



## Original Research

## Validation of a Novel Landmark-guided Intra-articular Postero-medial Surgeon-administered Injection Technique

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## ABSTRACT

**Background:** This study aimed to define an intra-articular surgeon-administered technique that may be comparable to ultrasound (US)-guided adductor canal block (ACB).

**Methods:** Five cadaver lower limbs were examined. An anesthesiologist administered a US-guided ACB using 20 mL of dilute indocyanine dye. An orthopedic surgeon performed a medial parapatellar arthrotomy and introduced an 18-gauge needle 1-2 cm proximal to the palpated adductor tubercle angled posteromedially. Needle position and dye spread were fluoroscopically documented.

**Results:** This technique consistently reached the infrapatellar branch of the saphenous nerve, nerve to the vastus medialis muscle, and posterior capsule, with minimal proximal dye spread.

**Conclusions:** This technique may be an efficient complement to ACB or surgeon infiltration or an alternative to US-guided ACB when it is not available.

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## Introduction

Total knee arthroplasty (TKA) is one of the most common elective surgical procedures, with approximately 1 million procedures performed annually within the United States [1-4]. With the aging population and an increase in knee osteoarthritis, the demand for TKA is predicted to undergo exponential growth [5,6]. While TKA effectively alleviates pain and restores function in those who have advanced arthritis, 10%-36% of patients experience moderate-to-severe postoperative pain, underscoring the need for enhanced postoperative pain management strategies [7,8]. Adequate pain management following TKA is critical because it facilitates prompt mobilization and range of motion exercises,

which have been shown to shorten recoveries, improve outcomes, and reduce hospital lengths of stay [9,10].

During the last decade, peripheral nerve blocks have emerged as an integral component of multimodal analgesia protocols for TKA [8]. Peripheral nerve blocks provide superior pain control compared with opioids alone while avoiding associated side effects [11]. Of the various approaches, femoral nerve blocks were once extensively used for their efficacy in managing postoperative pain. However, numerous studies have demonstrated that these blocks may lead to profound quadriceps muscle weakness and motor dysfunction that can delay rehabilitation and increase fall risk [12-14]. In contrast, adductor canal blocks (ACBs) have gained popularity as an alternative technique that primarily targets the sensory innervation of the knee via blockade of the saphenous nerve (SN) and its infrapatellar branch [15,16]. By sparing motor fibers, ACBs offer comparable analgesia to femoral blocks while better-preserving quadriceps muscle strength and function [17-19]. This facilitates earlier mobilization, rehabilitation, and safe ambulation,

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making ACBs ideally suited for fast-track TKA pathways [20]. Conventionally, ACBs are performed preoperatively under ultrasound (US) guidance by trained anesthesiologists, requiring proper equipment, expertise, and time. Surgeon-administered ACBs performed intraoperatively have recently been explored as an efficient and cost-effective alternative [21,22]. The exposure afforded by the surgical approach allows direct access to anatomic landmarks like the adductor tubercle. Surgeons can potentially use these reliable bony landmarks to guide ACBs and obviate the need for US [20]. Therefore, this cadaver study aimed to develop a landmark-guided intra-articular postero-medial surgeon-administered (IPSA) injection technique with optimal injectate volume that would be reproducible, standardized, and may be comparable to an anesthesiologist-performed US-guided ACB.

### Material and methods

There were 5 freshly frozen cadaver lower limbs examined. A total of 4 different surgeons were involved in the study and operated in pairs (ie, surgeons 1 and 2 and surgeons 3 and 4; Table 1). For the US-guided ACB, a board-certified regional anesthesiologist used a high-frequency linear probe to identify the adductor canal (AC) deep into the sartorius muscle. The SN was targeted with an in-plane needle approach and the injection of 10 mL of dilute indocyanine green dye. A second 10-mL injection targeted the nerve to the vastus medialis muscle (NVM) more proximally, where it enters the AC. An orthopaedic surgeon then performed a standard medial parapatellar arthrotomy on each cadaver knee, reflecting tissues to expose the joint. The adductor tubercle was identified by direct visual inspection and palpation approximately 2 cm proximal to the medial epicondyle, which was marked and verified by fluoroscopic imaging. With the knee extended, an 18-gauge bevel needle was introduced through the capsular pocket at 1-2 cm proximal to the adductor tubercle at the proximal border of the postero-medial femoral condyle. It was angled proximally and posteriorly and then advanced to contact the postero-medial capsule. The needle was buried in the hub in the medial gutter until it impacted the medial intermuscular septum inside the joint.

**Table 1**  
Dye injection procedures and structures dyed for each cadaver.

Cadaver	Surgeon-administered characteristics				Location of the ISN (relative to sartorius muscle)	Structures dyed	
	Surgeon	Needle length, inch <sup>a</sup>	Needle angle, ° posterior to femur	Time between injections, min		Green (US-guided ACB) <sup>b</sup>	Blue (surgeon-administered infiltration)
1	Surgeons 1 and 2	4	30	9	Superficial	SN NVM AC NA	None
2	Surgeons 3 and 4	1.5	40	5	Superficial		SN ISN NVM Posterior capsule
3	Surgeons 1 and 2	1.5	55	5	Within the AC	SN NVM AC	SN ISN NVM Posterior capsule
4 <sup>c</sup>	Surgeons 3 and 4	1.5	30	0	Superficial	NA	None
5 <sup>c</sup>	Surgeons 1 and 2	1.5	70	0	Within the AC	NA	SN ISN NVM

ACB, adductor canal block; AC, adductor canal; ISN, infrapatellar branch of the saphenous nerve; NA, not applicable; NVM, nerve to the vastus medialis muscle; SN, saphenous nerve; US, ultrasound.

