Evaluation of the iPACK block injectate spread: a cadaveric study

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ABSTRACT

Background and objectives Ultrasound-guided infiltration of the interspace between the popliteal artery and capsule of the knee (iPACK) block, a new regional analgesic technique, is believed to relieve posterior knee pain, after total knee arthroplasty, by targeting the articular branches innervating posterior aspect of the joint. The extent of injectate spread and the number of articular branches affected is currently unknown. This cadaveric study aimed to compare the area of dye spread and frequency of articular branches staining following a proximal versus distal injection technique.

Methods An ultrasound-guided iPACK injection (10 mL of methylene blue dye solution) was performed in 14 lightly embalmed specimens: 7 injected using a proximal injection technique (1 fingerbreadth above base of patella) and 7 using a distal injection technique (at the superior border of the femoral condyles). Following injection, dissection, digitization, and 3D modeling were performed to map the area of dye spread and determine the frequency of nerve staining.

Results Both injection techniques achieved a similar mean area of injectate spread. Of the four articular branches supplying the posterior knee joint capsule, the genicular branch of posterior division of obturator nerve was stained in all specimens. The proximal injection resulted in staining of superior medial genicular nerve, due to dye spread through the adductor hiatus, whereas superior lateral genicular nerve and anterior branch of common fibular nerve were consistently stained following distal injection. Other articular branches were stained with variable frequency.

Conclusions Both proximal and distal iPACK injection techniques provided a similar area of dye spread in the popliteal region and extensive staining of the articular branches supplying the posterior capsule. The proximal injection technique promoted greater anteromedial dye spread, while the distal injection had more anterolateral spread. Further clinical study is required to confirm our cadaveric findings.

INTRODUCTION

Total knee arthroplasty (TKA) is a common surgical procedure in patients with advanced knee osteoarthritis who do not respond to conservative treatment. The number of TKAs will continue to increase with an ageing population.[1] Pain following TKA can be severe, limiting early mobilization, rehabilitation and recovery.[2] Both femoral nerve block (FNB) and adductor canal/femoral triangle block (ACB/FTB) are commonly performed to provide postoperative analgesia by targeting sensory afferents supplying the anterior knee joint capsule.

More recently, a new block called infiltration of the interspace between the popliteal artery and capsule of the knee (iPACK) has been described to supplement FNB or ACB/FTB.[3] The iPACK block involves ultrasound-guided local anesthetic infiltration of the interspace between the popliteal artery and the posterior knee joint capsule. This block is believed to target only the terminal branches of the sciatic and posterior division of obturator nerves (PON) innervating the posterior knee joint capsule. However, due to the proximity of the tibial and common fibular nerves (CFN) to the targeted region of injection, there is a potential risk of unintentional motor blockade of these somatic nerves. The site of iPACK injection described by Dr Sanjay Sinha is approximately 1 fingerbreadth above the base of patella,[4] while Thobhani *et al*[3] and Reddy *et al*[5] performed this block more distally at the level of the femoral condyles. Although the iPACK block represents a promising adjunct to FNB or ACB/FTB, little is known about the extent of injectate distribution, articular nerve targets and/or optimal site of injection.

The purpose of this cadaveric study was: (1) to compare the dye spread distribution associated with two iPACK injection techniques—proximal dye injection superior to the base of patella versus distal injection at the level of the femoral condyles; and (2) to quantify the percentage of articular branches affected by each technique.

METHODS

Fourteen lightly embalmed cadaveric specimens with a mean age of 66.4±18.0 years (5 male/9 female) were used in this study. Seven specimens were injected using the proximal injection technique and the remaining seven specimens using the distal injection technique. Specimens with any visible signs of injury, pathology, or previous surgery were excluded from this study. No further demographic data were available.

Ultrasound-guided dye injection (10 mL containing 0.5 mL of methylene blue diluted in 9.5 mL of water) into the interspace between the popliteal artery and the posterior knee capsule was performed using a 2–5 MHz curvilinear probe (SonoSite Edge, Bothell). To facilitate localization of the popliteal artery a stainless steel wire was inserted into the vessel.

