion
Shah and Jain ⁷⁴ (2014)	Total knee arthroplasty	Adductor ropivacaine 0.75% (n = 48) 30 mL, then ropivacaine 0.25% 30 mL every 4 h until postoperative day 2	Femoral ropivacaine 0.75% (n = 50) 30 mL, then ropivacaine 0.25% 30 mL every 4 h until postoperative day 2	Improved ability to stand, sit, and ambulate, as well as climb stairs; decreased time until actual discharge (3.1 vs 3.9 d)
Sztain et al ⁵⁷ (2015)	Unicompartment knee arthroplasty	Adductor ropivacaine 0.2% (n = 15) 6–8 mL/h + 4 mL PCB [30]	Femoral ropivacaine 0.2% (n = 15) 2–6 mL/h + 4 mL PCB [30]	Fewer days until discharge readiness; improved ability to sit, stand, and ambulate; but higher resting pain scores than femoral infusion
Zhang et al ²⁰⁹ (2014)	Total knee arthroplasty	Adductor ropivacaine 0.2% (n = xx) 5 mL/h + 5 mL PCB [30]	Femoral ropivacaine 0.2% (n = x) 5 mL/h + 5 mL PCB [30]	Greater quadriceps femoris strength (52% vs 18% of baseline)
Femoral catheters				
Al-Zahrani et al ⁴⁴⁷ (2015)	Total knee arthroplasty	Femoral bupivacaine 0.2% (n = 25) 5 mL/h basal only (single-injection sciatic block 15 mL bupivacaine 0.25%)	Epidural bupivacaine 0.0625% + fentanyl 2 µg/mL (n = 25) 5–10 mL/h basal only	No differences between treatment groups detected
Sakai et al ¹⁹⁸ (2013)	Total knee arthroplasty	Femoral ropivacaine 0.15% (n = 30) 4 mL/h basal only	Epidural ropivacaine 0.15% (n = 30) 4 mL/h basal only	Shorter time to achieve 120° knee flexion (8 vs 15 d), improved dynamic analgesia, and lower supplemental analgesic requirements
Baranović et al ¹⁹⁶ (2011)	Total knee arthroplasty	Femoral levobupivacaine 0.25% (n = 35) 5–6 mL/h basal only	No catheter (n = 36)	Improved analgesia, improved knee flexion on postoperative day 2, lower intravenous morphine requirements, and dramatically lower opioid-related adverse events such as urinary retention, sedation, and nausea/vomiting

(Continued)

Table 3. Continued

First Author, Year	Surgical Procedure	Treatment Group	Control Group(s) During Catheter Utilization	Primary Positive Findings During Catheter Use (Treatment Group Superior Unless Otherwise Noted)
Peng et al ²¹⁶ (2014)	Total knee arthroplasty	Femoral ropivacaine 0.15% (n = 127) 5 mL/h + 5 mL [30]	No catheter (n = 123)	Less supplemental analgesics required and improved knee flexion during infusion, and lower incidence of chronic pain and improved knee flexion at 3 and 6 mo after surgery
Wu and Wong ¹⁹⁷ (2014)	Total knee arthroplasty	Femoral levobupivacaine 0.08% (n = 30) 8–12 mL/h basal only	No catheter (n = 30)	Lower intravenous opioid requirements, fewer opioid-related side effects, improved satisfaction with analgesia, and increased ambulation ability
Sciatic catheters				
Elliot et al ²⁰⁰ (2010)	Hind foot or ankle surgery	Bupivacaine 0.25% (n = 27) 4 mL/h + 1 mL [60]	Normal saline (n = 27) 4 mL/h + 1 mL [60]	Lower pain scores and less supplemental analgesic requirements
Saporito et al ¹⁹⁴ (2014)	Toes 2–5 osteotomy or hallux valgus correction	Ropivacaine 0.2% 5 mL/h + 5 mL PCB [60] Discharged day of surgery (n = 60)	Required to remain hospitalized 2 nights (n = 60)	Total costs of care were 79% lower in the early discharge group; no other differences between treatment groups including pain scores, complications, and readmission rates
Cappelleri et al ⁹⁶ (2011)	Total knee arthroplasty	Continuous posterior lumbar plexus blocks for all subjects Subgluteal levobupivacaine 0.06% (n = 19) 0.1 mL/kg/h	Subgluteal normal saline (n = 19) 0.1 mL/kg/h	Lower resting and dynamic pain scores, less supplemental opioids, lower incidence of nausea and vomiting, improved knee flexion and ambulation
Sato et al ²⁰¹ (2014)	Total knee arthroplasty	Continuous femoral nerve blocks for all subjects Subgluteal ropivacaine 0.2% (n = 30) 5 mL/h	Subgluteal normal saline (n = 30) 5 mL/h	Lower resting pain scores and less supplemental opioids
Wegener et al ^{97,220} (2011) and (2013)	Total knee arthroplasty	Continuous femoral nerve blocks for all subjects Parasacral levobupivacaine 0.125% (n = 30) 10 mL/h	• Parasacral single injection only (n = 30) • No block or catheter (n = 30)	Catheter group with lower dynamic pain scores compared with the other 2 treatment groups on postoperative days 1 and 2 during the infusion; and in a subset of the most initially disabled subjects preoperatively, joint stiffness was reduced at 3 and 12 mo, and dynamic pain reduced at 3 mo compared with the no block or catheter group

Due to publication limitations, includes selected reports published subsequent to a previously-published review article (Ilfeld⁴), and is not intended as an exhaustive list. In addition, investigations included in Table 2 are excluded.
 NRS, numeric rating scale for pain (0–10, 0: no pain, 10: worst imaginable); PCB, patient-controlled bolus volume (lockout period in minutes).
^aInfusions were discontinued morning of postoperative day 1 before endpoint evaluation.

BENEFITS

Novel indications for CPNB have been published within the past few years, suggesting benefits for an even wider array of morbidities.^{13,15,20–24,28–36,47,61–65} New RCTs have provided evidence that adding a perineural infusion after a single-injection peripheral nerve block improves postoperative analgesia (and in most cases decreases supplemental analgesic requirements) using interscalene,^{163,176,195} paravertebral,¹⁶⁷ adductor canal,^{47,61–65} femoral,^{196–199} and sciatic catheters (Table 3).^{96,97,200,201} Compared with epidural infusions,²⁰² CPNB provides similar analgesia²⁰³ but improves hemodynamic stability (presumably by inducing less sympathectomy)^{27,204,205} and after knee arthroplasty shortens the time to achieve flexion goals, improves analgesia, and lowers supplemental analgesic requirements.¹⁹⁸ Compared with intrathecal morphine, continuous posterior lumbar plexus blocks provide similar analgesia with lower supplemental opioid requirements and incidence of pruritis.²⁰⁶ Data continue to accumulate, demonstrating that CPNB provides

superior analgesia compared with continuous wound infusions.^{99,207,208}

Because of the association between continuous femoral nerve blocks and falling after knee arthroplasty,^{51,52,54} the past 5 years have seen a plethora of research validating adductor canal catheter effectiveness after major knee surgery^{47,61–65} based on the theory that any risk of falling will be decreased because of less induced quadriceps weakness compared with femoral infusion (Table 3).^{50,59} Of the 6 RCTs directly comparing continuous adductor canal and femoral nerve blocks,^{50,57–59,74,209} 3 demonstrated dramatic improvements for subjects with adductor catheters in the ability to stand, sit, ambulate, and climb stairs.^{50,57,58,74} One study did not investigate ambulation²⁰⁹; but the 2 remaining RCTs failed to detect mobilization improvements using an adductor infusion—although they did document and quantify improved quadriceps femoris strength (52% vs 18% of baseline in one).^{50,59} It is noteworthy that these 2 latter studies provided solely a fixed basal infusion (8 mL/h)

without either patient-controlled or repeated provider-administered bolus doses,^{50,59} which may have decreased adductor infusion effectiveness. In addition, 2 of the RCTs detected improved analgesia for subjects with femoral infusions at either rest (unicompartment arthroplasty)⁵⁷ or with movement (tricompartament arthroplasty),⁵⁸ whereas others failed to detect differences between the 2 catheter locations. Lastly, 1 of the investigations reported a decreased time until discharge favoring the adductor catheters (3.1 vs 3.9 days),⁷⁴ although there were issues raised regarding its protocol/findings⁶⁶⁻⁶⁸ and a similar RCT detected no decrease in time until discharge readiness or actual discharge,⁵⁸ albeit with slightly different criteria. What does appear likely is that continuous adductor canal blocks are associated with greater mobilization ability while providing similar analgesia compared with their femoral counterparts.⁶⁰ What remains unclear is the ideal catheter insertion location/protocol,^{70,71} optimal method of local anesthetic delivery (eg, basal infusion vs repeated bolus doses, basal rate, bolus volume), and if an optimized delivery regimen can shorten hospitalization duration.^{144,210,211}

In an effort to further improve analgesia after total knee arthroplasty,^{212,213} 3 recent RCTs have investigated the effects of adding a continuous sciatic nerve block to a continuous femoral or posterior lumbar plexus (psoas compartment) block.^{96,97,201} All demonstrated lower pain scores and decreased supplemental analgesic consumption,^{96,97,201} and 1 detected a lower incidence of nausea and vomiting as well as improved knee flexion and ambulation.²⁰¹ As has been previously opined, there are potential drawbacks to providing a continuous sciatic nerve block such as the extra time required to place a second catheter, an inability to fully evaluate sciatic nerve function postoperatively,²¹⁴ and interference with physical therapy goals (eg, foot drop, leg weakness).²¹⁵

Although there are relatively few demonstrated benefits of CPNB after catheter removal,¹ there are significant additions to our knowledge base within recently published data. Two RCTs found that a 2- to 3-day postoperative continuous interscalene or femoral nerve block resulted in less pain,^{176,216} opioid requirements,^{176,216} and sleep disturbances¹⁷⁶ on postoperative day 7 compared with a control group after shoulder and knee procedures, respectively. Similarly, 2 RCTs add to the previous evidence that a continuous femoral nerve block after total knee arthroplasty improves joint flexion for up to 6 months.^{198,216}

However, it is the possibility of decreasing persistent postsurgical pain that has perhaps garnered the most attention and optimism.^{217,218} Four new RCTs add data to the single previous positive study that involved the addition of a femoral catheter to a popliteal infusion for major ankle surgery.²¹⁹ One study reported that providing a continuous femoral nerve block after total knee arthroplasty reduced chronic pain at 3 and 6 months,²¹⁶ and another involving the same surgical procedure found that providing a continuous sciatic nerve block in addition to a femoral infusion resulted in a reduction of dynamic pain at 3 months (no difference at 12 months for either trial).²²⁰ Finally, 2 RCTs investigating continuous paravertebral blocks after mastectomy detected improvements in analgesia up to a full year

after surgery,^{177,221} including superior physical and mental health-related quality of life²²¹ and decreased pain-related physical and emotional dysfunction.¹⁷⁷

COMPLICATIONS

Probably the largest change in the CPNB literature of the past 5 to 6 years is the proportion of reports involving ultrasound guidance versus nerve stimulation with the former now eclipsing the latter to an overwhelming degree. This is undoubtedly multifactorial; but a predominant reason is probably that the risk of inaccurate and/or difficult catheter insertion is, on average, decreased with the use of ultrasound guidance.¹⁸⁷ However, the incidence for all CPNB-related complications can vary dramatically, most likely because of heterogeneous catheter insertion equipment, techniques, anatomic locations, and infusion protocols. For example, the reported frequency of catheter failure over the past few years varies between 0.5% and 26%.^{79,222} Accordingly, precise complication rates will not necessarily be widely applicable. This section reviews reports of adverse events published since the previous review article,¹ and readers are directed to that report for a complete examination of all possible complications.

Relatively few complications during insertion have been reported in recent years, perhaps because of the widespread adoption of ultrasound guidance (or possibly because all the adverse events had been previously published). However, new cases do include the inadvertent penetration of the epidural space^{113,223} and a catastrophic incident involving an unidentified intrathecal placement bolused on the wards.^{224,225} In addition, a single report describes the potential contamination of the surgical site caused by leakage from an interscalene catheter with the patient in a seated position.²²⁶ In contrast, reports of adverse events occurring during infusion are more common, including those reported previously such as hoarseness,²²⁷ dyspnea,^{169,228} and respiratory distress²²⁹ associated with continuous interscalene nerve blocks.¹⁶⁸ Although 1 healthy-volunteer study reported a catheter dislocation rate of 25% and 5% for femoral and interscalene catheters, respectively, over a period of 5 hours,²³⁰ the incidence of dislodgement reported in both RCTs and large series is dramatically lower,^{77,168} even for ambulatory pediatric patients.⁷⁹ Leakage at the catheter site continues to be an issue in a small minority of cases,^{79,168} but 2-octyl cyanoacrylate glue can decrease this problem by a factor of 10.²³¹

One case report describes a patient with an ambulatory popliteal sciatic block who fractured a metatarsal 2 days into the infusion, which was recognized only after the catheter was removed the next day.¹⁷⁴ In contrast, it is reassuring that there is 1 case of limb ischemia because of a surgically induced axillary artery injury and 3 reports of compartment syndrome all identified in a timely fashion by breakthrough pain not masked by the presence of a CPNB.²³²⁻²³⁵

Catheters have been accidentally cut during tunneling,²³⁶ suture removal,²³⁷ and for unknown reasons (most likely catheter withdrawal into the needle).²³⁸ Although it is common to leave a fractured epidural catheter remnant in situ, health care providers should be cognizant that many perineural catheters contain coiled wire, which is

at risk for heating during subsequent magnetic resonance imaging.²³⁹ Catheter retention during withdrawal can also occur caused by a perineural loop,¹⁶⁵ knot,²⁴⁰ kink,^{241,242} or adherence.^{171,179,243–247} Although multiple catheter designs have been involved with retained catheter reports,^{240,242} it is notable that within the past few years, 1 specific stimulating catheter (StimuCath; Teleflex, Morrisville, NC) has been overwhelmingly the predominant model described: 9 publications reporting a total of 18 separate cases.^{165,171,179,241,243–247} One investigator opined referring to these case reports, “While stimulating peripheral nerve catheters do have clinical utility, the expanding body of literature describing catheter entrapment is worrisome.”²⁴⁸

Regarding infusion-induced local anesthetic toxicity, both older¹ and more recent evidence suggest that perineural infusion-induced local anesthetic toxicity is very rare.^{159,249} Similarly, major hematoma formation is extraordinarily infrequent and usually occurs in the presence of anticoagulation and/or comorbidity such as myeloproliferative thrombocytosis.²⁵⁰ There is limited new information regarding the concurrent use of anticoagulants and perineural catheters,^{251–253} and no new recommendations from the American Society of Regional Anesthesia and Pain Medicine have been published since the previous review article.^{254,255} Of note, some investigators have advocated replacing epidural with paravertebral or TAP catheters in certain situations²⁵⁶ based on the theoretical premise that a hematoma in the peripheral nervous system carries less risk of catastrophic nerve injury.^{35,37} Minimal information regarding CPNB-related infection has been published in recent years,^{77,79,168} other than the identification of diabetes and obesity as risk factors for catheter-associated infection^{257,258} and a few new cases of previously described related complications such as abscess formation.^{259–262} Of note, although the incidence of infection increases with infusion duration, there remains no “maximum” time period for a perineural catheter (although there are various regulations regarding the maximum duration of local anesthetic contained within a reservoir); and the longest reported infusion of 88 days was recently published.⁷

In contrast, there has been a significant amount of data published in the past few years involving neurologic risk in the presence of a CPNB.²⁶³ In most cases of postoperative neurologic symptoms (PONS), it is problematic assigning causality to the surgical procedure, CPNB, or simply perioperative injuries (eg, tourniquet or positioning injuries on an unrelated part of the body). Interpreting the available data is further complicated because of a lack of controls and/or randomization, which lead to multiple types of bias. An excellent example is a prospective, uncontrolled cohort study of patients with continuous popliteal sciatic nerve blocks (n = 151) after foot and ankle surgery reporting an alarming 41% incidence of PONS within 2 weeks, 24% at 34 weeks, and 4% after 48 weeks.²⁶⁴ A similar retrospective study (n = 157) found a 1.9% incidence of unresolved PONS at 11 months.²⁶⁵ These risks are an order of magnitude higher than previous estimates for popliteal infusions (0%–0.4%)^{266,267} and are most likely because of numerous biases, beginning with selection bias.

Another relatively new retrospective investigation of 1182 continuous interscalene and femoral nerve blocks

identified 4 (0.3%) patients with PONS at any time point, with 1 of these cases resolving by 6 months.²⁶⁸ Of note, these investigators reported an increased incidence of PONS lasting >6 months among patients with continuous versus single-injection peripheral nerve blocks (0.24% vs 0.07%; *P* = .08).²⁶⁸ It is important to be aware of the very high risk of selection bias from this retrospective, nonrandomized cohort (eg, larger surgical procedures—with inherently higher neurologic risk—more represented in the catheter group). The most reliable, recently published data are derived from 2 prospective investigations of over 2500 interscalene and femoral catheters, reporting a PONS incidence of 4.9% to 5.3% resolving by 6 months with all but 0.3% to 0.7% of these resolving by 11 months.^{168,269} To emphasize, it is critical that practitioners are cognizant of the fact that these values approximate association and not necessarily causation: an unknown percentage of subjects with PONS would have experienced them without any regional analgesic because of the surgery itself or other factors. Unfortunately, the available data do not suggest that ultrasound guidance has a “meaningful impact on the incidence of PONS,” so switching from a different insertion technique is not expected to decrease the rate of PONS.²⁷⁰

The risk of falling after knee and hip arthroplasty has become better appreciated within the previous decade.^{271,272} Single-injection femoral nerve blocks do not appear to increase this risk²⁷³; but data from randomized, controlled trials suggest that a continuous femoral or psoas compartment block is associated with a 4 to 5 times increased risk of falling,^{51,54,274} although some investigators have questioned this correlation.^{275,276} Regardless of the relationship between CPNB and falls, this complication continues to occur even with the implementation of specific, intensive fall prevention programs.^{52,56,277,278} Although replacing continuous femoral nerve blocks with adductor canal infusions have been proposed as a method to decrease the risk of falling because of decreases induced quadriceps weakness,^{50,59} such an association has yet to be demonstrated.^{59,279}

ALTERNATIVE MODALITIES

While perineural infusion has become accepted and now routine within anesthesiology, there are a number of novel, alternative analgesic modalities either currently available or under development/investigation. Although numerous analgesic possibilities are available,^{99,207,280–282} publication limitations prohibit inclusion of every option.¹⁸² The current article compares and contrasts 4 of the most novel analgesic alternatives to CPNB.