<sup>a</sup> All needles were 18-gauge sharp.

<sup>b</sup> A US-guided ACB was performed in cadavers 1 and 3.

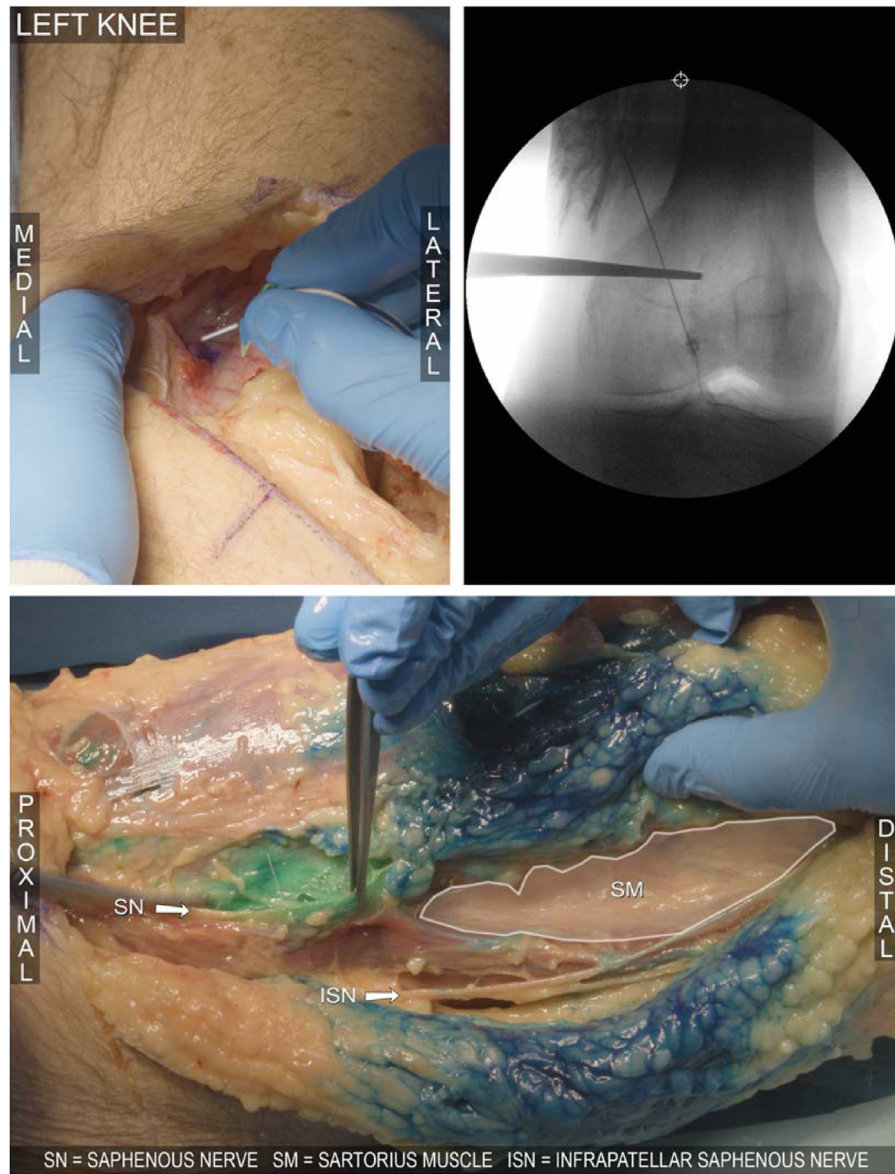
<sup>c</sup> Only landmark approach/methylene blue was administered in cadavers 4 and 5.

The needle angle and position relative to the femur were determined via fluoroscopy. A 10-mL bolus of dilute methylene blue and radiopaque dye was injected, and the needle was left in place. The spread of the dye was observed via fluoroscopy. A second 10-mL bolus was then injected. After the second injection, the knee was dissected by an anatomist, or under their direct supervision, to determine which anatomic structures were stained by dye and the extent of the spread of both approaches. The SN, infrapatellar branch of the SN (ISN), NVM, and femoral nerve and vascular structures were evaluated. Injectate volume, needle position, needle size, and timing between surgeon-administered boluses were adjusted for the subsequent 4 cadaver knees in an iterative fashion on the basis of the dissection findings of the previous knees. The needle size was adjusted from 4 inches for cadaver 1 to 1.5 inches for cadavers 2 through 5. The needle angle measured from vertical posterior relative to the axis of the femur for cadavers 1 through 5 was 30°, 40°, 55°, 30°, and 70°, respectively, with the needle tip directed proximally and posteriorly from the entry point and slightly medial to the axis of the femur toward the femoral head. The total volume injected was 20 mL for all knees, with timing that varied between cadavers 1 and 2 to determine the volume spread; the same timing between injections was used for cadavers 2 and 3. Because minimal proximal spread was observed, all 20 mL were injected at once in cadavers 4 and 5. The US-guided ACB was repeated in cadavers 1 and 3 to confirm the consistency of anatomic coverage.

### Results

Cadaver 1 was an 80-year-old man who had a body mass index (BMI) of 24.4 and a midhigh circumference of 47.5 cm. No blue staining from the surgeon-directed approach posterior was found within the AC, but rather only in the subcutaneous tissue (Fig. 1). The ISN was found to be superficial to the sartorius muscle along its entire course and was not stained by either the green or blue dyes.