Proximal injection technique

The proximal injection technique was performed as previously described.[4] The specimens were placed

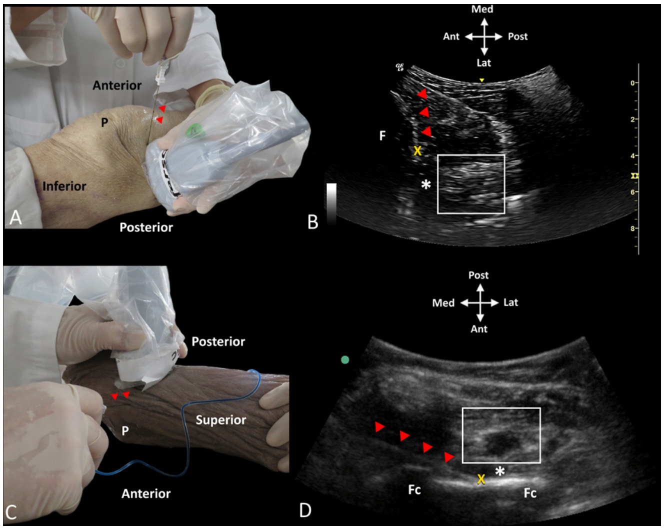

Figure 1 Methodology. Ultrasound-guided proximal and distal infiltration of the interspace between the popliteal artery and capsule of the knee (iPACK) injection techniques. (A) Proximal injection technique. The probe is placed over the anteromedial thigh with needle advancement in the anteromedial to posterolateral direction, approximately 1 fingerbreadth superior to the base of patella. (B) Sonogram showing in-plane proximal needle advancement adjacent to the femoral shaft. (C) Distal injection technique. The probe is placed over the popliteal region with needle advancement, from medial to lateral, at the level of the superior border of the femoral condyles. (D) Sonogram showing in-plane distal needle advancement to reach the intercondylar fossa. Arrowheads (red) indicate echogenic needle; asterisk (white), interspace between popliteal artery and capsule of knee; box (white), location of neurovascular bundle/popliteal fat. F, femoral shaft; Fc, femoral condyles; P, patella; X (yellow), site of needle tip location before injection.

supine. The ultrasound probe was positioned transversely over the anteromedial thigh, 1 fingerbreadth superior to the base of patella, and a 22 G, 80 mm echogenic needle (PAJUNK Germany) was inserted in-plane in the anteromedial to posterolateral direction. The needle was advanced to reach the interspace between the popliteal artery (indicated by the stainless steel wire) and the distal femoral shaft (figure 1A, B). The 10 mL dye solution was injected over 10 s into the interspace and incremental injection continued during needle withdrawal.

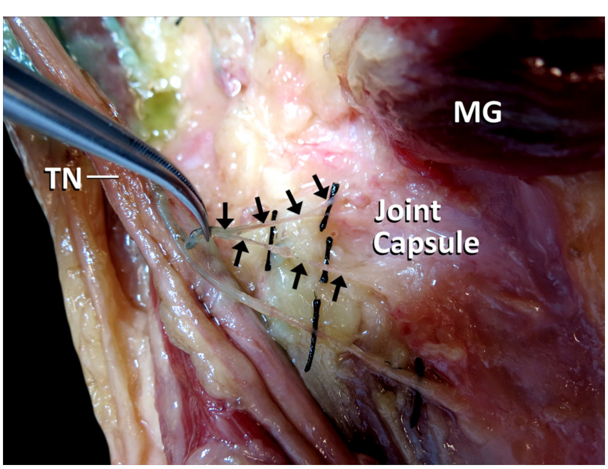

Figure 2 Methodology. Example of dissection of articular branches terminating in the posterior knee joint capsule. Arrows (black) indicate articular branches from the tibial nerve (TN). MG, medial head of the gastrocnemius muscle (reflected).

Distal injection technique

The distal injection technique was performed as previously described.[3 5] In the prone position, the ultrasound probe was placed posteriorly at the level immediately superior to the femoral condyles. A 22 G, 80 mm echogenic needle (PAJUNK Germany) was inserted in-plane from medial to lateral and advanced to the intercondylar fossa between the popliteal artery and posterior knee joint capsule (figure 1C, D). As in the proximal injection, 10 mL dye solution was injected over 10 s into the interspace with further incremental injection during needle withdrawal.

