

REGIONAL ANESTHESIA (CJL McCARTNEY, SECTION EDITOR)

# Peripheral Nerve Blockade for Total Knee Arthroplasty: An Evidence-Based Review

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Abstract Total knee arthroplasty (TKA) is associated with significant postoperative pain. Optimization of postoperative analgesia can improve rehabilitation and functional recovery. There is much debate regarding the best peripheral nerve blocks for optimization of postoperative analgesic and functional outcomes following TKA. Continuous femoral nerve block provides excellent postoperative analgesia. In comparison, adductor canal block may provide relative preservation of quadriceps motor weakness, however, its effect on analgesia, mobilization, longterm functional outcomes, and inpatient falls remains unclear. Sciatic nerve block provides effective analgesia in addition to continuous femoral nerve block, and its clinical benefit may be greatest in patients with opioid tolerance or chronic pain. Studies comparing local infiltration analgesia to femoral nerve block are difficult to interpret due to high risk of bias and methodological flaws. Addition of

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<sup>2</sup> Department of Anesthesiology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada obturator nerve block may improve postoperative analgesia, but the impact of this on functional outcomes remains unknown.

**Keywords** Total knee arthroplasty · Peripheral nerve block · Femoral nerve block · Sciatic nerve block · Local infiltration analgesia · Adductor canal block

# Introduction

Total knee arthroplasty (TKA) is a commonly performed orthopedic surgical procedure. 450,000 primary TKAs were performed in the United States in 2005, and this figure is projected to increase to 3.48 million by 2030 [1].

TKA is associated with significant postoperative pain, which may impair early postoperative knee rehabilitation [2]. Optimizing analgesia in the postoperative period can facilitate early mobilization, rehabilitation, and functional recovery.

Due to the complex sensory innervation to the knee, several different peripheral nerve blocks and combinations thereof can be utilized for postoperative analgesia. In addition, the use of continuous peripheral nerve blockade via perineural catheters extends the duration of analgesia.

This review aims to summarize the evidence base for the most common peripheral nerve blocks used for postoperative analgesia following TKA including femoral nerve block (FNB), sciatic nerve block (SNB), adductor canal block (ACB), obturator nerve block (ONB), and also local infiltration analgesia (LIA). The impact of these blocks on relevant postoperative outcomes including analgesia, opioid consumption, mobilization, rehabilitation, inpatient falls, and length of stay (LOS) is evaluated.

## **Femoral Nerve Block**

FNB provides postoperative analgesia to the anterior cutaneous and articular aspects of the knee following TKA. Historically, the term '3 in 1' block was used for the landmark-based technique on the assumption that the femoral, obturator, and lateral femoral cutaneous nerves could all be blocked effectively by a single injection via cephalad spread to the lumbar plexus. Both clinical and radiological studies have disproved this, demonstrating consistent blockade of the femoral and lateral femoral cutaneous nerves, with ineffective obturator nerve block-ade [3–5].

Single shot FNB results in significantly lower resting pain scores following TKA compared to intravenous patient-controlled analgesia (IV PCA) at 3–12 [6–8], 24 [8–10], and 48 h postoperatively [8, 9, 11]. Pain on movement is also reduced up to 48 h postoperatively [8]. Continuous femoral nerve block (cFNB) also produces significantly lower resting pain scores compared to IV PCA at 3–12 [12–16], 24 [12–14, 17, 18] and 48 h [13–15], and also on movement at the same time points [12, 13, 15, 19–22].

Data from a recent systematic review including both FNB and cFNB demonstrated the reduction in pain scores at rest to be significant up to 72 h postoperatively and on movement up to 48 h postoperatively following TKA compared to IV PCA [23•]. There was also a trend toward lower postoperative pain scores on movement up to 72 h.

Few studies report pain scores beyond 72 h, however, one recorded pain outcomes for 3 months comparing FNB, cFNB, and IV PCA [20]. There was no significant difference between groups after 48 h except at week two, where FNB was superior to IV PCA.

Several studies have demonstrated a significant reduction in opioid consumption up to 48 h postoperatively with FNB [6–11, 20, 24, 25] and cFNB, [12, 15, 16, 18, 20, 22, 26, 30] and this finding has been confirmed with metaanalysis [23•]. In addition, intermittent local anesthetic boluses via cFNB are associated with a reduction in IV opioid consumption compared to continuous infusion following TKA [31].