LOCAL ANESTHETIC ADJUVANTS

Single-injection peripheral nerve blocks have multiple benefits over their continuous infusion counterparts, including less time required for administration, management, follow-up; lower risk of infection; no risk of leakage, catheter dislodgement, or pump malfunction; and simply cost. Of course, the reason that CPNB is used despite these relative disadvantages is that the duration of treatment effects may be prolonged beyond the duration of a single-injection peripheral nerve block.¹ However, a single-injection block with a similar duration to what is possible with CPNB

would provide the benefits of a 1-shot block without the drawbacks of a perineural catheter and infusion.²⁸³ Toward this end, multiple medications—some in just the past few years—have been combined with (and without) local anesthetic, including opioids,^{284–287} clonidine,^{288,289} dexmedetomidine,^{290,291} dexamethasone,^{292–294} epinephrine, magnesium, midazolam, and tramadol.²⁹⁵

Unfortunately, most reported adjuvants prolong analgesia by fewer than 12 hours^{295,296} with even the most effective—buprenorphine and dexamethasone—reliably providing <24 hours of pain control.^{284–287,297} Many of the additives may increase the incidence of side effects such as pruritis,²⁹⁸ nausea/vomiting,^{287,298} hypotension,²⁸⁸ bradycardia,^{288,295} and sedation.^{288,295} Optimal doses remain unknown,²⁹⁹ and the risk of neurotoxicity remains a concern for multiple agents.²⁹⁵ Importantly, because systemic administration may result in similar or even superior³⁰⁰ prolongation of analgesic benefits versus perineural administration^{291,301–303}—although there are exceptions^{286,304}—and there is no adjuvant currently approved by the US FDA for perineural administration, the risk–benefit ratio of perineural administration remains in question at the time of this writing.

While there are no direct comparisons of CPNB and single-injection blocks including an adjuvant, it is unlikely that such studies will be conducted because most perineural catheters are inserted for use of at least 2 days,¹ and no adjuvant given by any route of administration has been shown to reliably extend analgesia even 1 full day. The 2 techniques do not, in fact, “compete” but are instead complementary, depending on the desired duration of block effects.

LIPOSOME LOCAL ANESTHETIC

Liposomes consist of 2 hydrophobic tails and a hydrophilic head³⁰⁵ and can form vesicles to act as a medication “depot” (Figure 1).^{306,307} After administration, the liposomes gradually break down, resulting in an extended release of medication.^{308,309} Combining liposomes and a local anesthetic (lidocaine) was first proposed in 1979,³¹⁰ initially used in humans in 1988,³¹¹ and first reported for postoperative

analgesia in 1994.^{310,312} Although multiple subsequent reports were published,^{313–321} a liposome local anesthetic was not approved by the US FDA until 2011 (Exparel liposome bupivacaine; Pacira Pharmaceuticals, Parsippany, NJ) for administration at the surgical site to provide postoperative analgesia in adults.³⁰⁷

Two multicenter RCTs demonstrated superior postoperative analgesia of this approved medication compared with placebo wound infiltration after hemorrhoidectomy³²² and unionectomy.³²³ In contrast, when compared with bupivacaine HCl (“standard” bupivacaine), 10 of the 12 currently published RCTs were negative for their primary (and most secondary) analgesic end points.^{324–330} Of the 2 positive RCTs versus bupivacaine HCl, 1 involved hemorrhoidectomy,³³¹ although another similar trial had negative results.³²⁴ The second positive RCT involved submuscular augmentation mammoplasty in which mean pain scores were reduced by <1 on the 0 to 10 numeric rating scale and the investigators concluded, “...it is our assertion that the additional cost of liposomal bupivacaine is unjustified for this particular use.”³³² Some of these 14 RCTs were dose–response studies, not powered to be a conclusive test of efficacy; and when combined with the placebo-controlled trials, there were some detected positive associations for secondary endpoints such as pain scores at individual time points,³³³ opioid use (although differences were minimal),³³³ and duration until first use of opioid analgesics.^{324,333} However, considering the new medication costs an estimated 100 times that of bupivacaine HCl, it is incumbent on those proposing the conversion to produce data conclusively demonstrating superiority.³³⁰ Various large RCTs currently ongoing should provide much-needed data to help practitioners make evidence-based decisions involving this analgesic modality (ClinicalTrials.gov NCT02713490, NCT02111746, NCT02197273).

There are no RCTs directly comparing CPNB with liposome bupivacaine wound infiltration.³³⁴ The only direct comparison to a single-injection femoral nerve block after total knee arthroplasty suggests that liposome bupivacaine

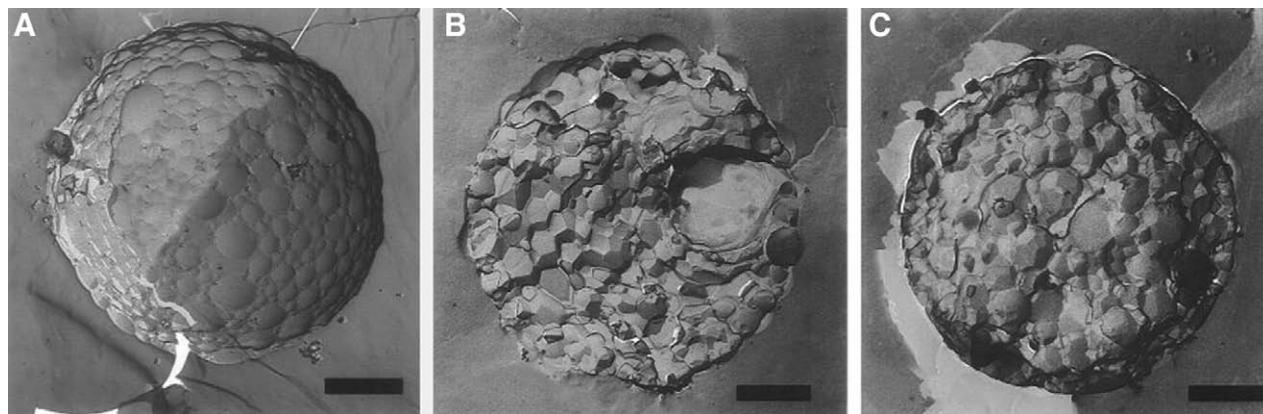


Figure 1. Liposome local anesthetic: (A) electron micrograph of a replica showing the outer surface of a multivesicular liposome. The abrupt change in the gray scale near the center of the multivesicular liposome is because of the shadowing effect of the freeze-fracture replica. The white region near the bottom is a crack in the replica, and (B and C) electron micrographs of freeze-fracture replicas showing cross sections through 2 multivesicular liposomes. The multivesicular liposomes are, on average, approximately 10 μm in diameter. The polyhedral interior compartments range from approximately 100 nm to several micrometers. The bars represent 2 μm . Reprinted with permission from Spector MS, Zasadzinski JA. Topology of multivesicular liposomes, a model biliquid foam. *Langmuir*. 1996;12:4704–4708. Copyright 1996 American Chemical Society.

infiltration provides inferior analgesia during the duration of the peripheral nerve block without subsequent analgesic differences between the 2 treatments.³³⁵ Considering that there are now 4 negative published RCTs comparing liposome bupivacaine with bupivacaine HCl infiltration after total knee arthroplasty,^{324,326–328} and the literature is replete with positive studies involving CPNB,¹ the evidence certainly does not suggest even equivalence between these 2 modalities.

In contrast to wound infiltration, recently published data from 1 RCT strongly suggest that liposome bupivacaine within a single-injection subcostal TAP block provides statistically and clinically superior analgesia to bupivacaine HCl up to 3 days after robotic-assisted hysterectomy.³³⁶ In a separate RCT, few differences were detected between a continuous subcostal TAP block and epidural infusion after open renal or hepatobiliary surgery,³⁶ although this investigation was designed as a superiority study and the negative findings should be viewed as inconclusive and not equivalent. Therefore, a randomized comparison of a TAP with liposome bupivacaine bolus compared with either an epidural infusion or a perineural local anesthetic TAP infusion appears warranted.^{337,338} Of note, the US FDA recently revised the label for the single approved liposome bupivacaine formulation explicitly including, “infiltration into the transversus abdominis plane (TAP) which is a field block technique [is] covered by the approved indication for EXPAREL.”

Although no liposome local anesthetic is currently approved for use within the epidural space³³⁹ or peripheral nerve blocks, a great deal of related research has been completed (if not all published).³⁰⁷ Both preclinical toxicology and clinical data indicate that liposome bupivacaine has a safety profile at least as favorable as bupivacaine HCl.^{340–350} Although phase 1 to 3 clinical trials involving the use of liposome bupivacaine have been reported for intercostal and ankle blocks,^{306,307,340} the most published data may be found for femoral nerve blocks.^{351,352} No direct comparisons with CPNB are available, but liposome bupivacaine in a femoral nerve block produced over 72 hours of analgesia with an incomplete motor block in healthy volunteers³⁵¹ and demonstrated analgesic activity for up to 72 hours versus placebo in subjects after total knee arthroplasty (albeit extraordinarily minimal analgesic differences after 24 hours).³⁵² Further sizable RCTs involving adductor canal, brachial plexus, and femoral nerve blocks with liposome bupivacaine are ongoing (ClinicalTrials.gov NCT02607579, NCT02713230, NCT02713178).

Theoretical benefits over CPNB include the avoidance of catheter insertion (eg, less procedure time, no catheter management/removal), the lack of an infusion pump and anesthetic reservoir to purchase/carry, a lower risk of infection, and no risk of catheter dislodgement or leakage.³⁵³ It is emphasized that at the time of this writing, there are no liposome bupivacaine local anesthetics approved for use in the epidural space³³⁹ or peripheral nerve blocks (other than the possible exception of TAP blocks, depending on how this block is categorized).

CRYOANALGESIA

Cryoneurolysis is the application of exceptionally low temperatures to reversibly ablate peripheral nerves, resulting



Figure 2. Cryoanalgesia: (A) the Joule-Thomson effect producing very cold temperatures resulting from gas flowing from a high- to low-pressure chamber (used with permission from B.M.I.), and (B) a portable cryoneurolytic device (lovera; Myoscience, Fremont, CA). Inset: 3-needle tip for cryoneurolysis of superficial nerves.

in temporary analgesia termed “cryoanalgesia.”³⁵⁴ The first cryosurgical apparatus was described in 1961,³⁵⁵ and modern cryoprobes transmit a gas (usually nitrous oxide or carbon dioxide) at high pressure down their length, through a minute opening, and into the sealed distal tip at a lower pressure (Figure 2A).³⁵⁶ Explained by the Joule-Thomson effect, a large drop in temperature occurs when the gas moves from a high to low pressure inducing brisk expansion and absorption of heat.³⁵⁷ The gas is returned out of the body through a larger diameter (low pressure) cylinder in the middle of the shaft. This closed circuit ensures that all gas exits the body. The intense cold temperature at the probe tip produces Wallerian degeneration—a reversible breakdown of the nerve axon—subsequently inhibiting transmission of afferent and efferent signals. However, because the temperature resulting in irreversible degeneration—approximately -100°C —is colder than the boiling point of the gas (carbon dioxide: -79°C ;

nitrous oxide: -88°C), the remaining endoneurium, perineurium, and epineurium remain intact and the axon regenerates at a rate of approximately 1 to 2 mm/d.³⁵⁶

Cryoneurolysis has been used via the surgical incision to treat acute pain after thoracotomy,^{358–374} tonsillectomy,³⁷⁵ and herniorrhaphy.^{376,377} Alternatively, ultrasound may be used to guide^{378,379} a percutaneously inserted probe to a peripheral nerve to provide analgesia and has been described for various chronic pain conditions.^{380–385} The combination of ultrasound and newly designed, FDA-approved handheld cryoneurolysis devices^{386,387} may now make percutaneous cryoanalgesia a valuable postoperative analgesic alternative to CPNB (Figure 2B).³⁵⁴ The largest limiting factors when applying this technique to acute pain states are (1) the inhibition of efferent signals effectively paralyzing innervated muscles; and (2) the relatively unpredictable duration of action measured in multiple weeks and often months. Therefore, the modality has historically been used to target sensory-only nerves,³⁸⁸ although mixed motor–sensory nerves have been cryoablated to treat spasticity,³⁸⁹ and pre-clinical studies found no lasting changes to the structure or function of motor nerves after remyelination.^{386,387}

Surgical procedures possibly amenable to cryoneurolysis include iliac crest bone harvesting (superficial superior cluneal nerves), total knee arthroplasty (anterior femoral cutaneous and infrapatellar saphenous nerves), various thumb surgeries (superficial branch of the radial nerve), rotator cuff repair (suprascapular nerve), and digit/limb amputations, among others.^{354,356} Although there are available cryoneurolysis devices currently approved by the US FDA for relief of pain, the use of cryoanalgesia to treat acute pain requires a great deal of further investigation with both RCTs and large series. It remains undetermined whether the duration of denervation can be shortened (eg, decreasing the freezing interval or number of cycles) and the incidence of adverse events such as

neuralgias after thoracotomy.^{372–374} Direct comparisons with CPNB are unavailable, but some theoretical benefits of cryoneurolysis include an ultralong duration of action, no catheter management/removal, the lack of an infusion pump and anesthetic reservoir to carry, a lower risk of infection, and no risk of local anesthetic toxicity, catheter dislodgement, or leakage.

PERCUTANEOUS PERIPHERAL NERVE STIMULATION

Electric current applied in both the central and the peripheral nervous systems induces analgesia. There are numerous theories regarding the mechanism of action,³⁹⁰ but most are usually based on “gate control theory” by Melzack and Wall³⁹¹: current activates large-diameter myelinated afferent peripheral nerves which then—within the spinal cord—impede pain signal transmission from small-diameter pain fibers to the central nervous system.^{392,393} Implanted spinal cord and peripheral nerve stimulators have since been used to treat multiple chronic pain states.^{394–398} In contrast, the use of peripheral nerve stimulation to treat acute/postoperative pain is extraordinarily rare,^{399–401} in no small part because of cutaneous pain fiber activation with transcutaneous electrical nerve stimulation³⁹² and the invasive requirement of surgically implanting/removing peripheral nerve electrodes/leads.^{402,403}

Electrical leads are now available with a diameter small enough to allow passage through a needle, allowing percutaneous insertion (Figure 3A).^{404–409} Precise placement is possible using ultrasound guidance^{410,411} and has been reported to treat chronic pain.^{412–415} More recently, postoperative pain was treated using ultrasound-guided percutaneous peripheral nerve stimulation.^{416–416c} In one report, femoral—and in 2 cases sciatic—leads were inserted in subjects ($n = 5$) 8 to 58 days after total knee arthroplasty.⁴¹⁶ Percutaneous peripheral nerve stimulation decreased pain an average of 93% at

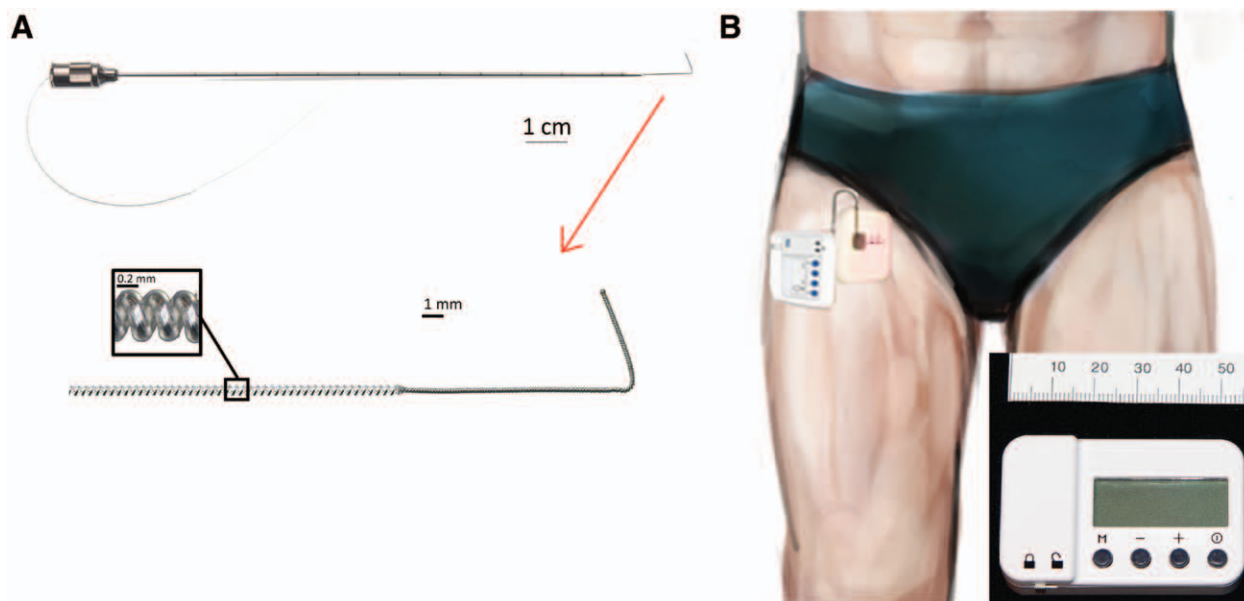


Figure 3. Percutaneous peripheral nerve stimulation: (A) a preloaded, small-diameter (0.2 mm), open-coiled, helical electrical lead with an anchoring wire preloaded within the 12.5-cm, 20-g insertion needle (MicroLead; SPR Therapeutics, Cleveland, OH) and (inset) a small-diameter (0.2 mm), open-coiled, helical electrical lead with an anchoring wire (MicroLead; SPR Therapeutics); and (B) a stimulator small enough to be simply adhered to the skin during use (SPR Therapeutics) (both used with permission from B.M.I.).

rest (reduced from a mean of 5.0 to 0.2 on a 0–10 numeric rating scale) with 4 of 5 subjects experiencing complete resolution of pain. During passive and active knee motion, pain decreased an average of 27% and 30%, respectively. Neither maximum passive nor active knee range of motion was consistently affected in this small cohort of subjects.