Cadaver 2 was an 81-year-old woman who had a BMI of 26.4 and a midhigh circumference of 47.5 cm. Upon dissection, blue staining from the surgeon-directed approach using a 1.5-inch needle



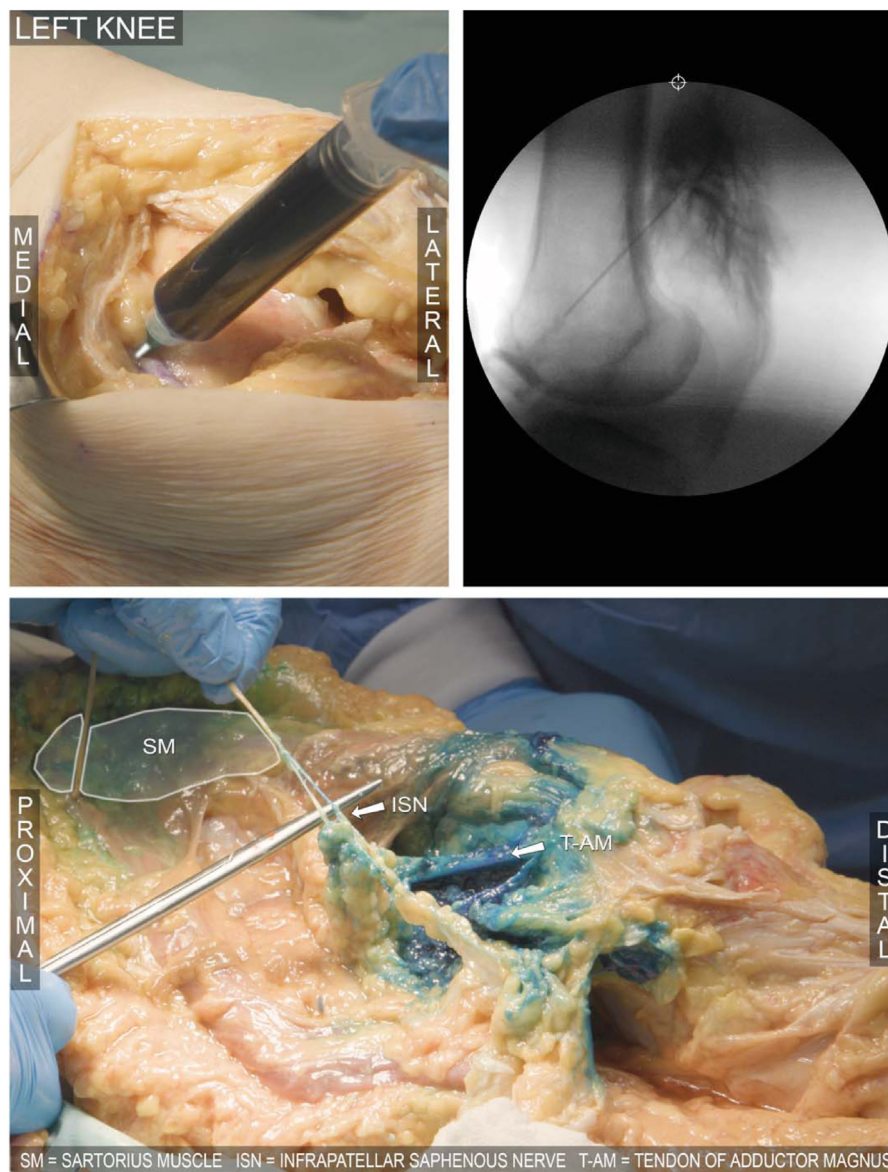
**Figure 1.** Clinical and radiographic representation of cadaver 1 showing no blue staining from the surgeon-directed block posterior was found within the adductor canal, but rather only in the subcutaneous tissue. The ISN was found to be superficial to the sartorius muscle along its entire course and was not stained by either the green or blue dyes. ISN, infrapatellar branch of the saphenous nerve.

inserted 20° medial and 45° posterior was observed, particularly in the interval between the vastus medialis muscle and the subcutaneous tissue (Fig. 2). The adductor magnus tendon and the hamstring tendon of the adductor magnus muscle were also stained. Some staining was noted in the interval between the vastus medialis muscle and the adductor magnus tendon. The ISN was located superficially to the sartorius muscle throughout its entire course. There was marked blue staining of the distal portion of the ISN as well as postero-medial staining of the posterior capsule. The anterior femoral cutaneous nerve branches, as well as the ISN, were observed to come off a common trunk of the anterior division of the femoral nerve, separate from the posterior division and the saphenous proper. The sartorius muscle was dissected and followed down to the distal attachment of the pes anserinus tendons on the antero-medial tibia. Blue staining was well confined in the interval between the pes and the capsule, indicating that there is a legitimate chance that superomedial genicular branches would be

covered by this approach. The tendon of the semimembranosus muscle was unstained; however, the area beneath that was well stained. There was no blue staining of the sciatic nerve in the region of the popliteal fossa. The posterior capsule was stained with blue dye all the way to the lateral condyle. There was no blue staining within the AC given that the staining remained distal to it.

Cadaver 3 was a 73-year-old man who had a BMI of 24.7 and a mid thigh circumference of 49.5 cm. The surgeon-directed approach with a 1.5-inch needle inserted 10° medial and 55° posterior demonstrated blue dye staining between the vastus medialis muscle and the adductor magnus tendon (Fig. 3). Most of the blue staining was located posterior to the intermuscular fascial septum that separates the anterior compartment from the medial compartment, keeping the dye in the medial and posterior compartments of the knee. Some blue dye spread was noted in the very distal aspect of the AC through the hiatus from the inferior border of the AC.