FNB is also associated with a reduction in nausea, vomiting [9, 12–15, 20, 22], and sedation [12, 13, 26], and improved patient satisfaction [10, 16, 22, 26, 30] compared to IV PCA. Postoperative knee range of motion is also greater with FNB compared to IV PCA [10, 15, 20–22, 27] but this does not translate into earlier mobilization [23•].

Four randomized controlled trials have directly compared FNB to cFNB for TKA [17, 20, 28, 29]. Two studies demonstrated significantly lower pain scores at rest and movement, and reduced opioid consumption up to 48 h postoperatively with cFNB [28, 29]. One study showed a significant reduction in opioid consumption up to 48 h postoperatively with trends to lower pain scores with cFNB [20] and another showed trends toward lower opioid consumption in the cFNB group [17].

One metaanalysis [32] used indirect statistical methods to compare data from two randomized controlled trials [17, 28] to conclude that addition of a cFNB to FNB did not reduce morphine consumption or pain scores. This conclusion, however, was based on Bayesian analysis; therefore, data were not randomized and are subject to the same bias as observational studies [33]. A more recent systematic review directly analyzed data from four studies and concluded that cFNB lowered pain scores and opioid consumption at 24 and 48 h compared to FNB [23•].

Evidence to date is overwhelmingly in favor of FNB compared to IV PCA following TKA in terms of postoperative pain scores, opioid consumption, opioid-related side effects, knee range of movement, and patient satisfaction. In addition, cFNB provides significantly lower pain scores and opioid consumption in the early postoperative period compared to FNB.

Due to its effects on quadriceps motor function, there is concern regarding a potential link between FNB and increased incidence of inpatient falls following TKA [34– 37]. A large retrospective study, however, failed to identify peripheral nerve blockade as an independent risk factor for inpatient falls following TKA [38•]. There is also data to suggest that multidisciplinary falls prevention programs, patient education, and use of a knee brace may contribute to a reduction in inpatient falls [39, 40]. Further prospective studies investigating inpatient falls as the primary outcome are required before firm conclusions can be made regarding causality. In addition, the impact of knee braces, assist devices for ambulation, and concentration of local anesthetic solution on inpatient falls following TKA requires further investigation.

# Sciatic Nerve Block

The sciatic nerve in addition to the femoral and obturator nerves provides sensory innervation to the knee. In three early studies, SNB combined with FNB resulted in lower pain scores at rest and lower opioid consumption during the first 24 h compared to FNB alone [41–43]. However, another study reported no difference in early or late pain scores at rest or on movement, and no difference in opioid consumption between the FNB group and the FNB + SNB group [44].

Two studies comparing cSNB + FNB to FNB alone [45, 46], reported a reduction in early pain scores with one also reporting reduced postoperative opioid consumption

following 12 hourly boluses of local anesthetic via the sciatic catheter [46]. The other study employed cSNB along with cFNB but postoperative infusion of local anesthetic through the cSNB was only commenced in the presence of poorly controlled posterior knee or calf pain [45]. Interestingly, 83 % of patients required infusion via the sciatic catheter, resulting in clinically significant reductions in pain scores. One study comparing cSNB + cFNB to cFNB did not report a difference in pain scores between groups, however, postoperative opioid consumption was significantly lower in the cFNB + cSNB group compared with the FNB group during the first 48 h [47].

Systematic review of the above studies concluded that SNB in addition to FNB produces lower pain scores and opioid requirements in the first 24 h post-TKA, however, the evidence was weak, with methodological flaws in most studies [48].

A more recent study investigated the effect of adding SNB or cSNB to cFNB on achieving discharge readiness, and demonstrated no difference between groups [49]. The SNB and cSNB groups did experience significantly lower pain scores on the day of surgery with cSNB significantly reducing pain scores at rest and mobilization during the first two postoperative days. No difference in long-term functional outcomes between groups at 3 and 12 months was observed [50]. Another similar study also demonstrated a reduction in opioid consumption and pain scores during the first 48 h with cSNB compared to SNB in the presence of cFNB, however, no difference in LOS was observed [51].