There are no direct comparisons with CPNB, but theoretical benefits of percutaneous peripheral nerve stimulation are numerous.^{416d} Leads function optimally when inserted 0.5 to 3.0 cm from a target peripheral nerve, negating the importance of location within a particular facial plane. Electrical generators are now so minute that their footprint is smaller than a business card and may be literally adhered to a patient's limb, so there is no large portable infusion pump or local anesthetic reservoir to carry (Figure 3B). Helically coiled leads are designed to minimize the risks of migration and fracture and decrease the infection risk to approximately 0.03 per 1000 indwelling days (or 1 infection for approximately every 33,000 indwelling days).^{416c} These characteristics permit a dramatically long duration of lead retention—well over a year in some cases^{417–419}—raising the possibility of preoperative insertion and continued postoperative stimulation for the entire interval of surgically related pain.^{417–421} There are theoretically no induced sensory, proprioception, or motor deficits, enabling full engagement in physical therapy and likely lacking any association with an increased falling risk. Obviously, there is no risk of local anesthetic toxicity or leakage. Conversely, practical implementation of percutaneous peripheral nerve stimulation to treat acute pain states is dependent on multiple factors that are currently undetermined: the time required for lead insertion, clinical efficacy and applicability, adverse event rate, the cost of leads and electrical generators, the maximum provided analgesia, and the future commercial availability of US FDA-approved equipment specifically approved for the treatment of acute pain.^{415,422}

CONCLUSIONS

Although the recently published evidence presented in this review helps to clarify questions previously unanswered, many unknown aspects of CPNB persist. Although the data demonstrating perineural local anesthetic infusion's many benefits continue to grow in quality, breadth, and depth, both older^{280,282,298,423} and novel^{1307,352,354,424} analgesic alternatives must be considered and investigated. Only through persistent, unbiased investigation will we be able to optimize analgesia for patients, whether from CPNB or an alternative modality.⁴²⁵

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DISCLOSURES

Name: Brian M. Ilfeld, MD, MS.

Contribution: This author helped design the study, conduct the study, and write the manuscript.

Attestation: Brian M. Ilfeld approved the final manuscript.

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REFERENCES

- Ilfeld BM. Continuous peripheral nerve blocks: a review of the published evidence. *Anesth Analg*. 2011;113:904–925.
- Ansbro FP. A method of continuous brachial plexus block. *Am J Surg*. 1946;71:716–722.
- Anghelescu DL, Faughnan LG, Baker JN, Yang J, Kane JR. Use of epidural and peripheral nerve blocks at the end of life in children and young adults with cancer: the collaboration between a pain service and a palliative care service. *Paediatr Anaesth*. 2010;20:1070–1077.
- Gemayel MC, Chidiac JE, Chidiac EJ. Ambulatory continuous interscalene blocks for cancer pain. *J Pain Palliat Care Pharmacother*. 2015;29:34–36.
- Sato S, Yamashita S, Iwai M, Mizuyama K, Satsumae T. Continuous interscalene block for cancer pain. *Reg Anesth*. 1994;19:73–75.
- Esch AT, Esch A, Knorr JL, Boezaart AP. Long-term ambulatory continuous nerve blocks for terminally ill patients: a case series. *Pain Med*. 2010;11:1299–1302.
- Pacenta HL, Kaddoum RN, Pereiras LA, Chidiac EJ, Burgoyne LL. Continuous tunnelled femoral nerve block for palliative care of a patient with metastatic osteosarcoma. *Anaesth Intensive Care*. 2010;38:563–565.
- Buchanan D, Brown E, Millar F, Mosgrove F, Bhat R, Levack P. Outpatient continuous interscalene brachial plexus block in cancer-related pain. *J Pain Symptom Manage*. 2009;38:629–634.
- Martin DP, Bhalla T, Rehman S, Tobias JD. Successive multisite peripheral nerve catheters for treatment of complex regional pain syndrome type I. *Pediatrics*. 2013;131:e323–e326.
- Gharaei H. Continuous peripheral nerve catheters in pediatric complex regional pain syndrome. *Anesth Pain Med*. 2015;5:e23414.
- Kato J, Gokan D, Ueda K, Shimizu M, Suzuki T, Ogawa S. Successful pain management of primary and independent spread sites in a child with CRPS type I using regional nerve blocks. *Pain Med*. 2011;12:174.
- Everett A, Mclean B, Plunkett A, Buckenmaier C. A unique presentation of complex regional pain syndrome type I treated with a continuous sciatic peripheral nerve block and parenteral ketamine infusion: a case report. *Pain Med*. 2009;10:1136–1139.
- Hashimoto A, Ito H, Sato Y, Fujiwara Y. [Automated intermittent bolus infusion for continuous sciatic nerve block: a case report]. *Masui*. 2011;60:873–875.
- Keskinbora K, Aydinli I. Perineural morphine in patients with chronic ischemic lower extremity pain: efficacy and long-term results. *J Anesth*. 2009;23:11–18.
- Ishiwa D, Okazaki K. [Continuous block of the sciatic nerve in the popliteal fossa for pain relief in three patients with intractable leg ulcer]. *Masui*. 2009;58:1456–1459.
- Tognù A, Borghi B, Gullotta S, White PF. Ultrasound-guided posterior approach to brachial plexus for the treatment of upper phantom limb syndrome. *Minerva Anesthesiol*. 2012;78:105–108.
- Borghi B, Bugamelli S, Stagni G, Missiroli M, Genco R, Colizza MT. Perineural infusion of 0.5% ropivacaine for successful treatment of phantom limb syndrome: a case report. *Minerva Anesthesiol*. 2009;75:661–664.
- Cheah J, Yap E, Naidu R. Attempting to prevent persistent postamputation phantom limb and stump pain. *A A Case Rep*. 2014;3:35–37.
- Ilfeld BM, Moeller-Bertram T, Hanling SR, et al. Treating intractable phantom limb pain with ambulatory continuous peripheral nerve blocks: a pilot study. *Pain Med*. 2013;14:935–942.
- Malhotra N, Madison SJ, Ward SR, Mariano ER, Loland VJ, Ilfeld BM. Continuous interscalene nerve block following adhesive capsulitis manipulation. *Reg Anesth Pain Med*. 2013;38:171–172.

21. Hutchins JL, Jacobs RA. Thoracic paravertebral catheter placement for acute rib pain in a pregnant patient with cystic fibrosis. *A A Case Rep.* 2015;4:31–32.
22. Cutshall C, Hutchins J. Ultrasound-guided continuous thoracic paravertebral catheter management of acute rib pain secondary to cystic fibrosis exacerbation in a pediatric patient. *A A Case Rep.* 2015;4:29–30.
23. Murata H, Salviz EA, Chen S, Vandepitte C, Hadzic A. Case report: ultrasound-guided continuous thoracic paravertebral block for outpatient acute pain management of multilevel unilateral rib fractures. *Anesth Analg.* 2013;116:255–257.
24. Flores RA Jr, Ortiz J, Markan S. Multilevel continuous intercostal nerve block catheter: a viable alternative to thoracic epidural for multiple rib fractures? *Anesthesiology.* 2013;119:994
25. Truitt MS, Mooty RC, Amos J, Lorenzo M, Mangram A, Dunn E. Out with the old, in with the new: a novel approach to treating pain associated with rib fractures. *World J Surg.* 2010;34:2359–2362.
26. Truitt MS, Murry J, Amos J, et al. Continuous intercostal nerve blockade for rib fractures: ready for primetime? *J Trauma.* 2011;71:1548–1552.
27. Mohta M, Verma P, Saxena AK, Sethi AK, Tyagi A, Girotra G. Prospective, randomized comparison of continuous thoracic epidural and thoracic paravertebral infusion in patients with unilateral multiple fractured ribs—a pilot study. *J Trauma.* 2009;66:1096–1101.
28. Miller EC, Szeto M, Boet S. Unilateral transversus abdominis plane block catheter for the treatment of abdominal wall pain in pregnancy: a case report. *Reg Anesth Pain Med.* 2015;40:720–722.
29. Stewart B, Tudur Smith C, Teebay L, Cunliffe M, Low B. Emergency department use of a continuous femoral nerve block for pain relief for fractured femur in children. *Emerg Med J.* 2007;24:113–114.
30. Herring AA, Liu B, Kiefer MV, Nagdev AD, Tsui BC. ED placement of perineural catheters for femoral fracture pain management. *Am J Emerg Med.* 2014;32:287.e1–287.e3.
31. Su HH, Lui PW, Yu CL, et al. The effects of continuous axillary brachial plexus block with ropivacaine infusion on skin temperature and survival of crushed fingers after microsurgical replantation. *Chang Gung Med J.* 2005;28:567–574.
32. Lang RS, Gorantla VS, Esper S, et al. Anesthetic management in upper extremity transplantation: the Pittsburgh experience. *Anesth Analg.* 2012;115:678–688.
33. Heil JW, Nakanote KA, Madison SJ, et al. Continuous transversus abdominis plane (TAP) blocks for postoperative pain control after hernia surgery: a randomized, triple-masked, placebo-controlled study. *Pain Med.* 2014;15:1957–1964.
34. Farag E, Guirguis MN, Helou M, et al. Continuous transversus abdominis plane block catheter analgesia for postoperative pain control in renal transplant. *J Anesth.* 2015;29:4–8.
35. Allcock E, Spencer E, Frazer R, Applegate G, Buckenmaier C III. Continuous transversus abdominis plane (TAP) block catheters in a combat surgical environment. *Pain Med.* 2010;11:1426–1429.
36. Niraj G, Kelkar A, Jeyapalan I, et al. Comparison of analgesic efficacy of subcostal transversus abdominis plane blocks with epidural analgesia following upper abdominal surgery. *Anaesthesia.* 2011;66:465–471.
37. Visoiu M, Yang C. Ultrasound-guided bilateral paravertebral continuous nerve blocks for a mildly coagulopathic patient undergoing exploratory laparotomy for bowel resection. *Paediatr Anaesth.* 2011;21:459–462.
38. Ponstein NA, Kim TW, Hsia J, Goode R, Borges P, Mariano ER. Continuous lesser palatine nerve block for postoperative analgesia after uvulopalatopharyngoplasty. *Clin J Pain.* 2013;29:e35–e38.
39. Osada R, Zukawa M, Seki E, Kimura T. Continuous peripheral nerve block in forearm for severe hand trauma. *Hand Surg.* 2011;16:239–244.
40. Gucev G, Karandikar K, Charlton T. Midcalf continuous peripheral nerve block anesthesia for hallux valgus surgery: case report. *Foot Ankle Int.* 2014;35:175–177.
41. Jaffe JD, Henshaw DS, Nagle PC. Ultrasound-guided continuous superficial peroneal nerve block below the knee for the treatment of nerve injury. *Pain Pract.* 2013;13:572–575.
42. Wallaert M, Courivaud P, Mati EH, Shiniara M, Guilbert JM. [Catheter for continuous interpectoral block and postoperative pain relief in breast surgery]. *Ann Fr Anesth Reanim.* 2014;33:269–271.
43. Pérez MF, Duany O, de la Torre PA. Redefining PECS blocks for postmastectomy analgesia. *Reg Anesth Pain Med.* 2015;40:729–730.
44. Chakraborty A, Goswami J, Patro V. Ultrasound-guided continuous quadratus lumborum block for postoperative analgesia in a pediatric patient. *A A Case Rep.* 2015;4:34–36.
45. Shaaban M, Esa WA, Maheshwari K, Elsharkawy H, Soliman LM. Bilateral continuous quadratus lumborum block for acute postoperative abdominal pain as a rescue after opioid-induced respiratory depression. *A A Case Rep.* 2015;5:107–111.
46. Visoiu M, Yakovleva N. Continuous postoperative analgesia via quadratus lumborum block - an alternative to transversus abdominis plane block. *Paediatr Anaesth.* 2013;23:959–961.
47. Jaeger P, Grevstad U, Henningsen MH, Gottschau B, Mathiesen O, Dahl JB. Effect of adductor-canal-blockade on established, severe post-operative pain after total knee arthroplasty: a randomised study. *Acta Anaesthesiol Scand.* 2012;56:1013–1019.
48. Burckett-St Laurant D, Peng P, Giron Arango L, et al. The nerves of the adductor canal and the innervation of the knee: an anatomic study. *Reg Anesth Pain Med.* 2016; 41: 321–327.
49. Davis JJ, Bond TS, Swenson JD. Adductor canal block: more than just the saphenous nerve? *Reg Anesth Pain Med.* 2009;34:618–619.
50. Jæger P, Zaric D, Fomsgaard JS, et al. Adductor canal block versus femoral nerve block for analgesia after total knee arthroplasty: a randomized, double-blind study. *Reg Anesth Pain Med.* 2013;38:526–532.
51. Ilfeld BM, Duke KB, Donohue MC. The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. *Anesth Analg.* 2010;111:1552–1554.
52. Finn DM, Agarwal RR, Ilfeld BM, et al. Association between the use of continuous peripheral nerve blocks and risk of falling following knee and hip arthroplasty. *MedSurg Nursing.* 2016;25:25–30.
53. Wasserstein D, Farlinger C, Brull R, Mahomed N, Gandhi R. Fall risk associated with continuous peripheral nerve blocks following knee and hip arthroplasty. *J Arthroplasty.* 2013;28:1121–1124.
54. Ilfeld BM. Single-injection and continuous femoral nerve blocks are associated with different risks of falling. *Anesthesiology.* 2014;121:668–669.
55. Mudumbai SC, Ganaway T, Kim TE, et al. Can bedside patient-reported numbness predict postoperative ambulation ability for total knee arthroplasty patients with nerve block catheters? *Korean J Anesthesiol.* 2016;69:32–36.
56. Pelt CE, Anderson AW, Anderson MB, Van Dine C, Peters CL. Postoperative falls after total knee arthroplasty in patients with a femoral nerve catheter: can we reduce the incidence? *J Arthroplasty.* 2014;29:1154–1157.
57. Sztain JF, Machi AT, Kormylo NJ, et al. Continuous adductor canal versus continuous femoral nerve blocks: relative effects on discharge readiness following unicompartment knee arthroplasty. *Reg Anesth Pain Med.* 2015;40:559–567.
58. Machi AT, Sztain JF, Kormylo NJ, et al. Discharge readiness after tricompartment knee arthroplasty: adductor canal versus femoral continuous nerve blocks—a dual-center, randomized trial. *Anesthesiology.* 2015;123:444–456.
59. Elkassabany NM, Antosh S, Ahmed M, et al. The risk of falls after total knee arthroplasty with the use of a femoral nerve block versus an adductor canal block: a double-blinded randomized controlled study. *Anesth Analg.* 2016;122:1696–1703.
60. Ilfeld BM, Hadzic A. Walking the tightrope after knee surgery: optimizing postoperative analgesia while minimizing quadriceps weakness. *Anesthesiology.* 2013;118:248–250.
61. Hanson NA, Allen CJ, Hostetter LS, et al. Continuous ultrasound-guided adductor canal block for total knee arthroplasty: a randomized, double-blind trial. *Anesth Analg.* 2014;118:1370–1377.