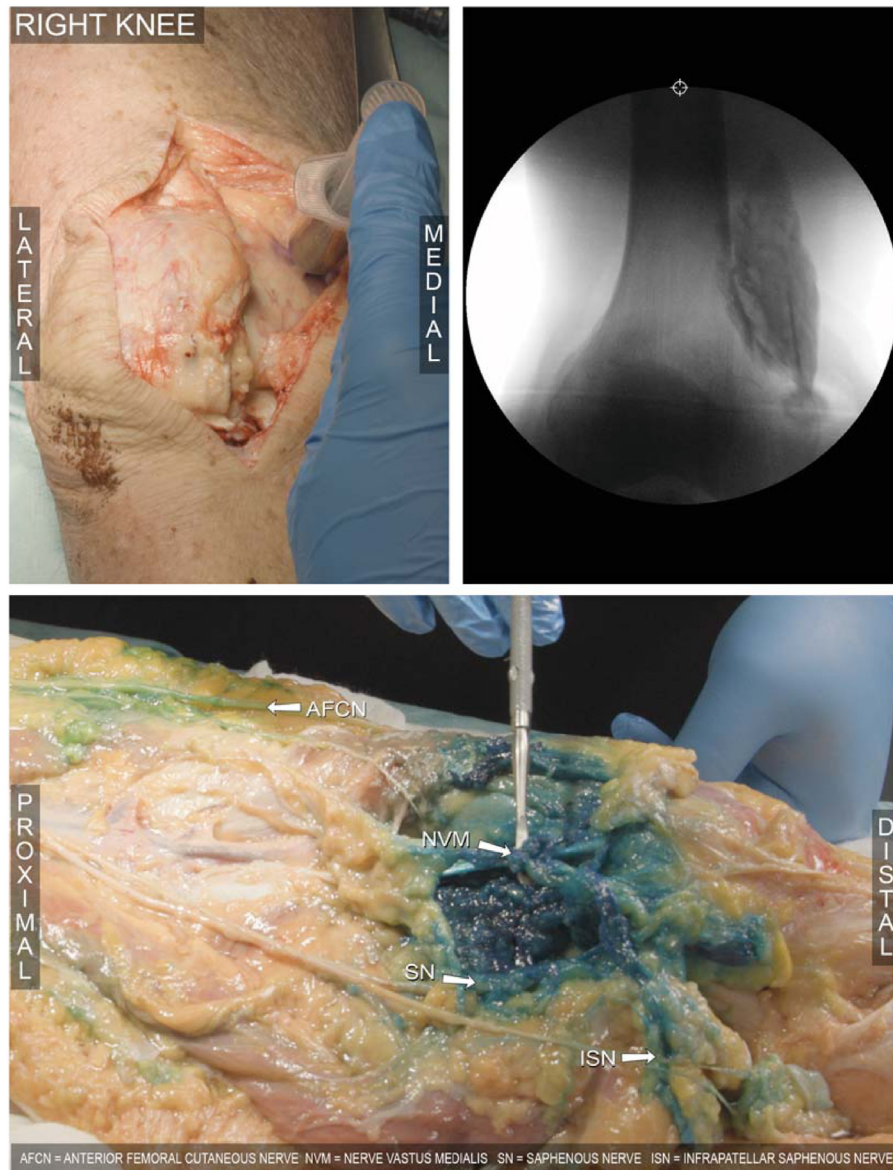
**Figure 2.** Clinical and radiographic representation of cadaver 2 showing blue staining from the surgeon-directed block using a 1.5-inch needle inserted 20° medial and 45° posterior observed in the interval between the vastus medialis muscle and the subcutaneous tissue. The adductor magnus tendon and the hamstring tendon of the adductor magnus muscle were also stained. Some staining was noted in the interval between the vastus medialis muscle and the adductor magnus tendon. The ISN was located superficially to the sartorius muscle throughout its entire course. There was marked blue staining of the distal portion of the ISN as well as postero-medial staining of the posterior capsule. The anterior femoral cutaneous nerve branches, as well as the ISN, were observed to come off a common trunk of the anterior division of the femoral nerve separate from the posterior division and the saphenous proper. Blue staining was well confined in the interval between the pes and the capsule, indicating that there is a legitimate chance that superomedial genicular branches would be covered by this approach. The posterior capsule was stained with blue dye all the way to the lateral condyle. ISN, infrapatellar branch of the saphenous nerve.

Cadaver 4 was an 83-year-old man who had a BMI of 22.2 and a midhigh circumference of 39.0 cm. The surgeon-directed approach with a 1.5-inch needle inserted 10° medial and 30° posterior demonstrated dye staining between the vastus medialis and sartorius muscles only, without crossing the intermuscular septum to the posterior capsule (Fig. 4).

Cadaver 5 was a 73-year-old man who had a BMI of 24.7 and a midhigh circumference of 49.5 cm. The surgeon-directed approach with a 1.5-inch needle inserted 10° medial and 70° posterior showed blue dye staining anterior to the adductor magnus muscle and of the posterior capsule on dissection (Fig. 5). No staining was present in the intermuscular septum or sartorius muscle space. Dye injection procedures and structures dyed for each cadaver are summarized in the Table 1.