Dissection, digitization and 3D modeling

Specimen dissection was performed using a 3.5× magnification lens. The skin and superficial fascia were removed from the anterior, medial and posterior compartments of the thigh and posterior compartment of the leg to expose the underlying muscles. The following nerves were exposed while preserving any branches that were found:

- Main trunk of the obturator nerve, tibial nerve (TN), and CFN.
- Articular branches in the posterior compartment—superior branches of tibial nerve (SBTN), inferior branches of tibial nerve (IBTN), posterior branch of common fibular nerve (PBCFN), and genicular branch of posterior division of obturator nerve (GBPON).
- Articular branches in the anterior compartment—anterior branch of common fibular nerve (ABCFN), saphenous nerve (SPN), nerve to vastus medialis (NVM), medial and lateral branches of nerve to vastus intermedius (MBNVI and LBNVI), nerve to vastus lateralis (NVL), superior lateral genicular nerve (SLGN) and superior medial genicular nerve (SMGN).

During dissection of the posterior compartment, the popliteal artery and vein were cleaned and delineated. Next, articular branches of each of the TN and CFN were identified and followed to their termination in the knee joint capsule (figure 2). In the popliteal fossa, the fatty lobules were meticulously removed while maintaining the integrity of articular branches and extent of dye spread (figure 3).

In all specimens, the area of dye distribution was exposed and digitized using a MicroScribe G2X Digitizer (Immersion, San Jose, CA, USA) along with custom data collection software developed in our laboratory. The digitized area of dye distribution in each specimen was modeled and superimposed onto a 3D CT reconstructed skeletal model of the knee joint to generate a dye distribution map (Maya 2016, Autodesk, San Rafael, CA; Amira for Life Sciences, Thermo Scientific, Waltham, MA; Paint.Net, dotPDN, Redmond, WA). All specimens were photographed throughout the dissection process.

Data analysis

The following data were collected and analyzed using descriptive statistics: (1) determination of which articular branches were present or absent in each specimen and quantification of percentage frequency; (2) determination of the nerves stained in each specimen and quantification of stain frequency in percentage; and (3) computation and comparison of dye spread area between the proximal and distal iPACK injection techniques. An independent-samples t-test ($p \geq 0.05$) was used to determine