62. Jenstrup MT, Jæger P, Lund J, et al. Effects of adductor canal-blockade on pain and ambulation after total knee arthroplasty: a randomized study. *Acta Anaesthesiol Scand*. 2012;56:357–364.
63. Jæger P, Koscielniak-Nielsen ZJ, Schrøder HM, et al. Adductor canal block for postoperative pain treatment after revision knee arthroplasty: a blinded, randomized, placebo-controlled study. *PLoS One*. 2014;9:e111951
64. Andersen HL, Gyryn J, Møller L, Christensen B, Zaric D. Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty. *Reg Anesth Pain Med*. 2013;38:106–111.
65. Grevstad U, Mathiesen O, Valentiner LS, Jaeger P, Hilsted KL, Dahl JB. Effect of adductor canal block versus femoral nerve block on quadriceps strength, mobilization, and pain after total knee arthroplasty: a randomized, blinded study. *Reg Anesth Pain Med*. 2015;40:3–10.
66. Chelly JE. Does the study design really compare apples to apples? *J Arthroplasty*. 2015;30:513–514.
67. Jaeger P, Dahl JB, Rasmussen LS. Surprising results in an article in press from your journal. *J Arthroplasty*. 2015;30:512–516.
68. Ilfeld BM, Turan A, Ball ST. Not all “continuous femoral nerve blocks” are equivalent. *J Arthroplasty*. 2015;30:896–897.
69. Chelly JE. Is the continuous saphenous block the right technique for postoperative pain management after total knee replacement? *Reg Anesth Pain Med*. 2013;38:461
70. Bendtsen TF, Moriggl B, Chan V, Pedersen EM, Børglum J. Redefining the adductor canal block. *Reg Anesth Pain Med*. 2014;39:442–443.
71. Bendtsen TF, Moriggl B, Chan V, Pedersen EM, Børglum J. Defining adductor canal block. *Reg Anesth Pain Med*. 2014;39:253–254.
72. Moore DM, O’Gara A, Duggan M. Continuous saphenous nerve block for total knee arthroplasty: when and how? *Reg Anesth Pain Med*. 2013;38:370–371.
73. Mariano ER, Kim TE, Wagner MJ, et al. A randomized comparison of proximal and distal ultrasound-guided adductor canal catheter insertion sites for knee arthroplasty. *J Ultrasound Med*. 2014;33:1653–1662.
74. Shah NA, Jain NP. Is continuous adductor canal block better than continuous femoral nerve block after total knee arthroplasty? Effect on ambulation ability, early functional recovery and pain control: a randomized controlled trial. *J Arthroplasty*. 2014;29:2224–2229.
75. Lam DK, Corry GN, Tsui BC. Evidence for the use of ultrasound imaging in pediatric regional anesthesia: a systematic review. *Reg Anesth Pain Med*. 2016;41:229–241.
76. Dadure C, Bringuier S, Nicolas F, et al. Continuous epidural block versus continuous popliteal nerve block for postoperative pain relief after major podiatric surgery in children: a prospective, comparative randomized study. *Anesth Analg*. 2006;102:744–749.
77. Walker BJ, Long JB, De Oliveira GS, et al; PRAN Investigators. Peripheral nerve catheters in children: an analysis of safety and practice patterns from the pediatric regional anesthesia network (PRAN). *Br J Anaesth*. 2015;115:457–462.
78. Visoiu M, Joy LN, Grudziak JS, Chelly JE. The effectiveness of ambulatory continuous peripheral nerve blocks for postoperative pain management in children and adolescents. *Paediatr Anaesth*. 2014;24:1141–1148.
79. Gurnaney H, Kraemer FW, Maxwell L, Muhly WT, Schleelein L, Ganesh A. Ambulatory continuous peripheral nerve blocks in children and adolescents: a longitudinal 8-year single center study. *Anesth Analg*. 2014;118:621–627.
80. Dadure C, Bringuier S, Raux O, et al. Continuous peripheral nerve blocks for postoperative analgesia in children: feasibility and side effects in a cohort study of 339 catheters. *Can J Anaesth*. 2009;56:843–850.
81. de José María B, Banús E, Navarro-Egea M, Banchs RJ. Tips and tricks to facilitate ultrasound-guided placement of peripheral nerve catheters in children. *Paediatr Anaesth*. 2011;21:974–979.
82. Ponde VC, Desai AP, Shah DM, Johari AN. Feasibility and efficacy of placement of continuous sciatic perineural catheters solely under ultrasound guidance in children: a descriptive study. *Paediatr Anaesth*. 2011;21:406–410.
83. Boretsky K, Visoiu M, Bigeleisen P. Ultrasound-guided approach to the paravertebral space for catheter insertion in infants and children. *Paediatr Anaesth*. 2013;23:1193–1198.
84. Tran DQ, Muñoz L, Russo G, Finlayson RJ. Ultrasonography and stimulating perineural catheters for nerve blocks: a review of the evidence. *Can J Anaesth*. 2008;55:447–457.
85. Gandhi K, Lindenmuth DM, Hadzic A, et al. The effect of stimulating versus conventional perineural catheters on post-operative analgesia following ultrasound-guided femoral nerve localization. *J Clin Anesth*. 2011;23:626–631.
86. Neal JM, Brull R, Horn JL, et al. The Second American Society of Regional Anesthesia and Pain Medicine Evidence-Based Medicine Assessment of Ultrasound-Guided Regional Anesthesia: executive summary. *Reg Anesth Pain Med*. 2016;41:181–194.
87. Schnabel A, Meyer-Frießem CH, Zahn PK, Pogatzki-Zahn EM. Ultrasound compared with nerve stimulation guidance for peripheral nerve catheter placement: a meta-analysis of randomized controlled trials. *Br J Anaesth*. 2013;111:564–572.
88. Bendtsen TF, Nielsen TD, Rohde CV, Kibak K, Linde F. Ultrasound guidance improves a continuous popliteal sciatic nerve block when compared with nerve stimulation. *Reg Anesth Pain Med*. 2011;36:181–184.
89. Danelli G, Bonarelli S, Tognú A, et al. Prospective randomized comparison of ultrasound-guided and neurostimulation techniques for continuous interscalene brachial plexus block in patients undergoing coracoacromial ligament repair. *Br J Anaesth*. 2012;108:1006–1010.
90. Danelli G, Ghisi D, Fanelli A, et al. The effects of ultrasound guidance and neurostimulation on the minimum effective anesthetic volume of mepivacaine 1.5% required to block the sciatic nerve using the subgluteal approach. *Anesth Analg*. 2009;109:1674–1678.
91. Li M, Xu T, Han WY, Wang XD, Jia DL, Guo XY. Use of ultrasound to facilitate femoral nerve block with stimulating catheter. *Chin Med J (Engl)*. 2011;124:519–524.
92. Maalouf D, Liu SS, Movahedi R, et al. Nerve stimulator versus ultrasound guidance for placement of popliteal catheters for foot and ankle surgery. *J Clin Anesth*. 2012;24:44–50.
93. Farag E, Atim A, Ghosh R, et al. Comparison of three techniques for ultrasound-guided femoral nerve catheter insertion: a randomized, blinded trial. *Anesthesiology*. 2014;121:239–248.
94. Soltesz S, Meiger D, Milles-Thieme S, Saxler G, Ziegeler S. Intermittent versus continuous sciatic block combined with femoral block for patients undergoing knee arthroplasty. A randomized controlled trial. *Int Orthop*. 2016. [epub ahead of print].
95. Svediene S, Andrijauskas A, Ivaskевичius J, Saikus A. The efficacy comparison of on-demand boluses with and without basal infusion of 0.1 % bupivacaine via perineural femoral catheter after arthroscopic ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2013;21:641–645.
96. Cappelleri G, Ghisi D, Fanelli A, Albertini A, Somalvico F, Aldegheri G. Does continuous sciatic nerve block improve postoperative analgesia and early rehabilitation after total knee arthroplasty? A prospective, randomized, double-blinded study. *Reg Anesth Pain Med*. 2011;36:489–492.
97. Wegener JT, van Ooij B, van Dijk CN, Hollmann MW, Preckel B, Stevens MF. Value of single-injection or continuous sciatic nerve block in addition to a continuous femoral nerve block in patients undergoing total knee arthroplasty: a prospective, randomized, controlled trial. *Reg Anesth Pain Med*. 2011;36:481–488.
98. Borgeat A, EkatoDRAMIS G, Guzzella S, Ruland P, Votta-Velis G, Aguirre J. Deltoid, triceps, or both responses improve the success rate of the interscalene catheter surgical block compared with the biceps response. *Br J Anaesth*. 2012;109:975–980.
99. Winkler T, Suda AJ, Dumitrescu RV, et al. Interscalene versus subacromial continuous infusion of ropivacaine after arthroscopic acromioplasty: a randomized controlled trial. *J Shoulder Elbow Surg*. 2009;18:566–572.
100. Hayashi H, Ueyama H. [Experience of ultrasound-guided popliteal sciatic nerve block and femoral nerve perineural catheter placement in a morbidly obese patient undergoing total knee arthroplasty]. *Masui*. 2010;59:1260–1262.

101. Ilfeld BM, Loland VJ, Sandhu NS, et al. Continuous femoral nerve blocks: the impact of catheter tip location relative to the femoral nerve (anterior versus posterior) on quadriceps weakness and cutaneous sensory block. *Anesth Analg*. 2012;115:721–727.
102. Zaragoza-Lemus G, Hernández-Gasca V, Espinosa-Gutiérrez A. [Ultrasound-guided continuous infraclavicular block for hand surgery: technical report arm position for perineural catheter placement]. *Cir Cir*. 2015;83:15–22.
103. Wang AZ, Gu L, Zhou QH, Ni WZ, Jiang W. Ultrasound-guided continuous femoral nerve block for analgesia after total knee arthroplasty: catheter perpendicular to the nerve versus catheter parallel to the nerve. *Reg Anesth Pain Med*. 2010;35:127–131.
104. Mariano ER, Kim TE, Funck N, et al. A randomized comparison of long-and short-axis imaging for in-plane ultrasound-guided femoral perineural catheter insertion. *J Ultrasound Med*. 2013;32:149–156.
105. Ilfeld BM, Fredrickson MJ, Mariano ER. Ultrasound-guided perineural catheter insertion: three approaches but few illuminating data. *Reg Anesth Pain Med*. 2010;35:123–126.
106. Salinas FV. Evidence basis for ultrasound guidance for lower-extremity peripheral nerve block: update 2016. *Reg Anesth Pain Med*. 2016;41:261–274.
107. Fredrickson MJ, Ball CM, Dalgleish AJ. Posterior versus anterolateral approach interscalene catheter placement: a prospective randomized trial. *Reg Anesth Pain Med*. 2011;36:125–133.
108. Schwenk ES, Gandhi K, Baratta JL, et al. Ultrasound-guided out-of-plane vs. in-plane interscalene catheters: a randomized, prospective study. *Anesth Pain Med*. 2015;5:e31111
109. Taketa Y, Fujitani T. A novel paralaminar in-plane approach for ultrasound-guided continuous thoracic paravertebral block using microconvex array transducer. *Reg Anesth Pain Med*. 2015;40:390
110. Elsharkawy H, Maheshwari A, Farag E, Mariano ER, Rosenquist RW. Development of technologies for placement of perineural catheters. *J Anesth*. 2016;30:138–147.
111. Luyet C, Seiler R, Herrmann G, Hatch GM, Ross S, Eichenberger U. Newly designed, self-coiling catheters for regional anesthesia—an imaging study. *Reg Anesth Pain Med*. 2011;36:171–176.
112. Luyet C, Meyer C, Herrmann G, Hatch GM, Ross S, Eichenberger U. Placement of coiled catheters into the paravertebral space. *Anaesthesia*. 2012;67:250–255.
113. Fuzier R, Izard P, Aziza R, Pouymayou J. Even a “pigtail” distal end catheter can enter the epidural space after continuous paravertebral block. *J Anesth*. 2016;30:503–505.
114. Rothe C, Steen-Hansen C, Madsen MH, Lange KH. A novel concept for continuous peripheral nerve blocks. Presentation of a new ultrasound-guided device. *Acta Anaesthesiol Scand*. 2015;59:232–237.
115. Rothe C, Steen-Hansen C, Madsen MH, et al. A novel suture method to place and adjust peripheral nerve catheters. *Anaesthesia*. 2015;70:791–796.
116. Fredrickson MJ. Randomised comparison of an end-hole, triple-hole and novel six-hole catheter for continuous interscalene analgesia. *Anaesth Intensive Care*. 2014;42:37–42.
117. Tsui BC, Tsui J. Less leakage and dislodgement with a catheter-over-needle versus a catheter-through-needle approach for peripheral nerve block: an ex vivo study. *Can J Anaesth*. 2012;59:655–661.
118. Ip VH, Tsui BC. The catheter-over-needle assembly facilitates delivery of a second local anesthetic bolus to prolong supraclavicular brachial plexus block without time-consuming catheterization steps: a randomized controlled study. *Can J Anaesth*. 2013;60:692–699.
119. Ip VH, Rockley MC, Tsui BC. The catheter-over-needle assembly offers greater stability and less leakage compared with the traditional counterpart in continuous interscalene nerve blocks: a randomized patient-blinded study. *Can J Anaesth*. 2013;60:1272–1273.
120. Tsui BC, Ip VH. Catheter-over-needle method reduces risk of perineural catheter dislocation. *Br J Anaesth*. 2014;112:759–760.
121. Yu B, Hu X, Zou T, He M, Cai G. Effects of postoperative continuous femoral nerve block analgesia with Braun continuous peripheral nerve block catheter set versus novel needle-over-cannula after total knee arthroplasty. *Med Sci Monit*. 2015;21:1843–1849.
122. Kan JM, Harrison TK, Kim TE, Howard SK, Kou A, Mariano ER. An *in vitro* study to evaluate the utility of the “air test” to infer perineural catheter tip location. *J Ultrasound Med*. 2013;32:529–533.
123. Johns J, Harrison TK, Steffel L, Howard SK, Kim TE, Kou A, Mariano ER. A pilot *in vitro* evaluation of the “air test” for perineural catheter tip localization by a novice regional anesthesiologist. *J Ultrasound Med*. 2014;33:2197–2200.
124. Takatani J, Takeshima N, Okuda K, Uchino T, Noguchi T. Ultrasound visibility of regional anesthesia catheters: an *in vitro* study. *Korean J Anesthesiol*. 2012;63:59–64.
125. Mariano ER, Yun RD, Kim TE, Carvalho B. Application of echogenic technology for catheters used in ultrasound-guided continuous peripheral nerve blocks. *J Ultrasound Med*. 2014;33:905–911.
126. Brookes J, Sondekoppam R, Armstrong K, Uppal V, Dhir S, Terlecki M, Ganapathy S. Comparative evaluation of the visibility and block characteristics of a stimulating needle and catheter vs an echogenic needle and catheter for sciatic nerve block with a low-frequency ultrasound probe. *Br J Anaesth*. 2015;115:912–919.
127. Clendenen SR, Robards CB, Clendenen NJ, Freidenstein JE, Greengrass RA. Real-time 3-dimensional ultrasound-assisted infraclavicular brachial plexus catheter placement: implications of a new technology. *Anesthesiol Res Pract*. 2010;2010:
128. Choquet O, Capdevila X. Case report: Three-dimensional high-resolution ultrasound-guided nerve blocks: a new panoramic vision of local anesthetic spread and perineural catheter tip location. *Anesth Analg*. 2013;116:1176–1181.
129. Elsharkawy H, Salmasi V, Abd-Elseyed A, Turan A. Identification of location of nerve catheters using pumping maneuver and M-Mode—a novel technique. *J Clin Anesth*. 2015;27:325–330.
130. Choromanski DW, Patel PS, Frederick JM, Lemos SE, Chidiac EJ. The effect of continuous interscalene brachial plexus block with 0.125% bupivacaine vs 0.2% ropivacaine on pain relief, diaphragmatic motility, and ventilatory function. *J Clin Anesth*. 2015;27:619–626.
131. Yang CW, Jung SM, Kang PS, et al. A randomized comparison of ropivacaine 0.1% and 0.2% for continuous interscalene block after shoulder surgery. *Anesth Analg*. 2013;116:730–733.
132. Bauer M, Wang L, Onibonjo OK, et al. Continuous femoral nerve blocks: decreasing local anesthetic concentration to minimize quadriceps femoris weakness. *Anesthesiology*. 2012;116:665–672.
133. Wilson SH, Auroux AS, Eloy JD, Merman RB, Chelly JE. Ropivacaine 0.1% versus 0.2% for continuous lumbar plexus nerve block infusions following total hip arthroplasty: a randomized, double blinded study. *Pain Med*. 2014;15:465–472.
134. Madison SJ, Monahan AM, Agarwal RR, et al. A randomized, triple-masked, active-controlled investigation of the relative effects of dose, concentration, and infusion rate for continuous popliteal-sciatic nerve blocks in volunteers. *Br J Anaesth*. 2015;114:121–129.
135. Yoshida T, Fujiwara T, Furutani K, Ohashi N, Baba H. Effects of ropivacaine concentration on the spread of sensory block produced by continuous thoracic paravertebral block: a prospective, randomised, controlled, double-blind study. *Anaesthesia*. 2014;69:231–239.
136. Buys MJ, Alphonso C. Novel use of perineural pregabalin infusion for analgesia in a rat neuropathic pain model. *Anesth Analg*. 2014;119:481–488.
137. Williams BA, Butt MT, Zeller JR, Coffee S, Pippi MA. Multimodal perineural analgesia with combined bupivacaine-clonidine-buprenorphine-dexamethasone: safe *in vivo* and chemically compatible in solution. *Pain Med*. 2015;16:186–198.
138. Mangar D, Karlowski RA, Sprenger CJ, et al. Knee strength retention and analgesia with continuous perineural fentanyl