## Discussion

This IPSA injection technique consistently reached the ISN, NVM, and posterior capsule with minimal proximal dye spread when a 20-mL volume was administered via a 1.5-inch 18-gauge needle at 40°–70° posterior relative to the axis of the femur and 10°–20° medial to the medial border of the femur (Fig. 6). While dye injected with the IPSA technique did not reach the AC, it did stain multiple nerves that are typically blocked for TKA pain via multiple injections and was more likely to contact the ISN than the US-guided ACB in these cadaver specimens. This cadaver study may lend insight into the reported variable clinical efficacy of ACBs. In this study, 3 of 5 cadavers had an anatomic variant noted in which the ISN coursed outside of the AC (beyond the midhigh) and was



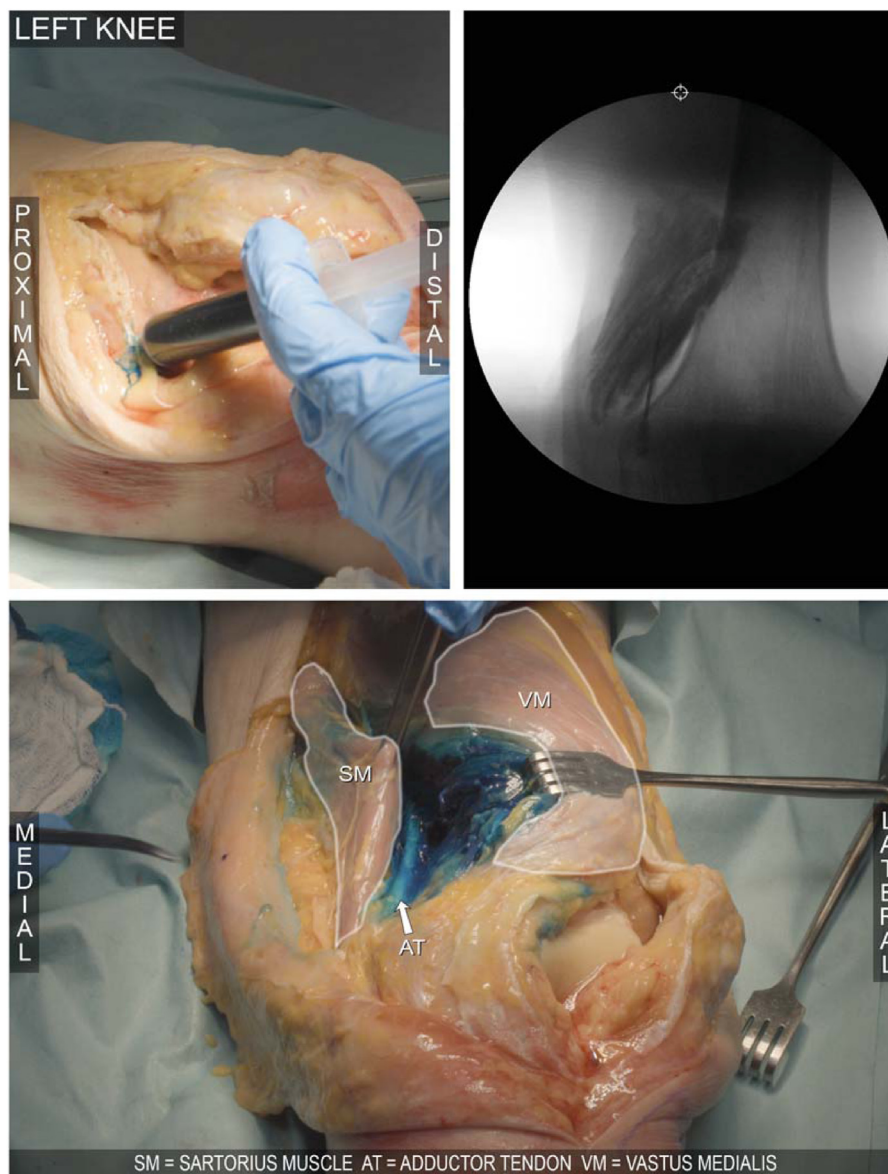
**Figure 3.** Clinical and radiographic representation of cadaver 3 showing a surgeon-directed block with a 1.5-inch needle inserted 10° medial and 55° posterior, demonstrating blue dye staining between the vastus medialis muscle and the adductor magnus tendon. Most of the blue staining was located posterior to the intermuscular fascial septum that separates the anterior compartment from the medial compartment, keeping the dye in the medial and posterior compartments of the knee. Some blue dye spread was noted in the very distal aspect of the adductor canal through the hiatus from the inferior border of the adductor canal.

not stained distally in the variant where a US-guided ACB was evaluated (cadaver 1). In contrast, the ISN, which is critical to the sensory innervation of the knee, was reliably and routinely bathed by the IPSA injection. Thus, this novel single-injection intra-articular postero-medial approach may be an efficient complement to a periarticular infiltration or a US-guided ACB. Further studies are warranted to confirm and validate these anatomic findings in terms of clinical outcomes.

Traditionally, ACBs have been performed preoperatively by trained regional anesthesiologists using US guidance [21]. However, there is increasing interest in evaluating surgeon-performed ACBs intraoperatively as an alternative approach to streamline care, reduce cost, and increase access [21]. Surgeon-performed blocks avoid the additional time, equipment, and specialized personnel required for preoperative US-guided ACBs. One study estimated that an anesthesiologist-performed ACB costs approximately \$1015 US dollars [23], so avoiding this additional

procedure could lead to major cost savings. In addition, the IPSA technique could provide comparable pain management to patients receiving operations in locations that lack the resources or personnel to perform US-guided ACB by an anesthesiologist [21]. Furthermore, intraoperative ACBs can be performed under direct visualization rather than with reliance on imaging. This allows the technique to be standardized and reliably implemented by orthopaedic surgeons. Notably, because the injection is administered within the joint, the location of needle infiltration is not impacted by body habitus, or more specifically, the presence of excessive soft tissue in the medial knee; this highlights the advantage of surgeon-performed alternatives over anesthesiologist-administered ACBs. Overall, surgeon-performed alternatives to US-guided ACBs have the potential to improve operating room efficiency, reduce expenses, eliminate risks of surgical site contamination, and provide a valuable option when regional anesthesia expertise is limited.