Cappelleri et al. compared SNB to cSNB in the presence of a continuous lumbar plexus block [52•]. There was a significant reduction in morphine consumption in the cSNB group at 30, 42, and 48 h postoperatively, and mean pain scores were significantly higher in the SNB group compared to the cSNB group at 30 and 42 h. Importantly, rehabilitation and functional outcomes were superior in the cSNB group, with patients ambulating further and demonstrating greater knee flexion at 48 h postoperatively. Unfortunately, this study did not include a placebo SNB group, as this would have provided valuable insight into the effect of SNB and cSNB on functional recovery compared to FNB alone.

Safa et al. compared SNB + FNB, posterior capsule LIA + FNB, and FNB following TKA [53•]. There was no significant difference in pain scores at rest or with movement between groups during the first 48 h. The SNB + FNB group did demonstrate lower opioid consumption at 4 and 8 h postoperatively; however, this did not have any effect on reducing opioid-related side effects and was deemed clinically insignificant. Of note, patients with FNB + SNB demonstrated reduced ability to ambulate with assistance on postoperative day one (POD1) but this did not translate to an increased incidence of falls or prolonged LOS.

Abdallah et al. demonstrated a significant reduction in posterior knee pain and PONV with proximal or distal SNB compared to placebo up to 8 h postoperatively in the presence of cFNB [54].

The evidence to date suggests that SNB in addition to FNB lowers pain scores and opioid requirements in the first 24 h post-TKA, and that cSNB extends this period to 48 h. Whether the reduction in opioid consumption provided by SNB in the presence of multimodal analgesia and IV PCA is clinically significant remains unclear, however, three studies have demonstrated a reduction in PONV with SNB [54] and cSNB [46, 52•].

Further contributing to the difficulty in interpreting these studies is the lack of differentiation of pain from the femoral and sciatic regions. Studies which attempted to isolate sciatic pain have all demonstrated a reduction in pain scores with SNB [40, 43, 49, 54]. Further studies using a confirmed functioning cFNB along with a preexisting sciatic nerve catheter which would be used upon patient reporting of posterior knee pain may improve clarity regarding specific benefits of SNB. This approach would also allow surgeons to exclude sciatic nerve palsy in the immediate postoperative period, before administration of local anesthetic through the sciatic nerve catheter. Further research is required to evaluate the effects of combined SNB + FNB compared to FNB alone on functional outcomes, and the impact of dose and rate of local anesthetic infusion on motor block.

## Local Infiltration Analgesia

LIA following TKA involves systematic infiltration of local anesthetic mixture often including adjunct agents such as ketorolac, adrenaline, morphine, or corticosteroids throughout the periarticular and subcutaneous tissues.

Several studies have reported reductions in early postoperative pain scores with LIA when compared to a control group or no injection group [55–69]. The majority of these studies, however, demonstrated significant bias due to incomplete blinding and lack of administration of systemic adjuncts such as ketorolac or morphine to the control group.

Systematic reviews have reported reduction in pain scores up to 48 h postoperatively when compared to control [70, 71, 72•], however, one review [72•] identified only two studies [57, 58] with a low risk of bias. In another review, 10 of 18 studies comparing single dose LIA to placebo or no injection reported no effect or minimal effect on pain scores [70]. This review also demonstrated no difference in postoperative morphine consumption between groups following sensitivity analysis.

The use of intra-articular LIA catheters has been associated with reduced pain scores up to 48 h postoperatively compared to placebo, however, study design did not allow differentiation between the effect of intraoperative LIA and the postoperative infusion or bolus via the catheter [72•]. Intra-articular catheters are not without risk, and one systematic review reported two cases of deep infection from 287 catheters [71].

Comparison of LIA to placebo does not provide an accurate reflection on current clinical practice, as there is no comparison to the gold standard technique. Several recent studies have attempted to address this issue by comparing LIA to FNB.

One study compared cFNB to continuous periarticular infusion in TKA patients, with both groups receiving posterior capsule LIA to control posterior knee pain [73]. Morphine consumption was significantly reduced in the cFNB group compared to the LIA group and there was a nonsignificant trend toward less pain at rest in the cFNB group. Additionally, the cFNB group ambulated further during the first two postoperative days and demonstrated better walking capacity, physical activity, and knee function at 6 weeks postoperatively. Two studies [74, 75] compared LIA to FNB and cFNB, respectively, and found no difference in postoperative pain scores. A randomized crossover trial for staged TKA allocated patients to cFNB or LIA for each stage of surgery and found no difference between groups in postoperative morphine consumption or pain scores [25].