- infusion after total knee replacement: randomized controlled trial. *J Anesth.* 2014;28:214–221.
139. Burlacu CL, Frizelle HP, Moriarty DC, Buggy DJ. Fentanyl and clonidine as adjunctive analgesics with levobupivacaine in paravertebral analgesia for breast surgery. *Anaesthesia.* 2006;61:932–937.
 140. Wajima Z, Nakajima Y, Kim C, et al. IV compared with brachial plexus infusion of butorphanol for postoperative analgesia. *Br J Anaesth.* 1995;74:392–395.
 141. Wajima Z, Shitara T, Nakajima Y, et al. Continuous brachial plexus infusion of butorphanol-mepivacaine mixtures for analgesia after upper extremity surgery. *Br J Anaesth.* 1997;78:83–85.
 142. Yaksh TL, Ilfeld BM, Wiese AJ. Perineural local anesthetic and adjuvant action: the meaning of an ex vivo data set for efficacy and safety. *Reg Anesth Pain Med.* 2012;37:366–368.
 143. Aguirre J, Del Moral A, Cobo I, Borgeat A, Blumenthal S. The role of continuous peripheral nerve blocks. *Anesthesiol Res Pract.* 2012;2012:560879
 144. Monahan AM, Sztain JF, Khatibi B, et al. Continuous adductor canal blocks: Does varying local anesthetic delivery method (automatic repeated bolus doses versus continuous basal infusion) influence cutaneous analgesia and quadriceps femoris strength? A randomized, double-masked, controlled, split-body volunteer study. *Anesth Analg.* 2016;122:1681–1688.
 145. Hamdani M, Chassot O, Fournier R. Ultrasound-guided continuous interscalene block: the influence of local anesthetic background delivery method on postoperative analgesia after shoulder surgery: a randomized trial. *Reg Anesth Pain Med.* 2014;39:387–393.
 146. Byeon GJ, Shin SW, Yoon JU, Kim EJ, Baek SH, Ri HS. Infusion methods for continuous interscalene brachial plexus block for postoperative pain control after arthroscopic rotator cuff repair. *Korean J Pain.* 2015;28:210–216.
 147. Shin SW, Byeon GJ, Yoon JU, et al. Effective analgesia with ultrasound-guided interscalene brachial plexus block for postoperative pain control after arthroscopic rotator cuff repair. *J Anesth.* 2014;28:64–69.
 148. Wei Y, Li M, Rong Y, Guo X. Effective background infusion rate of ropivacaine 0.2% for patient-controlled interscalene brachial plexus analgesia after rotator cuff repair surgery. *Chinese Med J.* 2014; 127: 4119–4123.
 149. Machi AT, Ilfeld BM. Continuous peripheral nerve blocks in the ambulatory setting: an update of the published evidence. *Curr Opin Anaesthesiol.* 2015;28:648–655.
 150. Lecoq JP, Jacquemin D, Lamy M, Fontaine R. [Analgesia for wound dressing by continuous peripheral nerve block]. *Rev Med Liege.* 2008;63:31–36.
 151. Borgeat A, Kalberer F, Jacob H, Ruetsch YA, Gerber C. Patient-controlled interscalene analgesia with ropivacaine 0.2% versus bupivacaine 0.15% after major open shoulder surgery: the effects on hand motor function. *Anesth Analg.* 2001;92:218–223.
 152. Charous MT, Madison SJ, Suresh PJ, et al. Continuous femoral nerve blocks: varying local anesthetic delivery method (bolus versus basal) to minimize quadriceps motor block while maintaining sensory block. *Anesthesiology.* 2011;115:774–781.
 153. Fredrickson MJ, Abeysekera A, Price DJ, Wong AC. Patient-initiated mandatory boluses for ambulatory continuous interscalene analgesia: an effective strategy for optimizing analgesia and minimizing side-effects. *Br J Anaesth.* 2011;106:239–245.
 154. Ilfeld BM, Enneking FK. Continuous peripheral nerve blocks at home: a review. *Anesth Analg.* 2005;100:1822–1833.
 155. Ilfeld BM. Continuous peripheral nerve blocks in the hospital and at home. *Anesthesiol Clin.* 2011;29:193–211.
 156. Yuan SC, Hanson NA, Auyong DB, Choi DS, Coy D, Strodtbeck WM. Fluoroscopic evaluation of contrast distribution within the adductor canal. *Reg Anesth Pain Med.* 2015;40:154–157.
 157. Taboada M, Rodríguez J, Bermudez M, et al. Comparison of continuous infusion versus automated bolus for postoperative patient-controlled analgesia with popliteal sciatic nerve catheters. *Anesthesiology.* 2009;110:150–154.
 158. Fibla JJ, Molins L, Mier JM, Hernandez J, Sierra A. A randomized prospective study of analgesic quality after thoracotomy: paravertebral block with bolus versus continuous infusion with an elastomeric pump. *Eur J Cardiothorac Surg.* 2015;47:631–635.
 159. Bleckner L, Solla C, Fileta BB, Howard R, Morales CE, Buckenmaier CC. Serum free ropivacaine concentrations among patients receiving continuous peripheral nerve block catheters: is it safe for long-term infusions? *Anesth Analg.* 2014;118:225–229.
 160. Mohseni M, Ebneshahidi A. The flow rate accuracy of elastomeric infusion pumps after repeated filling. *Anesth Pain Med.* 2014;4:e14989
 161. Weisman RS, Missair A, Pham P, Gutierrez JF, Gebhard RE. Accuracy and consistency of modern elastomeric pumps. *Reg Anesth Pain Med.* 2014;39:423–428.
 162. Macaire P, Nadhari M, Greiss H, et al. Internet remote control of pump settings for postoperative continuous peripheral nerve blocks: a feasibility study in 59 patients. *Ann Fr Anesth Reanim.* 2014;33:e1–e7.
 163. Fredrickson MJ, Fredrickson MJ, Ball CM, Dalgleish AJ. Analgesic effectiveness of a continuous versus single-injection interscalene block for minor arthroscopic shoulder surgery. *Reg Anesth Pain Med.* 2010;35:28–33.
 164. Fredrickson MJ, Ball CM, Dalgleish AJ. Catheter orifice configuration influences the effectiveness of continuous peripheral nerve blockade. *Reg Anesth Pain Med.* 2011;36:470–475.
 165. Gharabawy R, Abd-Elsayed A, Elsharkawy H, et al. The Cleveland Clinic experience with supraclavicular and popliteal ambulatory nerve catheters. *Scientific World J.* 2014;2014:572507
 166. Ilfeld BM, Shuster JJ, Theriaque DW, et al. Long-term pain, stiffness, and functional disability after total knee arthroplasty with and without an extended ambulatory continuous femoral nerve block: a prospective, 1-year follow-up of a multicenter, randomized, triple-masked, placebo-controlled trial. *Reg Anesth Pain Med.* 2011;36:116–120.
 167. Ilfeld BM, Madison SJ, Suresh PJ, et al. Treatment of post-mastectomy pain with ambulatory continuous paravertebral nerve blocks: a randomized, triple-masked, placebo-controlled study. *Reg Anesth Pain Med.* 2014;39:89–96.
 168. Fredrickson MJ, Leightley P, Wong A, Chaddock M, Abeysekera A, Frampton C. An analysis of 1505 consecutive patients receiving continuous interscalene analgesia at home: a multicentre prospective safety study. *Anaesthesia.* 2016;71:373–379.
 169. Chidiac EJ, Kaddoum R, Peterson SA. Patient survey of continuous interscalene analgesia at home after shoulder surgery. *Middle East J Anaesthesiol.* 2009;20:213–218.
 170. Fredrickson MJ, Stewart AW. Continuous interscalene analgesia for rotator cuff repair: a retrospective comparison of effectiveness and cost in 205 patients from a multi-provider private practice setting. *Anaesth Intensive Care.* 2008;36:786–791.
 171. Clendenen SR, Robards CB, Greengrass RA, Brull SJ. Complications of peripheral nerve catheter removal at home: case series of five ambulatory interscalene blocks. *Can J Anaesth.* 2011;58:62–67.
 172. Gallay SH, Lobo JJ, Baker J, Smith K, Patel K. Development of a regional model of care for ambulatory total shoulder arthroplasty: a pilot study. *Clin Orthop Relat Res.* 2008;466:563–572.
 173. Cruz Eng H, Riazi S, Veillette C, et al. An expedited care pathway with ambulatory brachial plexus analgesia is a cost-effective alternative to standard inpatient care after complex arthroscopic elbow surgery: a randomized, single-blinded study. *Anesthesiology.* 2015;123:1256–1266.
 174. Saporito A, Sturini E, Petri J, Borgeat A, Aguirre JA. Case report: unusual complication during outpatient continuous regional popliteal analgesia. *Can J Anaesth.* 2012;59:958–962.
 175. Yilmazlar A, Türker G, Atici T, Bilgen S, Bilgen OF. Functional results of conservative therapy accompanied by interscalene brachial plexus block and patient-controlled analgesia in cases with frozen shoulder. *Acta Orthop Traumatol Turc.* 2010;44:105–110.
 176. Salviz EA, Xu D, Frulla A, et al. Continuous interscalene block in patients having outpatient rotator cuff repair surgery: a prospective randomized trial. *Anesth Analg.* 2013;117:1485–1492.

177. Ilfeld BM, Madison SJ, Suresh PJ, et al. Persistent postmastectomy pain and pain-related physical and emotional functioning with and without a continuous paravertebral nerve block: a prospective 1-year follow-up assessment of a randomized, triple-masked, placebo-controlled study. *Ann Surg Oncol*. 2015;22:2017–2025.
178. Nye ZB, Horn JL, Crittenden W, Abrahams MS, Aziz MF. Ambulatory continuous posterior lumbar plexus blocks following hip arthroscopy: a review of 213 cases. *J Clin Anesth*. 2013;25:268–274.
179. Moran K, Arbona F, Khabiri B, et al. The need for patient teaching, follow up and physician availability for the prevention of outpatient perineural catheter complications. *J Pain Symptom Control Palliat Care*. 2011; 8: 1–4.
180. Dooley J, Fingerma M, Melton S, Klein SM. Contralateral local anesthetic spread from an outpatient interscalene catheter. *Can J Anaesth*. 2010;57:936–939.
181. Chelly JE, Greger J, Gebhard R. Ambulatory continuous perineural infusion: are we ready? *Anesthesiology*. 2000;93:581–582.
182. Rawal N. American Society of Regional Anesthesia and Pain Medicine 2010 Gaston Labat Lecture: Perineural catheter analgesia as a routine method after ambulatory surgery—effective but unrealistic. *Reg Anesth Pain Med*. 2012;37:72–78.
183. Pawa A, Devlin AP, Kochhar A. Interscalene catheters—should we give them the cold shoulder? *Anaesthesia*. 2016;71:359–362.
184. Fredrickson MJ. Orthopedic anesthesia subspecialization: the way forward to increase utilization of perineural infusions? *Reg Anesth Pain Med*. 2012;37:359–360.
185. Grant SA, Nielsen KC, Greengrass RA, Steele SM, Klein SM. Continuous peripheral nerve block for ambulatory surgery. *Reg Anesth Pain Med*. 2001;26:209–214.
186. Klein SM, Steele SM, Nielsen KC, et al. The difficulties of ambulatory interscalene and intra-articular infusions for rotator cuff surgery: a preliminary report. *Can J Anaesth*. 2003;50:265–269.
187. Russon K, Sardesai AM, Ridgway S, et al. Postoperative shoulder surgery initiative (POSSI): an interim report of major shoulder surgery as a day case procedure. *Br J Anaesth*. 2006;97:869–873.
188. McGraw RP III, Ilfeld BM. Toward outpatient arthroplasty: accelerating discharge with ambulatory continuous peripheral nerve blocks. *Int Anesthesiol Clin*. 2012;50:111–125.
189. Ilfeld BM, Mariano ER, Williams BA, Woodard JN, Macario A. Hospitalization costs of total knee arthroplasty with a continuous femoral nerve block provided only in the hospital versus on an ambulatory basis: a retrospective, case-control, cost-minimization analysis. *Reg Anesth Pain Med*. 2007;32:46–54.
190. Hunt KJ, Higgins TF, Carlston CV, Swenson JR, McEachern JE, Beals TC. Continuous peripheral nerve blockade as postoperative analgesia for open treatment of calcaneal fractures. *J Orthop Trauma*. 2010;24:148–155.
191. Ilfeld BM, Vandenborne K, Duncan PW, et al. Ambulatory continuous interscalene nerve blocks decrease the time to discharge readiness after total shoulder arthroplasty: a randomized, triple-masked, placebo-controlled study. *Anesthesiology*. 2006;105:999–1007.
192. White PF, Issioui T, Skrivaneck GD, Early JS, Wakefield C. The use of a continuous popliteal sciatic nerve block after surgery involving the foot and ankle: does it improve the quality of recovery? *Anesth Analg*. 2003;97:1303–1309.
193. Ilfeld BM, Meunier MJ, Macario A. Ambulatory continuous peripheral nerve blocks and the perioperative surgical home. *Anesthesiology*. 2015;123:1224–1226.
194. Saporito A, Sturini E, Borgeat A, Aguirre J. The effect of continuous popliteal sciatic nerve block on unplanned postoperative visits and readmissions after foot surgery—a randomized, controlled study comparing day-care and inpatient management. *Anaesthesia*. 2014;69:1197–1205.
195. Wei Y, Guo XY, Yang L, Rong YL, Xu CY, Li M. [Effects of continuous interscalene brachial plexus block plus general anesthesia versus general anesthesia alone on perioperative management of arthroscopic rotator cuff repair surgery]. *Zhonghua Yi Xue Za Zhi*. 2012;92:2327–2330.
196. Baranović S, Maldini B, Milosević M, Golubić R, Nikolić T. Peripheral regional analgesia with femoral catheter versus intravenous patient controlled analgesia after total knee arthroplasty: a prospective randomized study. *Coll Antropol*. 2011;35:1209–1214.
197. Wu JW, Wong YC. Elective unilateral total knee replacement using continuous femoral nerve blockade versus conventional patient-controlled analgesia: perioperative patient management based on a multidisciplinary pathway. *Hong Kong Med J*. 2014;20:45–51.
198. Sakai N, Inoue T, Kunugiza Y, Tomita T, Mashimo T. Continuous femoral epidural block for attainment of 120° knee flexion after total knee arthroplasty: a randomized controlled trial. *J Arthroplasty*. 2013;28:807–814.
199. Hadzic A, Houle TT, Capdevila X, Ilfeld BM. Femoral nerve block for analgesia in patients having knee arthroplasty. *Anesthesiology*. 2010;113:1014–1015.
200. Elliot R, Pearce CJ, Seifert C, Calder JD. Continuous infusion versus single bolus popliteal block following major ankle and hindfoot surgery: a prospective, randomized trial. *Foot Ankle Int*. 2010;31:1043–1047.
201. Sato K, Adachi T, Shirai N, Naoi N. Continuous versus single-injection sciatic nerve block added to continuous femoral nerve block for analgesia after total knee arthroplasty: a prospective, randomized, double-blind study. *Reg Anesth Pain Med*. 2014;39:225–229.
202. Barrington MJ, Olive D, Low K, Scott DA, Brittain J, Choong P. Continuous femoral nerve blockade or epidural analgesia after total knee replacement: a prospective randomized controlled trial. *Anesth Analg*. 2005;101:1824–1829.
203. Nishio S, Fukunishi S, Juichi M, et al. Comparison of continuous femoral nerve block, caudal epidural block, and intravenous patient-controlled analgesia in pain control after total hip arthroplasty: a prospective randomized study. *Orthop Rev (Pavia)*. 2014;6:5138.
204. Pintaric TS, Potocnik I, Hadzic A, Stupnik T, Pintaric M, Novak Jankovic V. Comparison of continuous thoracic epidural with paravertebral block on perioperative analgesia and hemodynamic stability in patients having open lung surgery. *Reg Anesth Pain Med*. 2011;36:256–260.
205. Patel N, Solovyova O, Matthews G, Arumugam S, Sinha SK, Lewis CG. Safety and efficacy of continuous femoral nerve catheter with single shot sciatic nerve block vs epidural catheter anesthesia for same-day bilateral total knee arthroplasty. *J Arthroplasty*. 2015;30:330–334.
206. Fredrickson MJ, Danesh-Crough TK. Spinal anaesthesia with adjunctive intrathecal morphine versus continuous lumbar plexus blockade: a randomised comparison for analgesia after hip replacement. *Anaesth Intensive Care*. 2015;43:449–453.
207. Delaunay L, Souron V, Lafosse L, Marret E, Toussaint B. Analgesia after arthroscopic rotator cuff repair: subacromial versus interscalene continuous infusion of ropivacaine. *Reg Anesth Pain Med*. 2005;30:117–122.
208. Beausang DH, Pozek JJ, Chen AF, et al. A randomized controlled trial comparing adductor canal catheter and intraarticular catheter after primary total knee arthroplasty. *J Arthroplasty*. 2016. [epub ahead of print].
209. Zhang W, Hu Y, Tao Y, Liu X, Wang G. Ultrasound-guided continuous adductor canal block for analgesia after total knee replacement. *Chin Med J (Engl)*. 2014;127:4077–4081.
210. Jæger P, Jenstrup MT, Lund J, et al. Optimal volume of local anaesthetic for adductor canal block: using the continual reassessment method to estimate ED95. *Br J Anaesth*. 2015;115:920–926.
211. Jæger P, Koscielniak-Nielsen ZJ, Hilsted KL, Fabritius ML, Dahl JB. Adductor canal block with 10 ml versus 30 ml local anesthetics and quadriceps strength: a paired, blinded, randomized study in healthy volunteers. *Reg Anesth Pain Med*. 2015;40:553–558.
212. Morin AM, Kratz CD, Eberhart LH, et al. Postoperative analgesia and functional recovery after total-knee replacement: comparison of a continuous posterior lumbar plexus (psoas compartment) block, a continuous femoral nerve block, and