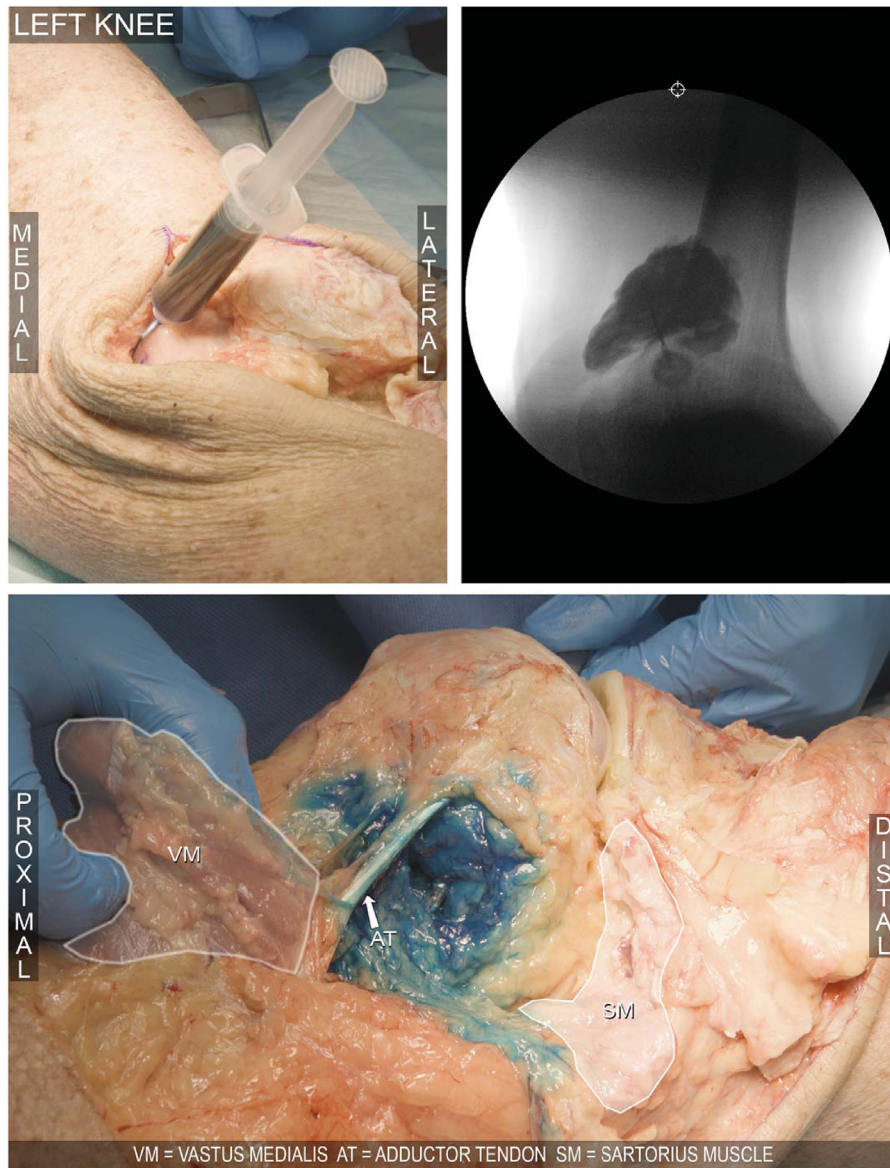


**Figure 4.** Clinical and radiographic representation of cadaver 4 showing a surgeon-directed block with a 1.5-inch needle inserted 10° medial and 30° posterior demonstrated dye staining between the vastus medialis and sartorius muscles only, without crossing the intermuscular septum to the posterior capsule.

Pepper et al. [24] were the first to perform a cadaver study on 11 knees to evaluate different ACB techniques that could be performed intraoperatively by surgeons. The authors first exposed each knee through a standard medial parapatellar arthrotomy. After retracting the patella laterally, blunt finger dissection was undertaken along the superomedial aspect of the suprapatellar pouch. The 3 ACB techniques were then tested. The first technique used a blunt 1.5-inch, 18-gauge needle aimed at the proximal AC. The needle was directed posteriorly at the adductor tubercle and angled medially until syringe hub resistance was met. The second approach involved a longer 3.5-inch, 20-gauge spinal needle directed proximally to the AC through the suprapatellar pouch in a parallel manner, advancing the full needle length until contacting the vastus medialis muscle origin. In addition, the third approach used a 1.5-inch 18-gauge blunt fill needle but maintained the same proximal trajectory. After testing all 3 approaches, the authors dissected each knee to directly visualize the dye placement and measure proximity to femoral vessels. The distal injection using a

shorter blunt needle yielded the highest accuracy at 86% while completely avoiding any vascular punctures. In contrast, the proximal 3.5-inch spinal needle had the lowest accuracy rate (14%) and the highest risk of injuring the femoral artery. This is in accordance with our findings, in which a 1.5-inch 18-gauge needle, compared with a 4-inch needle, consistently reached the ISN, NVM, and posterior capsule. Based on the observed staining, dye from the IPSA injection may have also reached the genicular nerves, although the deep genicular nerves were not dissected in this study, and additional confirmation is needed. Moreover, this study found that successful targeting can be achieved using a wide range of posterior angles, from 40° to 70°.