In one systematic review, the authors were unable to draw conclusions on the benefit of LIA compared to FNB due to high risk of bias, methodological flaws in study design, and variability in nerve block techniques [72•]. Another systematic review concluded that there was no evidence for improvement in pain at any time point following TKA when LIA with or without postoperative infusion was compared to FNB [71]. Two systematic reviews demonstrated an association between LIA and earlier postoperative mobilization compared to placebo or FNB, but this did not translate into a reduction in LOS [70, 71].

Several studies compared LIA to SNB with both groups receiving FNB [53•, 76–78]. Two of these studies [76, 78] showed no difference between groups in pain scores or opioid consumption, one study demonstrated lower pain scores in the LIA group at 12–24 h [77] and another showed a significant reduction in cumulative opioid consumption in the SNB group at 8 h [53•]. Of note, these studies did not administer ketorolac in the LIA solution.

Two studies compared LIA to SNB + FNB [79, 80]. One unblinded study reported lower pain scores and opioid consumption on the day of surgery in the SNB + FNB group with a small reduction in LOS in the LIA group [79], and the other reported no difference in pain scores between groups [80].

In two studies, liposomal bupivacaine produced inferior postoperative analgesia compared to conventional LIA solution [81] and FNB [82], but was associated with a small reduction in LOS in the latter study.

In summary, LIA may reduce postoperative pain scores for up to 48 h compared to placebo, however, the majority of relevant studies demonstrated severe methodological flaws including inadequate blinding, and lack of systemic matching of analgesic adjuncts such as ketorolac in the placebo groups. This is a highly confounding factor as ketorolac injection in LIA has been demonstrated to produce plasma concentrations equivalent to an intramuscular injection of the same dose [83•].

A more clinically relevant comparison of LIA to FNB does not demonstrate any improvement in pain scores following TKA, however, LIA may facilitate earlier postoperative mobilization compared to FNB with no concurrent reduction in LOS. Addition of posterior LIA to FNB may provide similar analgesia compared to SNB, but no clinical benefit over FNB alone.

Well-designed large randomized controlled trials comparing LIA to the gold standard technique of cFNB are required, with matched systemic analgesia in control groups. These studies should aim to isolate anterior knee pain through the use of posterior LIA or SNB. Further research is also required investigating the impact of any benefit in improved postoperative mobilization with LIA compared to cFNB or SNB on length of hospital stay and the ability to generalize this across different orthopedic units. The role of liposomal bupivacaine remains uncertain, and large comparative studies with cFNB are required.

# **Adductor Canal Block**

ACB is a relatively new approach to postoperative analgesia following TKA. In addition to the femoral artery and vein, the adductor canal contains the saphenous nerve, nerve to vastus medialis, posterior branch of obturator, and the medial cutaneous nerve. The only motor branch to the quadriceps passing through the adductor canal is the nerve to vastus medialis [84].

Compared to placebo, ACB results in lower pain scores in the early postoperative period [85–87]. This difference disappears when patients in the placebo group receive an ACB [85, 86], however, despite concurrent administration of LIA, 78 % of patients still report at least moderate movement-related pain following ACB [86]. cACB also reduces pain scores [88] and opioid consumption [89] in the early postoperative period compared to placebo, and improves ambulation on the day of surgery [88].

Significant preservation of quadriceps strength is observed with ACB compared to FNB in volunteers (51 vs. 92 % of baseline) [90•], in addition to better postoperative balance [91] and mobilization [90•]. Extrapolation of these results to TKA patients is, however, difficult, as volunteers did not undergo knee arthroplasty.

Two retrospective studies compared patient outcomes in TKA patients following a change in practice from cFNB to cACB [92] or cFNB + SNB to ACB [93]. Patients receiving cACB ambulated further on POD1 and POD2 than patients with cFNB in the setting of LIA and multimodal analgesia, but there was no difference in LOS, opioid consumption, or pain scores. Patients receiving LIA + ACB walked longer distances on POD1, and demonstrated lower pain scores and opioid consumption compared to the cFNB + SNB group during the first 24 h. Both of these studies, however, are retrospective in design and prone to significant bias, creating difficulty in drawing firm conclusions on causality.