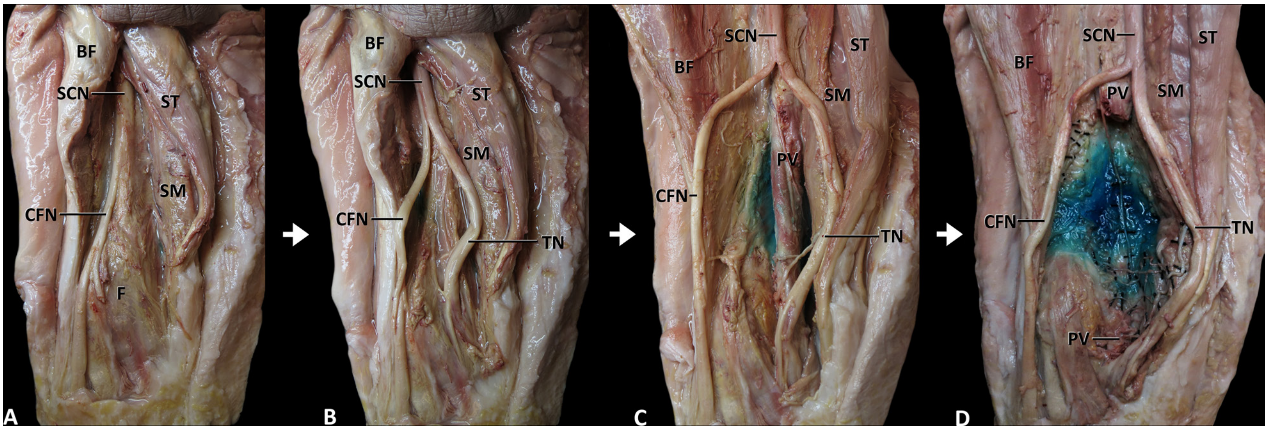

Figure 3 Methodology. Serial dissection of popliteal fossa following dye injection. (A) Biceps femoris and semitendinosus/semimembranosus were separated to expose the contents of the popliteal fossa. No dye was observed. (B) Tibial nerve was exposed by removing popliteal fat and then reflected. No dye was observed. (C) Fascial sheath around the popliteal vessels was removed posteriorly to expose the popliteal artery and underlying vein. Note the fat and fascia on the popliteal surface of the femur, lateral and deep to the vessels, are stained with dye. (D) Popliteal vessels were excised revealing dye spread staining the fat and fascia covering the popliteal surface of the femur. BF, biceps femoris muscle; CFN, main trunk of common fibular nerve; F, popliteal fat and fascia covering contents of popliteal fossa; PV, popliteal vessels; SCN, sciatic nerve; SM, semimembranosus muscle; ST, semitendinosus muscle; TN, main trunk of tibial nerve.

if there was a significant difference between the mean areas of dye spread of the two injection techniques.

RESULTS

A total of 12 articular branches were identified: 4 innervating the posterior knee joint capsule and 8 to the anterior knee joint. The eight articular branches supplying the anterior knee capsule (ABCFN, SPN, NVM, MBNVI, LBNVI, NVL, SLGN and SMGN) were identified in all specimens. Of the four articular branches innervating the posterior knee joint capsule, only two (IBTN, GBPON) were found in all specimens while the presence of the other two branches (SBTN and PBCFN) varied (table 1).

The mean area of dye spread was comparable for both the proximal and distal injection techniques, 48.43±10.44 mm^2 and 45.71±11.79 mm^2, respectively. However, the extent of distribution differed (figure 4). The cephalad-caudad dye spread associated with the proximal injection technique was between the adductor hiatus and the level of the superior border of the femoral condyles (figure 5A–C). This was more proximal than the dye spread of the distal injection technique which spanned

Table 1 Summary of articular nerve staining between iPACK injection techniques

	SBTN	IBTN	PBCFN	ABCFN	GBPON	SPN	SMGN	SLGN	MBNVI	LBNVI	NVM	NVL	n/T	%
Proximal injection														
SP 1	Y	X	–	Y	Y	Y	Y	Y	Y	X	X	X	7/11	63
SP 2	Y	X	Y	Y	Y	X	Y	Y	Y	X	X	X	7/12	58
SP 3	Y	Y	–	Y	Y	X	Y	Y	Y	X	X	X	7/11	63
SP 4	–	Y	Y	Y	Y	X	Y	Y	X	X	X	X	6/11	54
SP 5	X	X	–	Y	Y	X	Y	Y	X	X	X	X	4/11	36
SP 6	–	X	X	X	Y	Y	Y	X	Y	X	X	X	4/11	36
SP 7	–	X	X	X	Y	Y	Y	X	Y	X	X	X	4/11	36
Mean* %: 49.4±12.9														
Distal injection														
SP 1	Y	Y	Y	Y	Y	X	Y	Y	X	X	X	X	7/12	58
SP 2	Y	Y	–	Y	Y	X	X	Y	X	X	X	X	5/11	45
SP 3	Y	X	–	Y	Y	Y	Y	Y	X	X	X	X	6/11	55
SP 4	Y	X	X	Y	Y	X	X	Y	X	X	X	X	4/12	33
SP 5	X	X	Y	Y	Y	Y	Y	Y	X	X	X	X	6/12	50
SP 6	Y	Y	Y	Y	Y	Y	X	Y	X	X	X	X	7/12	58
SP 7	Y	X	Y	Y	Y	Y	Y	Y	X	X	X	X	7/12	58
Mean* %: 50.86±9.3														

n/T indicates number of nerves stained out of total nerves present; % denotes percentage of nerves stained; – indicates not found.
*No significant difference (p≥0.05) between the numbers of nerves captured using proximal and distal injection techniques.
ABCFN, anterior branch of common fibular nerve; GBPON, genicular branch of posterior division of obturator nerve; IBTN, inferior branches of tibial nerve; LBNVI, lateral branch of nerve to vastus intermedius; MBNVI, medial branch of nerve to vastus intermedius; NVL, nerve to vastus lateralis; NVM, nerve to vastus medialis; PBCFN, posterior branch of common fibular nerve; SBTN, superior branches of tibial nerve; SLGN, superior lateral genicular nerve; SMGN, superior medial genicular nerve; SP, specimen; SPN, saphenous nerve; X, not stained; Y, stained; iPACK, infiltration of the interspace between the popliteal artery and capsule of the knee.