In another cadaver study, Vanamala et al. [25] evaluated a surgeon-performed intraoperative ACB technique based purely on anatomic landmarks that could be readily identified during a medial parapatellar knee arthrotomy. In 27 cadaver knees, the technique used to inject dye into the AC involved first inserting a 10-mL syringe equipped with a blunt 22-gauge needle. The needle was oriented at a

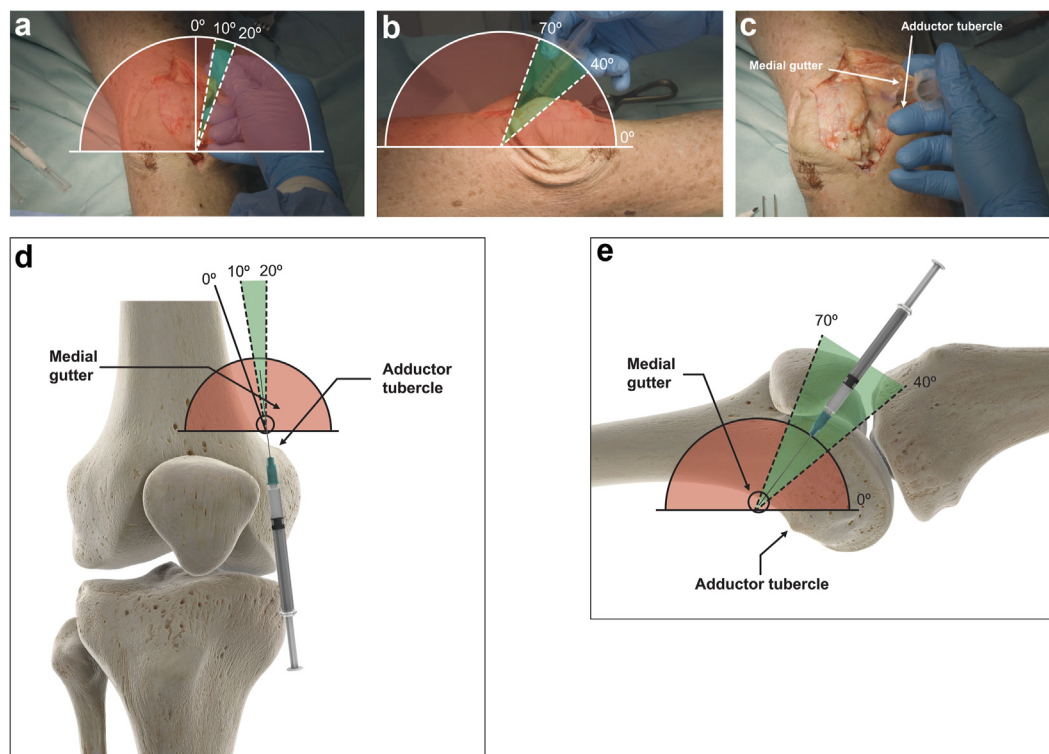


**Figure 5.** Clinical and radiographic representation of cadaver 5 showing a surgeon-directed approach with a 1.5-inch needle inserted 10° medial and 70° posterior showed blue dye staining anterior to the adductor magnus muscle and of the posterior capsule on dissection. No staining was present in the intermuscular septum or sartorius muscle space.

15°–20° angle in the coronal plane, aimed toward the adductor tubercle. It was advanced until resistance was felt against the tendon of the adductor magnus muscle. At that point, the needle tip was redirected cranially into the AC itself before injecting the India ink dye. This straightforward, anatomically guided approach successfully stained both the SN and NVM in all knees. Overall, this study demonstrated that surgeons can successfully perform intraoperative infiltration that stains the ISN, NVM, and posterior capsule using simple palpable bony landmarks to identify the adductor tubercle target site [26–28].

The promising results from cadaver studies showing the feasibility of surgeon-performed intraoperative ACBs have led to recent clinical research evaluating this technique in patients undergoing TKA. Several studies have compared intraoperative ACBs to traditional, anesthesiologist-performed ACBs [26,29–31]. A randomized controlled trial by Greenky et al. [23] compared anesthesiologist-performed US-guided ACBs ( $n = 34$ ) versus surgeon-performed ACBs ( $n = 29$ ) in patients undergoing TKA. For the

anesthesiologist-performed blocks, 15 mL of 0.5% ropivacaine was injected under US guidance. The surgeon-performed ACBs were done by injecting 15 mL of 0.5% ropivacaine through the medial parapatellar approach using an 18-gauge needle directed toward the adductor tubercle based on anatomic landmarks as described by Pepper et al. [24]. The results showed that the surgeon group had statistically significant higher pain scores on the day of surgery, with a mean visual analog scale pain score of 56.5 compared with 45.5 in the anesthesiologist group ( $P = .038$ ). However, this relatively small difference of 11 points did not meet the thresholds to be considered clinically relevant. There were no differences between groups in any other outcomes assessed, including opioid consumption, range of motion, length of stay, patient satisfaction, Knee Injury and Osteoarthritis Outcome, Short Form 12 Health Survey, and timed up and go scores. Other studies have found similar results when comparing surgeon-performed direct ACBs to anesthesiologist-performed US-guided ACBs in patients undergoing TKA [26,29–31]. In general, these early clinical studies



**Figure 6.** Needle angles for the intra-articular postero-medial surgeon-administered (IPSA) injection technique. (a) The medial angle was 0°–20° from the medial border of the femur. (b) The posterior angle was 40°–70° from the antero-posterior axis of the femur. (c) Visualization of needle insertion to the medial gutter and proximal to the adductor tubercle. (d) The IPSA technique needle angle from an anterior view. The needle should be directed from the insertion site parallel to or within 20° medial to the medial border of the femur, aiming toward the proximal postero-medial aspect of the knee. (e) The IPSA technique needle angle from a lateral view. 40°–70° represents the posterior orientation of the syringe and needle for the injection site along the vertical axis of the femur. To watch a video and description of the IPSA technique, access this link: <https://vimeo.com/904612040>.

demonstrate that surgeon-performed intraoperative ACBs provide pain control and patient outcomes that are comparable to anesthesiologist-performed ACBs. The techniques appear safe and effective when performed by surgeons using anatomic landmarks and familiar surgical approaches. However, it is notable that the staining results from the present cadaver study call into question whether surgeon-performed ACBs are routinely administered in the AC. Additional larger randomized trials will help further define the optimal utilization of these blocks, but the current evidence supports the integration of intraoperative ACBs into multimodal pathways to improve analgesia after TKA without requiring specialized personnel or equipment.