- the combination of a continuous femoral and sciatic nerve block. *Reg Anesth Pain Med.* 2005;30:434–445.
213. Pham Dang C, Gautheron E, Guilley J, et al. The value of adding sciatic block to continuous femoral block for analgesia after total knee replacement. *Reg Anesth Pain Med.* 2005;30:128–133.
 214. Ben-David B, Schmalenberger K, Chelly JE. Analgesia after total knee arthroplasty: is continuous sciatic blockade needed in addition to continuous femoral blockade? *Anesth Analg.* 2004;98:747–749.
 215. Ilfeld BM, Madison SJ. The sciatic nerve and knee arthroplasty: to block, or not to block—that is the question. *Reg Anesth Pain Med.* 2011;36:421–423.
 216. Peng L, Ren L, Qin P, et al. Continuous femoral nerve block versus intravenous patient controlled analgesia for knee mobility and long-term pain in patients receiving total knee replacement: a randomized controlled trial. *Evid Based Complement Alternat Med.* 2014;2014:569107
 217. Wijayasinghe N, Andersen KG, Kehlet H. Neural blockade for persistent pain after breast cancer surgery. *Reg Anesth Pain Med.* 2014;39:272–278.
 218. Brennan TJ, Kehlet H. Preventive analgesia to reduce wound hyperalgesia and persistent postsurgical pain: not an easy path. *Anesthesiology.* 2005;103:681–683.
 219. Blumenthal S, Borgeat A, Neudörfer C, Bertolini R, Espinosa N, Aguirre J. Additional femoral catheter in combination with popliteal catheter for analgesia after major ankle surgery. *Br J Anaesth.* 2011;106:387–393.
 220. Wegener JT, van Ooij B, van Dijk CN, et al. Long-term pain and functional disability after total knee arthroplasty with and without single-injection or continuous sciatic nerve block in addition to continuous femoral nerve block: a prospective, 1-year follow-up of a randomized controlled trial. *Reg Anesth Pain Med.* 2013;38:58–63.
 221. Karmakar MK, Samy W, Li JW, et al. Thoracic paravertebral block and its effects on chronic pain and health-related quality of life after modified radical mastectomy. *Reg Anesth Pain Med.* 2014;39:289–298.
 222. Ahsan ZS, Carvalho B, Yao J. Incidence of failure of continuous peripheral nerve catheters for postoperative analgesia in upper extremity surgery. *J Hand Surg Am.* 2014;39:324–329.
 223. Lucas SD, Higdon T, Boezaart AP. Unintended epidural placement of a thoracic paravertebral catheter in a patient with severe chest trauma. *Pain Med.* 2011;12:1284–1289.
 224. Yanovski B, Gaitini L, Volodarski D, Ben-David B. Catastrophic complication of an interscalene catheter for continuous peripheral nerve block analgesia. *Anaesthesia.* 2012;67:1166–1169.
 225. Fredrickson M, Harrop-Griffiths W. Death by regional block: can the analgesic benefits ever outweigh the risks? *Anaesthesia.* 2012;67:1071–1075.
 226. Ip V, Bouliane M, Tsui B. Potential contamination of the surgical site caused by leakage from an interscalene catheter with the patient in a seated position: a case report. *Can J Anaesth.* 2012;59:1125–1129.
 227. Shakespeare TJ, Tsui BC. Intermittent hoarseness with continuous interscalene brachial plexus catheter infusion due to deficient carotid sheath. *Acta Anaesthesiol Scand.* 2013;57:1085–1086.
 228. Tsui BC, Dillane D. Reducing and washing off local anesthetic for continuous interscalene block. *Reg Anesth Pain Med.* 2014;39:175–176.
 229. Ip VH, Tsui BC. Continuous interscalene block: the good, the bad and the refined spread. *Acta Anaesthesiol Scand.* 2012;56:526–530.
 230. Marhofer D, Marhofer P, Triffiterer L, Leonhardt M, Weber M, Zeitlinger M. Dislocation rates of perineural catheters: a volunteer study. *Br J Anaesth.* 2013;111:800–806.
 231. Gurnaney H, Kraemer FW, Ganesh A. Dermabond decreases pericatheter local anesthetic leakage after continuous perineural infusions. *Anesth Analg.* 2011;113:206
 232. Walker BJ, Noonan KJ, Bosenberg AT. Evolving compartment syndrome not masked by a continuous peripheral nerve block: evidence-based case management. *Reg Anesth Pain Med.* 2012;37:393–397.
 233. Munk-Andersen H, Laustrup TK. Compartment syndrome diagnosed in due time by breakthrough pain despite continuous peripheral nerve block. *Acta Anaesthesiol Scand.* 2013;57:1328–1330.
 234. Cometa MA, Esch AT, Boezaart AP. Did continuous femoral and sciatic nerve block obscure the diagnosis or delay the treatment of acute lower leg compartment syndrome? A case report. *Pain Med.* 2011;12:823–828.
 235. Nair GS, Soliman LM, Maheshwari K, Esa WA. Importance of vigilant monitoring after continuous nerve block: lessons from a case report. *Ochsner J.* 2013;13:267–269.
 236. Rose GL, McLarney JT. Retained continuous lumbar plexus block catheter. *J Clin Anesth.* 2009;21:464–465.
 237. Despond O, Kohut GN. Broken interscalene brachial plexus catheter: surgical removal or not? *Anesth Analg.* 2010;110:643–644.
 238. Reisig F, Breitbarth J, Ott B, Büttner J. [Sheared catheter in regional anaesthesia: causes and follow-up of an axillary plexus catheter]. *Anaesthesist.* 2011;60:942–945.
 239. Owens S, Erturk MA, Ouanes JP, Murphy JD, Wu CL, Bottomley PA. Evaluation of epidural and peripheral nerve catheter heating during magnetic resonance imaging. *Reg Anesth Pain Med.* 2014;39:534–539.
 240. Bures E, Rivet P, Estebe JP. [Difficulty of regional anaesthesia catheter withdrawing due to a knot: three case reports]. *Ann Fr Anesth Reanim.* 2009;28:493–495.
 241. Presta MV, Byram SW, Reis CL, Sniderman M. Noninvasive removal of an entrapped supraclavicular catheter. *J Clin Anesth.* 2012;24:350–352.
 242. Bowens C Jr, Briggs ER, Malchow RJ. Brachial plexus entrapment of interscalene nerve catheter after uncomplicated ultrasound-guided placement. *Pain Med.* 2011;12:1117–1120.
 243. Abrahams MS, Noles LM, Cross R, Horn JL. Retained stimulating perineural catheters: a report of four cases. *Reg Anesth Pain Med.* 2011;36:476–480.
 244. Wiesmann T, Wallot P, Nentwig L, et al. Separation of stimulating catheters for continuous peripheral regional anesthesia during their removal - two case reports and a critical appraisal of the use of steel-coil containing stimulating catheters. *Local Reg Anesth.* 2015;8:15–19.
 245. Brenier G, Salces A, Maguès JP, Fuzier R. Peripheral nerve catheter entrapment is not always related to knotting. *Can J Anaesth.* 2010;57:183–184.
 246. Duclax R Jr, Robards CB, Ladie BL, Clendenen SR. Tip adhesions complicate infraclavicular catheter removal. *Can J Anaesth.* 2011;58:482–483.
 247. Rogers WK, Jacobs R, Donnelly MJ. Retained stimulating perineural catheter placed with hydrodissection but without nerve stimulation. *Can J Anaesth.* 2012;59:997–998.
 248. Schroeder KM, Jacobs RX, Amlong CA, Rogers WK. Dangers associated with cutting and entrapment of stimulating peripheral nerve catheters. *J Clin Anesth.* 2013;25:83–84.
 249. Fagenholz PJ, Bowler GM, Carnochan FM, Walker WS. Systemic local anaesthetic toxicity from continuous thoracic paravertebral block. *Br J Anaesth.* 2012;109:260–262.
 250. Warner NS, Duncan CM, Kopp SL. Acute retroperitoneal hematoma after psoas catheter placement in a patient with myeloproliferative thrombocytosis and aspirin therapy. *A A Case Rep.* 2016;6:28–30.
 251. Idestrup C, Sawhney M, Nix C, Kiss A. The incidence of hematoma formation in patients with continuous femoral catheters following total knee arthroplasty while receiving rivaroxaban as thromboprophylaxis: an observational study. *Reg Anesth Pain Med.* 2014;39:414–417.
 252. Chelly JE, Clark LD, Gebhard RE, Raw RM, Atchabahian A. Consensus of the orthopedic anesthesia, pain, and rehabilitation society on the use of peripheral nerve blocks in patients receiving thromboprophylaxis. *J Clin Anesth.* 2014;26:69–74.
 253. Levy JH, Faraoni D, Spring JL, Douketis JD, Samama CM. Managing new oral anticoagulants in the perioperative and intensive care unit setting. *Anesthesiology.* 2013;118:1466–1474.
 254. Horlocker TT, Wedel DJ, Rowlingson JC, Enneking FK; American College of Chest Physicians. Executive summary: regional anesthesia in the patient receiving antithrombotic

- or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med.* 2010;35:102–105.
255. Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med.* 2010;35:64–101.
 256. Forero M, Neira VM, Heikkilä AJ, Paul JE. Continuous lumbar transversus abdominis plane block may spread to supraumbilical dermatomes. *Can J Anaesth.* 2011;58:948–951.
 257. Bomberg H, Kubulus C, List F, et al; German Network for Regional Anaesthesia Investigators. Diabetes: a risk factor for catheter-associated infections. *Reg Anesth Pain Med.* 2015;40:16–21.
 258. Bomberg H, Albert N, Schmitt K, et al. Obesity in regional anesthesia—a risk factor for peripheral catheter-related infections. *Acta Anaesthesiol Scand.* 2015;59:1038–1048.
 259. Landy C, Polycarpe A, Boulland P, Favier JC, Plancade D. [Complication of a continuous popliteal sciatic nerve block]. *Ann Fr Anesth Reanim.* 2012;31:564–565.
 260. Tucker CJ, Kirk KL, Ficke JR. Posterior thigh abscess as a complication of continuous popliteal nerve catheter. *Am J Orthop (Belle Mead NJ).* 2010;39:E25–E27.
 261. Ceron PC, Iselin I, Hoffmeyer P, Fournier R. Cervical abscess complicating an ultrasound-guided interscalene catheter. *A Case Rep.* 2014;3:53–55.
 262. Maheshwari A, George JE 3rd, Esa WA, Turan A, Mounir-Soliman L. Images in anesthesiology: severe posterior thigh abscess as a complication of popliteal sciatic nerve catheter. *Anesthesiology.* 2013;118:955
 263. Henningsen MH, Jaeger P, Hilsted KL, Dahl JB. Prevalence of saphenous nerve injury after adductor-canal-blockade in patients receiving total knee arthroplasty. *Acta Anaesthesiol Scand.* 2013;57:112–117.
 264. Gartke K, Portner O, Taljaard M. Neuropathic symptoms following continuous popliteal block after foot and ankle surgery. *Foot Ankle Int.* 2012;33:267–274.
 265. Hajek V, Dussart C, Klack F, et al. Neuropathic complications after 157 procedures of continuous popliteal nerve block for hallux valgus surgery. A retrospective study. *Orthop Traumatol Surg Res.* 2012;98:327–333.
 266. Capdevila X, Pirat P, Bringuier S, et al; French Study Group on Continuous Peripheral Nerve Blocks. Continuous peripheral nerve blocks in hospital wards after orthopedic surgery: a multicenter prospective analysis of the quality of postoperative analgesia and complications in 1,416 patients. *Anesthesiology.* 2005;103:1035–1045.
 267. Borgeat A, Blumenthal S, Lambert M, Theodorou P, Vienne P. The feasibility and complications of the continuous popliteal nerve block: a 1001-case survey. *Anesth Analg.* 2006;103:229–233.
 268. Sites BD, Taenzer AH, Herrick MD, et al. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. *Reg Anesth Pain Med.* 2012;37:478–482.
 269. Fredrickson MJ, Kilfoyle DH. Neurological complication analysis of 1000 ultrasound guided peripheral nerve blocks for elective orthopaedic surgery: a prospective study. *Anaesthesia.* 2009;64:836–844.
 270. Neal JM. Ultrasound-guided regional anesthesia and patient safety: update of an evidence-based analysis. *Reg Anesth Pain Med.* 2016;41:195–204.
 271. Jørgensen CC, Kehlet H; Lundbeck Foundation Centre for Fast-track Hip and Knee Replacement Collaborative Group. Fall-related admissions after fast-track total hip and knee arthroplasty - cause of concern or consequence of success? *Clin Interv Aging.* 2013;8:1569–1577.
 272. Ackerman DB, Trousdale RT, Bieber P, Henely J, Pagnano MW, Berry DJ. Postoperative patient falls on an orthopedic inpatient unit. *J Arthroplasty.* 2010;25:10–14.
 273. Memtsoudis SG, Danninger T, Rasul R, et al. Inpatient falls after total knee arthroplasty: the role of anesthesia type and peripheral nerve blocks. *Anesthesiology.* 2014;120:551–563.
 274. Johnson RL, Kopp SL, Hebl JR, Erwin PJ, Mantilla CB. Falls and major orthopaedic surgery with peripheral nerve blockade: a systematic review and meta-analysis. *Br J Anaesth.* 2013;110:518–528.
 275. Lucic A, Chelly JE. The relationship between ropivacaine infusions and postoperative falls after joint replacement: where is the evidence? *Anesth Analg.* 2011;113:428–429.
 276. Chelly JE. Do continuous 'lumbar plexus' blocks really increase the risk of falls? *Br J Anaesth.* 2014;112:386
 277. Johnson RL, Duncan CM, Ahn KS, Schroeder DR, Horlocker TT, Kopp SL. Fall-prevention strategies and patient characteristics that impact fall rates after total knee arthroplasty. *Anesth Analg.* 2014;119:1113–1118.
 278. Cui Q, Schapiro LH, Kinney MC, Simon P, Poole A, Novicoff WM. Reducing costly falls of total knee replacement patients. *Am J Med Qual.* 2013;28:335–338.
 279. Veal C, Auyong DB, Hanson NA, Allen CJ, Strodtbeck W. Delayed quadriceps weakness after continuous adductor canal block for total knee arthroplasty: a case report. *Acta Anaesthesiol Scand.* 2014;58:362–364.
 280. Kehlet H, Andersen LØ. Local infiltration analgesia in joint replacement: the evidence and recommendations for clinical practice. *Acta Anaesthesiol Scand.* 2011;55:778–784.
 281. Carli F, Clemente A, Asenjo JF, et al. Analgesia and functional outcome after total knee arthroplasty: periarticular infiltration vs continuous femoral nerve block. *Br J Anaesth.* 2010;105:185–195.
 282. Dauri M, Polzoni M, Fabbi E, et al. Comparison of epidural, continuous femoral block and intraarticular analgesia after anterior cruciate ligament reconstruction. *Acta Anaesthesiol Scand.* 2003;47:20–25.
 283. Schug SA, Chong C. Pain management after ambulatory surgery. *Curr Opin Anaesthesiol.* 2009;22:738–743.
 284. Kosel J, Bobik P, Tomczyk M. Buprenorphine—the unique opioid adjuvant in regional anesthesia. *Expert Rev Clin Pharmacol.* 2016;9:375–383.
 285. Candido KD, Franco CD, Khan MA, Winnie AP, Raja DS. Buprenorphine added to the local anesthetic for brachial plexus block to provide postoperative analgesia in outpatients. *Reg Anesth Pain Med.* 2001;26:352–356.
 286. Candido KD, Winnie AP, Ghaleb AH, Fattouh MW, Franco CD. Buprenorphine added to the local anesthetic for axillary brachial plexus block prolongs postoperative analgesia. *Reg Anesth Pain Med.* 2002;27:162–167.
 287. Candido KD, Hennes J, Gonzalez S, et al. Buprenorphine enhances and prolongs the postoperative analgesic effect of bupivacaine in patients receiving infraglutal sciatic nerve block. *Anesthesiology.* 2010;113:1419–1426.
 288. Pöpping DM, Elia N, Marret E, Wenk M, Tramèr MR. Clonidine as an adjuvant to local anesthetics for peripheral nerve and plexus blocks: a meta-analysis of randomized trials. *Anesthesiology.* 2009;111:406–415.
 289. McCartney CJ, Duggan E, Apatu E. Should we add clonidine to local anesthetic for peripheral nerve blockade? A qualitative systematic review of the literature. *Reg Anesth Pain Med.* 2007;32:330–338.
 290. Abdallah FW, Brull R. Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: a systematic review and meta-analysis. *Br J Anaesth.* 2013;110:915–925.
 291. Abdallah FW, Dwyer T, Chan VW, et al. IV and perineural dexmedetomidine similarly prolong the duration of analgesia after interscalene brachial plexus block: a randomized, three-arm, triple-masked, placebo-controlled trial. *Anesthesiology.* 2016;124:683–695.
 292. De Oliveira GS Jr, Castro Alves LJ, Nader A, Kendall MC, Rahangdale R, McCarthy RJ. Perineural dexamethasone to improve postoperative analgesia with peripheral nerve blocks: a meta-analysis of randomized controlled trials. *Pain Res Treat.* 2014;2014:179029
 293. Choi S, Rodseth R, McCartney CJ. Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: a systematic review and meta-analysis of randomized trials. *Br J Anaesth.* 2014;112:427–439.