A crossover study comparing ACB to FNB following bilateral TKA showed no difference in early postoperative VAS scores, quadriceps strength, functional outcomes, or patient satisfaction [94]. Qualitatively, more patients reported better pain control in the FNB limb compared to the ACB limb at 24 h. Both groups experienced significant reduction in quadriceps strength over 80 % from baseline, however, interpretation is difficult due to the presence of epidural analgesia.

Several recent randomized controlled trials directly compared ACB to FNB in patients undergoing TKA. Jaeger et al. demonstrated a significant reduction in quadriceps strength at 24 h with cFNB compared to cACB (18 vs. 52 % of baseline) following TKA [95]. There was no significant difference in pain outcomes, but there was a trend toward higher pain scores in the cACB group, and the study was not adequately powered for these secondary outcome measures. Despite the difference in quadriceps strength, there was no difference in postoperative mobilization at 24 h between groups.

Kim et al. also compared ACB to FNB following TKA, however, both groups also received an epidural with a patient-controlled bolus function [96]. The ACB group exhibited significant sparing of quadriceps strength at 6–8 h postoperatively and demonstrated non-inferior pain scores and opioid consumption up to 48 h compared to FNB. Data on postoperative mobilization, LOS, or falls were not provided in this study, and the use of epidural PCA in both groups creates difficultly with interpretation of the results.

Shah et al. demonstrated a significantly better performance in postoperative mobilization tests and total ambulation distance with cACB, compared to cFNB [97•]. There was no significant difference in pain scores during the first 24 h, and cACB patients demonstrated a significant reduction in LOS compared to cFNB.

Grevstad et al. compared ACB to FNB in patients with established postoperative pain following TKA [98]. At 2 h following block placement, quadriceps strength was significantly increased from postoperative baseline in the ACB group with a median change of 193 versus 16 %. The TUG test was performed significantly faster in the ACB group at this time interval.

In summary, the evidence suggests that ACB provides better early postoperative analgesia and ambulation compared to placebo. Despite this, most patients with ACB still report at least moderate pain on knee flexion following TKA and there is no evidence for any benefit beyond 24 h postoperatively.

Compared to FNB, ACB is associated with quadriceps strength preservation. This difference varies across studies, but is much less prominent than that seen in volunteer studies, suggesting a surgical contribution to quadriceps weakness [99]. Equivalence of analgesia outcomes has yet to be demonstrated convincingly, and an RCT with pain scores or opioid consumption as the primary outcome is awaited. The evidence regarding the effect of ACB on postoperative mobilization compared to FNB remains conflicting, with one early study showing no difference between groups and a more recent study showing better mobilization and reduced LOS with ACB. In addition, there is no direct evidence demonstrating a reduction in inpatient falls associated with ACB following TKA.

Further large, well-designed randomized controlled trials adequately powered for postoperative pain scores, mobilization, and LOS are required directly comparing cACB to cFNB. In addition, large studies comparing frequency of inpatient falls including evaluation of the protective effect of knee braces and patient education programs would further enhance our knowledge in this area. Studies investigating the optimum volume and concentration of ACB infusion are required along with the optimum insertion position on the thigh to minimize motor block while preserving analgesia.

# **Obturator Nerve Block**

The obturator nerve divides into anterior and posterior branches in the proximal thigh. The anterior branch has variable cutaneous innervation and most commonly innervates the skin over the lower medial aspect of thigh, while the posterior branch contributes to the innervation of the posterior knee joint [84]. ONB alone is of no benefit following TKA [27], however, patients receiving a combined FNB and SNB still complain of postoperative pain.

Two studies have investigated the additive effect of ONB following TKA. McNamee et al. randomized patients to FNB + SNB or FNB + SNB + ONB following general anesthetic for TKA [100]. The ONB group demonstrated a significantly longer time until first request for analgesia and

used significantly less opioid in the first 48 h compared to the FNB + SNB group. Macalou et al. randomized patients to receive FNB, FNB + ONB, or placebo FNB prior to general anesthetic for TKA [101]. In the first 6 h postoperatively, morphine consumption and VAS scores were significantly lower in the FNB + ONB group compared to the other groups, with less opioid-related side effects.