This cadaver study has several potential limitations. As with all cadaver-based analyses, direct clinical correlations are inherently limited. The relatively small sample size of 5 cadavers may not fully encompass the anatomic variability present in a large patient population. The methylene blue dye used does not perfectly mimic local anesthetic solutions that would be used clinically; the staining provides a useful visualization of spread, but may not identically represent the pharmacodynamics of anesthetic medications. Also, clinical outcomes such as pain scores, quadriceps muscle strength, and functional results were not assessed because this was an anatomic study looking only at nerve coverage and dye spread patterns.

## Conclusions

This landmark-guided IPSA injection technique may be an efficient complement or alternative to US-guided ACB when regional anesthesiologists are unavailable to perform the blocks. If administered consistently across patients, IPSA has the potential

to avoid the additional time and resources required for preoperative anesthesiologist administration and possibly allow injectates to more reliably reach the ISN. Overall, the IPSA injection technique consistently reached the ISN, NVM, and posterior capsule with minimal proximal dye spread when a 20-mL volume was administered via a 1.5-inch, 18-gauge needle at 40° to 70° posterior relative to the axis of the femur and 10°–20° medial relative to the medial border of the femur. Further clinical studies are needed to validate and better define the optimal utilization, safety, and clinical efficacy of this approach within multimodal anesthesia pathways. Altogether, the current evidence supports further developing and potentially integrating surgeon-performed injection techniques as part of a comprehensive analgesia protocol to improve outcomes during rapid-recovery total joint arthroplasty.

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## Conflicts of interest

The authors declare the following financial interests/personal relationships that may be considered as potential competing interests: **Nicolas S. Piuze** has received consultancy fees from Stryker; received research support from Osteal Therapeutics, Pепtilogics, RegenLab, Signature Orthopaedics, and Zimmer Biomet; serves on the editorial or governing board for the *Journal of Hip Surgery* and the *Journal of Knee Surgery*; and serves as a board member or on a committee for the American Association of Hip and Knee Surgeons, the International Society for Cell and Gene Therapy, and the Orthopaedic Research Society. **Andrew I. Spitzer** has received speaker compensation and research support from DePuy and Pacira BioSciences and has received consultancy fees from DePuy, Pacira BioSciences, and TraumaCad. **Jason Mussell** has received consultancy fees from Pacira BioSciences. **Ignacio Pasqualini** has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article. **Stan Dysart** and **Jeffrey Gonzales** are employees of Pacira BioSciences and may hold stock or stock options in the company. **Michael A. Mont** has received consultancy fees from Stryker, 3M, CERAS Health, Exactech, Johnson & Johnson, MirrorAR, Next Science, Pacira BioSciences, Peerwell, Smith & Nephew, and US Medical Innovations; has received royalties from Stryker; serves on the editorial/governing board of the *Journal of Arthroplasty*, *Journal of Knee Surgery*, *Surgical Technology International*, and *Orthopaedics*; and serves as a board member or on a committee for the Knee Society and the Hip Society. **Jess H. Lonner** has received royalties from Smith & Nephew and Zimmer Biomet; received speaker fees from Zimmer Biomet; received consultancy fees from Force Therapeutics, Pacira BioSciences, Smith & Nephew, and Zimmer Biomet; holds stock or stock options in Force Therapeutics and Proteonova; has received research support from Force Therapeutics, Heron Therapeutics, Smith & Nephew, and Zimmer Biomet; has received royalties, financial or material support from Saunders/Mosby-Elsevier, Springer, Wolters Kluwer Health-Lippincott Williams & Williams, and Smith & Nephew; and serves as a board member or on a committee for the American Association of Hip and Knee Surgeons and the Knee Society. **William Mihalko** has received royalties from Aesculap/B Braun; received speaker and consulting fees from Aesculap B Braun and Pacira BioSciences; holds stock or stock options in Medtronic; has received research support from the American Association of Hip and Knee Surgeons, the United States Food and Drug Administration, and Medacta; has received royalties, financial or material support from Saunders/Mosby-Elsevier; serves on the editorial or governing board for the *Journal of Arthroplasty*, *Journal of Long Term Effects of Medical Implants*, *Journal of Orthopaedic Research*, and *Orthopedic Clinics of North America*; and serves as a board member or on a committee for the American Association of Hip and Knee Surgeons, American Academy of Orthopaedic Surgeons, ASTM International, Campbell Foundation, Hip Society, International Society for Cell and Gene Therapy, Knee Society, and the Orthopaedic Research Society.

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## CRediT authorship contribution statement

**Nicolas S. Piuze**: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Conceptualization. **Andrew I. Spitzer**: Writing – review & editing, Methodology, Investigation, Conceptualization. **Jason Mussell**: Writing – review & editing, Investigation, Conceptualization. **Ignacio Pasqualini**: Writing – review & editing, Writing –

original draft. **Stan Dysart**: Writing – review & editing, Conceptualization. **Jeffrey Gonzales**: Writing – review & editing, Investigation, Conceptualization. **Michael A. Mont**: Writing – review & editing. **Jess H. Lonner**: Writing – review & editing, Methodology, Investigation, Conceptualization. **William Mihalko**: Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Investigation, Conceptualization.

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