294. Albrecht E, Kern C, Kirkham KR. A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks. *Anaesthesia*. 2015;70:71–83.
295. Kirksey MA, Haskins SC, Cheng J, Liu SS. Local anesthetic peripheral nerve block adjuvants for prolongation of analgesia: a systematic qualitative review. *PLoS One*. 2015;10:e0137312
296. Brummett CM, Williams BA. Additives to local anesthetics for peripheral nerve blockade. *Int Anesthesiol Clin*. 2011;49:104–116.
297. Cummings KC 3rd, Napierkowski DE, Parra-Sanchez I, et al. Effect of dexamethasone on the duration of interscalene nerve blocks with ropivacaine or bupivacaine. *Br J Anaesth*. 2011;107:446–453.
298. Picard PR, Tramèr MR, McQuay HJ, Moore RA. Analgesic efficacy of peripheral opioids (all except intra-articular): a qualitative systematic review of randomised controlled trials. *Pain*. 1997;72:309–318.
299. Noss CD, MacKenzie LD, Kostash MA. Adjuvant dexamethasone: innovation, farce, or folly? *Reg Anesth Pain Med*. 2014;39:540–545.
300. Mannion S, Hayes I, Loughnane F, Murphy DB, Shorten GD. Intravenous but not perineural clonidine prolongs postoperative analgesia after psoas compartment block with 0.5% levobupivacaine for hip fracture surgery. *Anesth Analg*. 2005;100:873–878, table of contents.
301. Fredrickson Fanzca MJ, Danesh-Clough TK, White R. Adjuvant dexamethasone for bupivacaine sciatic and ankle blocks: results from 2 randomized placebo-controlled trials. *Reg Anesth Pain Med*. 2013;38:300–307.
302. Desmet M, Braems H, Reynvoet M, et al. I.V. and perineural dexamethasone are equivalent in increasing the analgesic duration of a single-shot interscalene block with ropivacaine for shoulder surgery: a prospective, randomized, placebo-controlled study. *Br J Anaesth*. 2013;111:445–452.
303. Rahangdale R, Kendall MC, McCarthy RJ, et al. The effects of perineural versus intravenous dexamethasone on sciatic nerve blockade outcomes: a randomized, double-blind, placebo-controlled study. *Anesth Analg*. 2014;118:1113–1119.
304. Leurcharusmee P, Aliste J, Van Zundert TC, et al. A multicenter randomized comparison between intravenous and perineural dexamethasone for ultrasound-guided infraclavicular block. *Reg Anesth Pain Med*. 2016;41:328–333.
305. Bangham AD, Standish MM, Miller N. Cation permeability of phospholipid model membranes: effect of narcotics. *Nature*. 1965;208:1295–1297.
306. Ilfeld BM. Liposomal bupivacaine: its role in regional anesthesia and postoperative analgesia. *Advances in Anesthesia*. 2014; 32: 133–147.
307. Charous MT, Ilfeld BM: Liposome bupivacaine for postoperative analgesia: one formulation approved for clinical use within the United States. *Curr Anesthesiol Rep*. 2015; 5: 235–242.
308. Howell SB. Clinical applications of a novel sustained-release injectable drug delivery system: DepoFoam technology. *Cancer J*. 2001;7:219–227.
309. Viscusi ER. Liposomal drug delivery for postoperative pain management. *Reg Anesth Pain Med*. 2005;30:491–496.
310. Grant GJ, Bansinath M. Liposomal delivery systems for local anesthetics. *Reg Anesth Pain Med*. 2001;26:61–63.
311. Gesztes A, Mezei M. Topical anesthesia of the skin by liposome-encapsulated tetracaine. *Anesth Analg*. 1988;67:1079–1081.
312. Boogaerts JG, Lafont ND, Declercq AG, et al. Epidural administration of liposome-associated bupivacaine for the management of postsurgical pain: a first study. *J Clin Anesth*. 1994;6:315–320.
313. Holte K, Werner MU, Lacouture PG, Kehlet H. Dexamethasone prolongs local analgesia after subcutaneous infiltration of bupivacaine microcapsules in human volunteers. *Anesthesiology*. 2002;96:1331–1335.
314. Grant GJ, Barenholz Y, Bolotin EM, et al. A novel liposomal bupivacaine formulation to produce ultralong-acting analgesia. *Anesthesiology*. 2004;101:133–137.
315. Raeder JC, Drösdahl S, Klaastad O, et al. Axillary brachial plexus block with ropivacaine 7.5 mg/ml. A comparative study with bupivacaine 5 mg/ml. *Acta Anaesthesiol Scand*. 1999;43:794–798.
316. Kopacz DJ, Lacouture PG, Wu D, Nandy P, Swanton R, Landau C. The dose response and effects of dexamethasone on bupivacaine microcapsules for intercostal blockade (T9 to T11) in healthy volunteers. *Anesth Analg*. 2003;96:576–582.
317. Kopacz DJ, Bernards CM, Allen HW, et al. A model to evaluate the pharmacokinetic and pharmacodynamic variables of extended-release products using *in vivo* tissue microdialysis in humans: bupivacaine-loaded microcapsules. *Anesth Analg*. 2003;97:124–131.
318. Movafegh A, Razazian M, Hajimaohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. *Anesth Analg*. 2006;102:263–267.
319. Pedersen JL, Lillesø J, Hammer NA, et al. Bupivacaine in microcapsules prolongs analgesia after subcutaneous infiltration in humans: a dose-finding study. *Anesth Analg*. 2004;99:912–918.
320. Ginosar Y, Haroutounian S, Kagan L, Naveh M, Aharon A, Davidson EM. Proliposomal ropivacaine oil: pharmacokinetic and pharmacodynamic data after subcutaneous administration in volunteers. *Anesth Analg*. 2016;122:1673–1680.
321. Davidson EM, Haroutounian S, Kagan L, Naveh M, Aharon A, Ginosar Y. A novel proliposomal ropivacaine oil: pharmacokinetic-pharmacodynamic studies after subcutaneous administration in pigs. *Anesth Analg*. 2016;122:1663–1672.
322. Gorfine SR, Onel E, Patou G, Krivokapic ZV. Bupivacaine extended-release liposome injection for prolonged postsurgical analgesia in patients undergoing hemorrhoidectomy: a multicenter, randomized, double-blind, placebo-controlled trial. *Dis Colon Rectum*. 2011;54:1552–1559.
323. Golf M, Daniels SE, Onel E. A phase 3, randomized, placebo-controlled trial of DepoFoam® bupivacaine (extended-release bupivacaine local analgesic) in bunionectomy. *Adv Ther*. 2011;28:776–788.
324. Bergese SD, Ramamoorthy S, Patou G, Bramlett K, Gorfine SR, Candiotti KA. Efficacy profile of liposome bupivacaine, a novel formulation of bupivacaine for postsurgical analgesia. *J Pain Res*. 2012;5:107–116.
325. Smoot JD, Bergese SD, Onel E, Williams HT, Hedden W. The efficacy and safety of DepoFoam bupivacaine in patients undergoing bilateral, cosmetic, submuscular augmentation mammoplasty: a randomized, double-blind, active-control study. *Aesthet Surg J*. 2012;32:69–76.
326. Bramlett K, Onel E, Viscusi ER, Jones K. A randomized, double-blind, dose-ranging study comparing wound infiltration of DepoFoam bupivacaine, an extended-release liposomal bupivacaine, to bupivacaine HCl for postsurgical analgesia in total knee arthroplasty. *Knee*. 2012;19:530–536.
327. Collis PN, Hunter AM, Vaughn MD, Carreon LY, Huang J, Malkani AL. Periarticular injection after total knee arthroplasty using liposomal bupivacaine vs a modified ranawat suspension: a prospective, randomized study. *J Arthroplasty*. 2016;31:633–636.
328. Schroer WC, Diesfeld PG, LeMarr AR, Morton DJ, Reedy ME. Does extended-release liposomal bupivacaine better control pain than bupivacaine after total knee arthroplasty (TKA)? A prospective, randomized clinical trial. *J Arthroplasty*. 2015;30:64–67.
329. Knight RB, Walker PW, Keegan KA, et al. A randomized controlled trial for pain control in laparoscopic urologic surgery: 0.25% bupivacaine versus long-acting liposomal bupivacaine. *J Endourol*. 2015;29:1019–1024.
330. Noviasky J, Pierce DP, Whalen K, Guharoy R, Hildreth K. Bupivacaine liposomal versus bupivacaine: comparative review. *Hosp Pharm*. 2014;49:539–543.
331. Haas E, Onel E, Miller H, Ragupathi M, White PF. A double-blind, randomized, active-controlled study for post-hemorrhoidectomy pain management with liposome bupivacaine, a novel local analgesic formulation. *Am Surg*. 2012;78:574–581.
332. Nadeau MH, Saraswat A, Vasko A, Elliott JO, Vasko SD. Bupivacaine versus liposomal bupivacaine for postoperative pain control after augmentation mammoplasty: a prospective, randomized, double-blind trial. *Aesthet Surg J*. 2016;36:NP47–NP52.

333. Dasta J, Ramamoorthy S, Patou G, Sinatra R. Bupivacaine liposome injectable suspension compared with bupivacaine HCl for the reduction of opioid burden in the postsurgical setting. *Curr Med Res Opin.* 2012;28:1609–1615.
334. Ilfeld BM. Liposome bupivacaine in peripheral nerve blocks and epidural injections to manage postoperative pain. *Expert Opin Pharmacother.* 2013;14:2421–2431.
335. Surdam JW, Licini DJ, Baynes NT, Arce BR. The use of exparel (liposomal bupivacaine) to manage postoperative pain in unilateral total knee arthroplasty patients. *J Arthroplasty.* 2015;30:325–329.
336. Hutchins J, Delaney D, Vogel RI, et al. Ultrasound guided subcostal transversus abdominis plane (TAP) infiltration with liposomal bupivacaine for patients undergoing robotic assisted hysterectomy: a prospective randomized controlled study. *Gynecol Oncol.* 2015;138:609–613.
337. Hutchins J, Vogel RI, Ghebre R, et al. Ultrasound-guided subcostal transversus abdominis plane infiltration with liposomal bupivacaine for patients undergoing robotic-assisted hysterectomy: a retrospective study. *Int J Gynecol Cancer.* 2015;25:937–941.
338. Ayad S, Babazade R, Elsharkawy H, et al. Comparison of transversus abdominis plane infiltration with liposomal bupivacaine versus continuous epidural analgesia versus intravenous opioid analgesia. *PLoS One.* 2016;11:e0153675
339. Viscusi ER, Candiotti KA, Onel E, Morren M, Ludbrook GL. The pharmacokinetics and pharmacodynamics of liposome bupivacaine administered via a single epidural injection to healthy volunteers. *Reg Anesth Pain Med.* 2012;37:616–622.
340. Ilfeld BM, Viscusi ER, Hadzic A, et al. Safety and side effect profile of liposome bupivacaine (Exparel) in peripheral nerve blocks. *Reg Anesth Pain Med.* 2015;40:572–582.
341. Viscusi ER, Sinatra R, Onel E, Ramamoorthy SL. The safety of liposome bupivacaine, a novel local analgesic formulation. *Clin J Pain.* 2014;30:102–110.
342. Richard BM, Newton P, Ott LR, et al. The safety of EXPAREL® (bupivacaine liposome injectable suspension) administered by peripheral nerve block in rabbits and dogs. *J Drug Deliv.* 2012;2012:962101
343. McAlvin JB, Padera RF, Shankarappa SA, et al. Multivesicular liposomal bupivacaine at the sciatic nerve. *Biomaterials.* 2014;35:4557–4564.
344. McAlvin JB, Reznor G, Shankarappa SA, Stefanescu CF, Kohane DS. Local toxicity from local anesthetic polymeric microparticles. *Anesth Analg.* 2013;116:794–803.
345. Damjanovska M, Cvetko E, Hadzic A, et al. Neurotoxicity of perineural vs intraneural-extraneural injection of liposomal bupivacaine in the porcine model of sciatic nerve block. *Anaesthesia.* 2015;70:1418–1426.
346. Kharitonov V. A review of the compatibility of liposome bupivacaine with other drug products and commonly used implant materials. *Postgrad Med.* 2014;126:129–138.
347. Naseem A, Harada T, Wang D, et al. Bupivacaine extended release liposome injection does not prolong QTc interval in a thorough QT/QTc study in healthy volunteers. *J Clin Pharmacol.* 2012;52:1441–1447.
348. Boogaerts J, Declercq A, Lafont N, et al. Toxicity of bupivacaine encapsulated into liposomes and injected intravenously: comparison with plain solutions. *Anesth Analg.* 1993;76:553–555.
349. Curley J, Castillo J, Hotz J, et al. Prolonged regional nerve blockade. Injectable biodegradable bupivacaine/polyester microspheres. *Anesthesiology.* 1996;84:1401–1410.
350. Estebe JP, Le Corre P, Du Plessis L, et al. The pharmacokinetics and pharmacodynamics of bupivacaine-loaded microspheres on a brachial plexus block model in sheep. *Anesth Analg.* 2001;93:447–455.
351. Ilfeld BM, Malhotra N, Furnish TJ, Donohue MC, Madison SJ. Liposomal bupivacaine as a single-injection peripheral nerve block: a dose-response study. *Anesth Analg.* 2013;117:1248–1256.
352. Hadzic A, Minkowitz HS, Melson TI, et al. Liposome bupivacaine femoral nerve block for postsurgical analgesia after total knee arthroplasty. *Anesthesiology.* 2016;124:1372–1383.
353. Rice DC, Cata JP, Mena GE, Rodriguez-Restrepo A, Correa AM, Mehran RJ. Posterior intercostal nerve block with liposomal bupivacaine: an alternative to thoracic epidural analgesia. *Ann Thorac Surg.* 2015;99:1953–1960.
354. Ilfeld BM, Preciado J, Trescot AM. Cryoneurolysis for the treatment of sensory and motor peripheral nerves. *Expert Rev Med Dev.* 2016;13:713–725.
355. Gage AA. History of cryosurgery. *Semin Surg Oncol.* 1998;14:99–109.
356. Trescot AM. Cryoanalgesia in interventional pain management. *Pain Physician.* 2003;6:345–360.
357. Gage AA, Baust JM, Baust JG. Experimental cryosurgery investigations in vivo. *Cryobiology.* 2009;59:229–243.
358. Gwak MS, Yang M, Hahm TS, Cho HS, Cho CH, Song JG. Effect of cryoanalgesia combined with intravenous continuous analgesia in thoracotomy patients. *J Korean Med Sci.* 2004;19:74–78.
359. Yang MK, Cho CH, Kim YC. The effects of cryoanalgesia combined with thoracic epidural analgesia in patients undergoing thoracotomy. *Anaesthesia.* 2004;59:1073–1077.
360. Momenzadeh S, Elyasi H, Valaie N, et al. Effect of cryoanalgesia on post-thoracotomy pain. *Acta Med Iran.* 2011;49:241–245.
361. Moorjani N, Zhao F, Tian Y, Liang C, Kaluba J, Maiwand MO. Effects of cryoanalgesia on post-thoracotomy pain and on the structure of intercostal nerves: a human prospective randomized trial and a histological study. *Eur J Cardiothorac Surg.* 2001;20:502–507.
362. Miguel R, Hubbell D. Pain management and spirometry following thoracotomy: a prospective, randomized study of four techniques. *J Cardiothorac Vasc Anesth.* 1993;7:529–534.
363. Roberts D, Pizzarelli G, Lepore V, al-Khaja N, Belboul A, Dernevik L. Reduction of post-thoracotomy pain by cryotherapy of intercostal nerves. *Scand J Thorac Cardiovasc Surg.* 1988;22:127–130.
364. Rooney SM, Jain S, McCormack P, Bains MS, Martini N, Goldiner PL. A comparison of pulmonary function tests for postthoracotomy pain using cryoanalgesia and transcutaneous nerve stimulation. *Ann Thorac Surg.* 1986;41:204–207.
365. Katz J, Nelson W, Forest R, Bruce DL. Cryoanalgesia for post-thoracotomy pain. *Lancet.* 1980;1:512–513.
366. Pastor J, Morales P, Cases E, et al. Evaluation of intercostal cryoanalgesia versus conventional analgesia in postthoracotomy pain. *Respiration.* 1996;63:241–245.
367. Bucerius J, Metz S, Walther T, et al. Pain is significantly reduced by cryoablation therapy in patients with lateral mini-thoracotomy. *Ann Thorac Surg.* 2000;70:1100–1104.
368. Tovar EA, Roethe RA, Weissig MD, et al. Muscle-sparing minithoracotomy with intercostal nerve cryoanalgesia: an improved method for major lung resections. *Am Surg.* 1998;64:1109–1115.
369. Brichon PY, Pison C, Chaffanjon P, et al. Comparison of epidural analgesia and cryoanalgesia in thoracic surgery. *Eur J Cardiothorac Surg.* 1994;8:482–486.
370. Khanbhai M, Yap KH, Mohamed S, Dunning J. Is cryoanalgesia effective for post-thoracotomy pain? *Interact Cardiovasc Thorac Surg.* 2014;18:202–209.
371. Roxburgh JC, Markland CG, Ross BA, Kerr WF. Role of cryoanalgesia in the control of pain after thoracotomy. *Thorax.* 1987;42:292–295.
372. Mustola ST, Lempinen J, Saimanen E, Vilkkio P. Efficacy of thoracic epidural analgesia with or without intercostal nerve cryoanalgesia for postthoracotomy pain. *Ann Thorac Surg.* 2011;91:869–873.
373. Ju H, Feng Y, Yang BX, Wang J. Comparison of epidural analgesia and intercostal nerve cryoanalgesia for post-thoracotomy pain control. *Eur J Pain.* 2008;12:378–384.
374. Müller LC, Salzer GM, Ransmayr G, Neiss A. Intraoperative cryoanalgesia for postthoracotomy pain relief. *Ann Thorac Surg.* 1989;48:15–18.
375. Robinson SR, Purdie GL. Reducing post-tonsillectomy pain with cryoanalgesia: a randomized controlled trial. *Laryngoscope.* 2000;110:1128–1131.