Although the number of studies investigating the additive effect of ONB for TKA is limited, the existing evidence suggests an improvement in postoperative analgesia with a reduction in opioid consumption. This suggests that pain in the obturator distribution contributes to postoperative pain following TKA. Further studies are required to evaluate the impact of ONB on postoperative mobilization, the use of ultrasound guided ONB, and the duration of additive analgesia provided.

## Conclusion

There is strong evidence supporting the use of cFNB for postoperative analgesia following TKA. (Table 1) Concerns regarding a delay in functional recovery and risk of inpatient falls have led some clinicians to abandon cFNB in favor of ACB. Evidence remains conflicting regarding the magnitude of relative quadriceps motor preservation with ACB and the impact of this on postoperative mobility. Equivalence of postoperative analgesia between techniques has yet to be convincingly demonstrated by adequately powered RCTs. Further research is required to evaluate the impact of any improvement in early postoperative mobility on long-term functional outcomes following ACB, and to directly compare the rate of inpatient falls between these techniques.

The addition of SNB to FNB results in a reduction in early postoperative pain scores and opioid consumption following TKA and this effect is prolonged with cSNB. Evidence regarding the clinical significance of this remains conflicting, but several studies have demonstrated a reduction in opioid-related side effects. SNB may be of most benefit in patients with preoperative chronic pain or high opioid tolerance. Preoperative insertion of a sciatic nerve catheter in these patients can allow rapid control of pain in the immediate postoperative period following confirmation of motor function. The effect of SNB on functional outcomes and the impact of variation in local anesthetic dose on motor function requires further investigation.

Studies comparing LIA and FNB are difficult to interpret due to high risk of bias and methodological inadequacies, however, this technique has not been shown to provide superior pain control to FNB following TKA. Posterior LIA may provide similar analgesia to SNB following TKA but no clinical benefit over FNB alone. High levels of postoperative pain in studies investigating ACB with concurrent LIA administration following TKA remain a concern [86, 88].

Addition of ONB for postoperative analgesia following TKA does appear to improve postoperative analgesia;

Table 1 Summary of evidence for peripheral nerve blocks following TKA

	Strengths	Weaknesses
FNB	Improved analgesic and functional outcomes compared to IV PCA	Conflicting evidence regarding association with inpatient falls
	cFNB provides superior analgesic outcomes compared to FNB	
SNB	Reduced pain scores and opioid consumption when added to FNB compared to FNB alone	Conflicting evidence regarding impact on functional outcomes
	Further prolongation of analgesic effect with cSNB	Conflicting data on clinical significance of reduction in opioid requirements
	Reduction in opioid-related side effects in some studies	Most studies did not isolate posterior knee pain
LIA	Reduction in early postoperative pain scores compared to placebo	Difficulty making direct comparisons with FNB alone due to lack of systemic ketorolac in most studies
	Addition of LIA to FNB provides no clinical benefit over FNB alone	The role of liposomal bupivacaine requires further investigation
	Improved analgesic outcomes compared to placebo	Most patients still report significant postoperative pain despite ACB
ACB	Preservation of quadriceps strength compared to FNB	Equivalence of analgesia with FNB not demonstrated in adequately powered study
		Conflicting evidence on postoperative mobilization compared to FNB
		Conflicting evidence on magnitude of relative quadriceps preservation
		No evidence for reduction in inpatient falls rate
ONB	Addition of ONB improves analgesic outcomes compared to FNB or FNB + SNB alone	Further studies are required to investigate the impact on mobilization and functional outcomes

however, the impact of this on functional outcomes remains unknown.

In conclusion, cFNB remains the gold standard peripheral nerve block for TKA. Addition of SNB is supported by an increasing body of evidence and should at the very least be considered in patients with high opioid tolerance or chronic pain. ONB may have an additive analgesic effect in these patients, but impact on functional recovery remains unknown. The secondary motor effects from these blocks may delay mobilization in the early postoperative period compared to LIA or ACB, but evidence for a difference in functional recovery beyond this period is lacking. High quality studies comparing the analgesic and long-term functional outcomes of these techniques are required.

#### **Compliance with Ethics Guidelines**

**Conflict of Interest** Lloyd Turbitt, Stephen Choi, and Colin J.L. McCartney declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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