376. Wood GJ, Lloyd JW, Bullingham RE, Britton BJ, Finch DR. Postoperative analgesia for day-case herniorrhaphy patients. A comparison of cryoanalgesia, paravertebral blockade and oral analgesia. *Anaesthesia*. 1981;36:603–610.
377. Callesen T, Bech K, Thorup J, et al. Cryoanalgesia: effect on postherniorrhaphy pain. *Anesth Analg*. 1998;87:896–899.
378. Onik G, Gilbert J, Hoddick W, et al. Sonographic monitoring of hepatic cryosurgery in an experimental animal model. *AJR Am J Roentgenol*. 1985;144:1043–1047.
379. Onik G, Cobb C, Cohen J, Zabkar J, Porterfield B. US characteristics of frozen prostate. *Radiology*. 1988;168:629–631.
380. Moesker AA, Karl HW, Trescot AM. Treatment of phantom limb pain by cryoneurolysis of the amputated nerve. *Pain Pract*. 2014;14:52–56.
381. Yoon JH, Grechushkin V, Chaudhry A, Bhattacharji P, Durkin B, Moore W. Cryoneurolysis in patients with refractory chronic peripheral neuropathic pain. *J Vasc Interv Radiol*. 2016;27:239–243.
382. Rhame EE, Debonet AF, Simopoulos TT. Ultrasonographic guidance and characterization of cryoanalgesic lesions in treating a case of refractory sural neuroma. *Case Rep Anesthesiol*. 2011;2011:691478.
383. Friedman T, Richman D, Adler R. Sonographically guided cryoneurolysis: preliminary experience and clinical outcomes. *J Ultrasound Med*. 2012;31:2025–2034.
384. Campos NA, Chiles JH, Plunkett AR. Ultrasound-guided cryoablation of genitofemoral nerve for chronic inguinal pain. *Pain Physician*. 2009;12:997–1000.
385. Byas-Smith MG, Gulati A. Ultrasound-guided intercostal nerve cryoablation. *Anesth Analg*. 2006;103:1033–1035.
386. Hsu M, Stevenson FF. Reduction in muscular motility by selective focused cold therapy: a preclinical study. *J Neural Transm (Vienna)*. 2014;121:15–20.
387. Hsu M, Stevenson FF. Wallerian degeneration and recovery of motor nerves after multiple focused cold therapies. *Muscle Nerve*. 2015;51:268–275.
388. Zhou L, Craig J, Parekh N: Current concepts of neurolysis and clinical applications. *J Analgesics*. 2014;2:16–22.
389. Kim PS, Ferrante FM. Cryoanalgesia: a novel treatment for hip adductor spasticity and obturator neuralgia. *Anesthesiology*. 1998;89:534–536.
390. Guan Y. Spinal cord stimulation: neurophysiological and neurochemical mechanisms of action. *Curr Pain Headache Rep*. 2012;16:217–225.
391. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science*. 1965;150:971–979.
392. Campbell JN, Taub A. Local analgesia from percutaneous electrical stimulation. A peripheral mechanism. *Arch Neurol*. 1973;28:347–350.
393. Wall PD, Sweet WH. Temporary abolition of pain in man. *Science*. 1967;155:108–109.
394. Deer TR, Mekhail N, Petersen E, et al; Neuromodulation Appropriateness Consensus Committee. The appropriate use of neurostimulation: stimulation of the intracranial and extracranial space and head for chronic pain. Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17:551–570.
395. Deer TR, Thomson S, Pope JE, Russo M, Luscombe F, Levy R. International neuromodulation society critical assessment: guideline review of implantable neurostimulation devices. *Neuromodulation*. 2014;17:678–685.
396. Deer TR, Mekhail N, Provenzano D, et al; Neuromodulation Appropriateness Consensus Committee. The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17:515–550; discussion 550.
397. Deer TR, Mekhail N, Provenzano D, et al; Neuromodulation Appropriateness Consensus Committee. The appropriate use of neurostimulation: avoidance and treatment of complications of neurostimulation therapies for the treatment of chronic pain. Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17:571–597; discussion 597–8.
398. Deer TR, Krames E, Mekhail N, et al; Neuromodulation Appropriateness Consensus Committee. The appropriate use of neurostimulation: new and evolving neurostimulation therapies and applicable treatment for chronic pain and selected disease states. Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17:599–615; discussion 615.
399. Hymes AC, Raab DE, Yonehiro EG, Nelson GD, Printy AL. Electrical surface stimulation for control of acute postoperative pain and prevention of ileus. *Surg Forum*. 1973;24:447–449.
400. VanderArk GD, McGrath KA. Transcutaneous electrical stimulation in treatment of postoperative pain. *Am J Surg*. 1975;130:338–340.
401. Rakel BA, Zimmerman MB, Geasland K, et al. Transcutaneous electrical nerve stimulation for the control of pain during rehabilitation after total knee arthroplasty: a randomized, blinded, placebo-controlled trial. *Pain*. 2014;155:2599–2611.
402. Hassenbusch SJ, Stanton-Hicks M, Schoppa D, Walsh JG, Covington EC. Long-term results of peripheral nerve stimulation for reflex sympathetic dystrophy. *J Neurosurg*. 1996;84:415–423.
403. Picaza JA, Hunter SE, Cannon BW. Pain suppression by peripheral nerve stimulation. Chronic effects of implanted devices. *Appl Neurophysiol*. 1977;40:223–234.
404. Yu DT, Chae J, Walker ME, Fang ZP. Percutaneous intramuscular neuromuscular electric stimulation for the treatment of shoulder subluxation and pain in patients with chronic hemiplegia: a pilot study. *Arch Phys Med Rehabil*. 2001;82:20–25.
405. Goldman HB, Amundsen CL, Mangel J, et al. Dorsal genital nerve stimulation for the treatment of overactive bladder symptoms. *Neurourol Urodyn*. 2008;27:499–503.
406. Deer TR, Levy RM, Rosenfeld EL. Prospective clinical study of a new implantable peripheral nerve stimulation device to treat chronic pain. *Clin J Pain*. 2010;26:359–372.
407. Weiner RL. Peripheral nerve neurostimulation. *Neurosurg Clin N Am*. 2003;14:401–408.
408. Weiner RL, Reed KL. Peripheral neurostimulation for control of intractable occipital neuralgia. *Neuromodulation*. 1999;2:217–221.
409. Weiner RL. Occipital neurostimulation for treatment of intractable headache syndromes. *Acta Neurochir Suppl*. 2007;97:129–133.
410. Huntoon MA, Hoelzer BC, Burgher AH, Hurdle MF, Huntoon EA. Feasibility of ultrasound-guided percutaneous placement of peripheral nerve stimulation electrodes and anchoring during simulated movement: part two, upper extremity. *Reg Anesth Pain Med*. 2008;33:558–565.
411. Huntoon MA, Huntoon EA, Obray JB, Lamer TJ. Feasibility of ultrasound-guided percutaneous placement of peripheral nerve stimulation electrodes in a cadaver model: part one, lower extremity. *Reg Anesth Pain Med*. 2008;33:551–557.
412. Huntoon MA, Burgher AH. Ultrasound-guided permanent implantation of peripheral nerve stimulation (PNS) system for neuropathic pain of the extremities: original cases and outcomes. *Pain Med*. 2009;10:1369–1377.
413. Rauck RL, Kapural L, Cohen SP, et al. Peripheral nerve stimulation for the treatment of postamputation pain—a case report. *Pain Pract*. 2012;12:649–655.
414. Rauck RL, Cohen SP, Gilmore CA, et al. Treatment of post-amputation pain with peripheral nerve stimulation. *Neuromodulation*. 2014;17:188–197.
415. Deer T, Pope J, Benyamin R, et al. Prospective, multicenter, randomized, double-blinded, partial crossover study to assess the safety and efficacy of the novel neuromodulation system in the treatment of patients with chronic pain of peripheral nerve origin. *Neuromodulation*. 2016;19:91–100.
416. Ilfeld BM, Gilmore CA, Grant SA, et al. Ultrasound-guided percutaneous peripheral nerve stimulation for analgesia following total knee arthroplasty: a prospective feasibility study. *J Orthop Surg Res*. In Press.
- 416a. Ilfeld BM, Grant SA, et al. Neurostimulation for post-surgical analgesia: a novel system enabling ultrasound-guided

- percutaneous peripheral nerve stimulation. *Pain Practice*. In Press.
- 416b. Grant SA, Ilfeld BM, Martin G, et al. Percutaneous peripheral nerve stimulation for the treatment of perioperative pain during total knee arthroplasty [abstract]. *Reg Anesth Pain Med*. 2016; A1542.
- 416c. Ilfeld BM, Gabriel RA, Saulino MF, et al. Infection rate of electrical leads used for percutaneous neuromuscular stimulation of the peripheral nervous system. *Pain Practice*. In Press.
- 416d. Ilfeld BM, Grant SA. Ultrasound-guided percutaneous peripheral nerve stimulation for postoperative analgesia: could neurostimulation replace continuous peripheral nerve blocks? *Reg Anesth Pain Med*. In Press.
417. Marsolais EB, Kobetic R. Implantation techniques and experience with percutaneous intramuscular electrodes in the lower extremities. *J Rehabil Res Dev*. 1986;23:1-8.
418. Shimada Y, Matsunaga T, Misawa A, Ando S, Itoi E, Konishi N. Clinical application of peroneal nerve stimulator system using percutaneous intramuscular electrodes for correction of foot drop in hemiplegic patients. *Neuromodulation*. 2006;9:320-327.
419. Onders RP, Elmo M, Khansarinia S, et al. Complete worldwide operative experience in laparoscopic diaphragm pacing: results and differences in spinal cord injured patients and amyotrophic lateral sclerosis patients. *Surg Endosc*. 2009;23:1433-1440.
420. Scheiner A, Polando G, Marsolais EB. Design and clinical application of a double helix electrode for functional electrical stimulation. *IEEE Trans Biomed Eng*. 1994;41:425-431.
421. Shimada Y, Sato K, Kagaya H, Konishi N, Miyamoto S, Matsunaga T. Clinical use of percutaneous intramuscular electrodes for functional electrical stimulation. *Arch Phys Med Rehabil*. 1996;77:1014-1018.
422. Stanton-Hicks M, Panourias IG, Sakas DE, Slavin KV. The future of peripheral nerve stimulation. *Prog Neurol Surg*. 2011;24:210-217.
423. Tran KM, Ganley TJ, Wells L, Ganesh A, Minger KI, Cucchiaro G. Intraarticular bupivacaine-clonidine-morphine versus femoral-sciatic nerve block in pediatric patients undergoing anterior cruciate ligament reconstruction. *Anesth Analg*. 2005;101:1304-1310.
424. Ilfeld BM, Yaksh TL. The end of postoperative pain—a fast-approaching possibility? And, if so, will we be ready? *Reg Anesth Pain Med*. 2009;34:85-87.
425. Ilfeld BM, Mariano ER. Evaluating clinical research and bloodletting. (Seriously). *Reg Anesth Pain Med*. 2010;35:488-489.
426. Jones HG, Stoneham MD. Continuous cervical plexus block for carotid body tumour excision in a patient with Eisenmenger's syndrome. *Anaesthesia*. 2006;61:1214-1218.
427. Koh WU, Kim HJ, Park HS, Choi WJ, Yang HS, Ro YJ. A randomised controlled trial comparing continuous supraclavicular and interscalene brachial plexus blockade for open rotator cuff surgery. *Anaesthesia*. 2016;71:692-699.
428. Vandepitte C, Gautier P, Xu D, Salviz EA, Hadzic A. Effective volume of ropivacaine 0.75% through a catheter required for interscalene brachial plexus blockade. *Anesthesiology*. 2013;118:863-867.
429. Torrillo TM, Rosenblatt MA. Ultrasound-guided interscalene catheters performed under general anesthesia in a patient with Huntington's disease. *Minerva Anesthesiol*. 2010;76:645-648.
430. Gelpi B, Telang PR, Samuelson CG, Hamilton CS, Billioudaux S. Bilateral ultrasound-guided supraclavicular block in a patient with severe electrocution injuries of the upper extremities. *J La State Med Soc*. 2014;166:60-62.
431. Elsharkawy HA, Abd-Elsayed AA, Cummings KC 3rd, Soliman LM. Analgesic efficacy and technique of ultrasound-guided suprascapular nerve catheters after shoulder arthroscopy. *Ochsner J*. 2014;14:259-263.
432. Mariano ER, Sandhu NS, Loland VJ, et al. A randomized comparison of infraclavicular and supraclavicular continuous peripheral nerve blocks for postoperative analgesia. *Reg Anesth Pain Med*. 2011;36:26-31.
433. Mariano ER, Loland VJ, Ilfeld BM. Comparing axillary with infraclavicular perineural catheters for post-operative analgesia. *Acta Anaesthesiol Scand*. 2011;55:1283-1284.
434. Harrison TK, Kim TE, Howard SK, et al. Comparative effectiveness of infraclavicular and supraclavicular perineural catheters for ultrasound-guided through-the-catheter bolus anesthesia. *J Ultrasound Med*. 2015;34:333-340.
435. Choi SS, Lee MK, Kim JE, Kim SH, Yeo GE. Ultrasound-guided continuous axillary brachial plexus block using a nerve stimulating catheter: EpiStim® Catheter. *Korean J Pain*. 2015;28:287-289.
436. Maxwell BG, Hansen JA, Talley J, Curtin CM, Mariano ER. Ultrasound-guided continuous median nerve block to facilitate intensive hand rehabilitation. *Clin J Pain*. 2013;29:86-88.
437. Buggy DJ, Kerin MJ. Paravertebral analgesia with levobupivacaine increases postoperative flap tissue oxygen tension after immediate latissimus dorsi breast reconstruction compared with intravenous opioid analgesia. *Anesthesiology*. 2004;100:375-380.
438. Wu J, Buggy D, Fleischmann E, et al. Thoracic paravertebral regional anesthesia improves analgesia after breast cancer surgery: a randomized controlled multicentre clinical trial. *Can J Anaesth*. 2015;62:241-251.
439. Buckenmaier CC 3rd, Bleckner L. Primum non nocere. *Reg Anesth Pain Med*. 2014;39:87-88.
440. Ilfeld BM, Madison SJ. Continuous paravertebral blocks for analgesia following mastectomy: the jury is still out. *Reg Anesth Pain Med*. 2014;39:355
441. Buckenmaier CC 3rd, Kwon KH, Howard RS, et al. Double-blinded, placebo-controlled, prospective randomized trial evaluating the efficacy of paravertebral block with and without continuous paravertebral block analgesia in outpatient breast cancer surgery. *Pain Med*. 2010;11:790-799.
442. Maeda A, Shibata SC, Okitsu K, et al. Pain management with bilateral continuous thoracic paravertebral block in a patient with fontan-associated hepatocellular carcinoma undergoing hepatectomy. *Reg Anesth Pain Med*. 2015;40:718-719.
443. Chen H, Liao Z, Fang Y, et al. Continuous right thoracic paravertebral block following bolus initiation reduced post-operative pain after right-lobe hepatectomy: a randomized, double-blind, placebo-controlled trial. *Reg Anesth Pain Med*. 2014;39:506-512.
444. Kadam VR, Moran JL. Epidural infusions versus transversus abdominis plane (TAP) block infusions: retrospective study. *J Anesth*. 2011;25:786-787.
445. Nie H, Yang YX, Wang Y, Liu Y, Zhao B, Luan B. Effects of continuous fascia iliaca compartment blocks for postoperative analgesia in hip fracture patients. *Pain Res Manag*. 2015;20:210-212.
446. Fredrickson MJ, Danesh-Clough TK. Ultrasound-guided femoral catheter placement: a randomised comparison of the in-plane and out-of-plane techniques. *Anaesthesia*. 2013;68:382-390.
447. Al-Zahrani T, Doais KS, Aljassir F, Alshaygy I, Albishi W, Terkawi AS. Randomized clinical trial of continuous femoral nerve block combined with sciatic nerve block versus epidural analgesia for unilateral total knee arthroplasty. *J Arthroplasty*. 2015;30:149-154.
448. Beebe MJ, Allen R, Anderson MB, Swenson JD, Peters CL. Continuous femoral nerve block using 0.125% bupivacaine does not prevent early ambulation after total knee arthroplasty. *Clin Orthop Relat Res*. 2014;472:1394-1399.
449. Abdallah FW, Chan VW, Gandhi R, Koshkin A, Abbas S, Brull R. The analgesic effects of proximal, distal, or no sciatic nerve block on posterior knee pain after total knee arthroplasty: a double-blind placebo-controlled randomized trial. *Anesthesiology*. 2014;121:1302-1310.
450. Thomas K, Barrett B, Tupper R, Dacenko-Grawe L, Holm K. Pain management after total knee arthroplasty: a case-control study of continuous nerve block therapy. *Orthop Nurs*. 2014;33:268-276.

451. Krämer S, Wenk M, Fischer G, Möllmann M, Pöpping DM. Continuous spinal anesthesia versus continuous femoral nerve block for elective total knee replacement. *Minerva Anesthesiol.* 2011;77:394–400.
452. Mudumbai SC, Kim TE, Howard SK, et al. Continuous adductor canal blocks are superior to continuous femoral nerve blocks in promoting early ambulation after TKA. *Clin Orthop Relat Res.* 2013; 473: 1377–1383.
453. Leng JC, Harrison TK, Miller B, et al. A pilot study to assess adductor canal catheter tip migration in a cadaver model. *J Anesth.* 2015;29:308–312.
454. Webb CA, Kim TE, Funck N, et al. Comparison of catheter tip migration using flexible and stimulating catheters inserted into the adductor canal in a cadaver model. *J Anesth.* 2015;29:471–474.
455. Rasmussen M, Kim E, Kim TE, et al. A retrospective comparative provider workload analysis for femoral nerve and adductor canal catheters following knee arthroplasty. *J Anesth.* 2015;29:303–307.
456. Perlas A, Kirkham KR, Billing R, et al. The impact of analgesic modality on early ambulation following total knee arthroplasty. *Reg Anesth Pain Med.* 2013;38:334–339.
457. Luiten WE, Schepers T, Luitse JS, et al. Comparison of continuous nerve block versus patient-controlled analgesia for postoperative pain and outcome after talar and calcaneal fractures. *Foot Ankle Int.* 2014;35:1116–1121.
458. Saporito A, Petri GJ, Sturini E, Borgeat A, Aguirre JA. Safety and effectiveness of bilateral continuous sciatic nerve block for bilateral orthopaedic foot surgery: a cohort study. *Eur J Anaesthesiol.* 2014;31:620–625.
459. Fisker AK, Iversen BN, Christensen S, et al. Combined saphenous and sciatic catheters for analgesia after major ankle surgery: a double-blinded randomized controlled trial. *Can J Anaesth.* 2015;62:875–882.