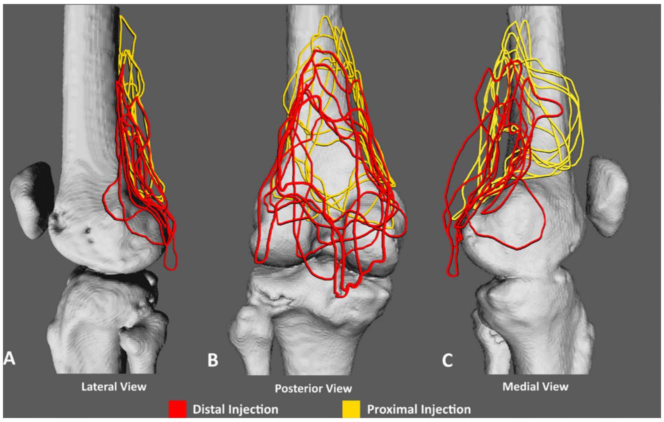

Figure 4 Dye distribution map of the proximal and distal infiltration of the interspace between the popliteal artery and capsule of the knee (iPACK) injection. (A) Lateral spread. (B) Posterior spread. (C) Medial spread.

between the adductor hiatus and the knee joint line (figure 5D–F; see also figure 4B).

Dye spread in the medial-lateral direction also differed. With the proximal injection technique, dye spread to the medial aspect of the knee joint was extensive, with extension as far anterior as the suprapatellar bursa (figure 6A–C). On the other hand, medial dye spread was more limited with the distal injection and only reached as far as the adductor tubercle and medial femoral epicondyle (figures 6D–F and 7A, see also figure 4C). Dye spread to the lateral epicondyle was noted only with the distal injection (figures 7 and 8B, see also figure 4A).

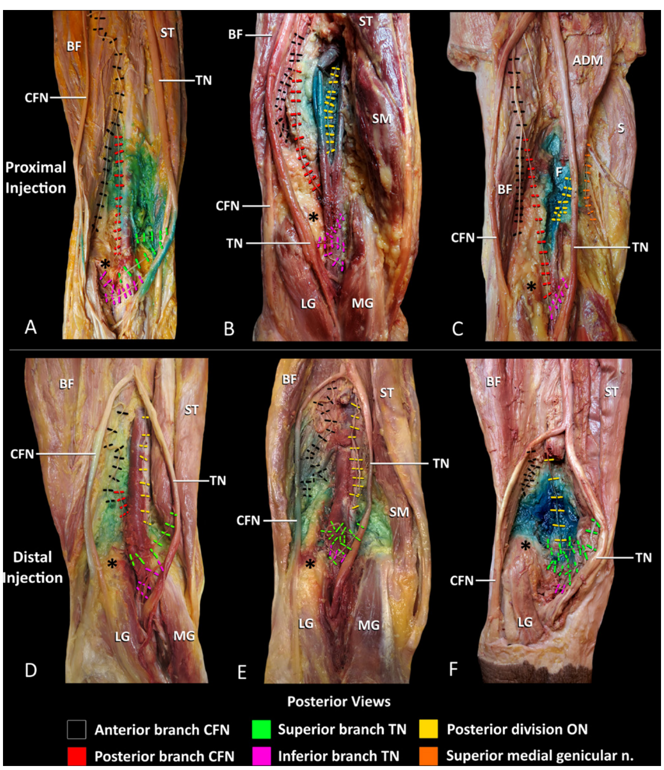

Figure 5 Posterior dye spread in the popliteal fossa following proximal and distal infiltration of the interspace between the popliteal artery and capsule of the knee (iPACK) injections. (A–C) Proximal iPACK injection. (D–F) Distal iPACK injection. Asterisk (black) denotes lateral femoral condyle. ADM, adductor magnus muscle; BF, biceps femoris muscle; CFN, main trunk of common fibular nerve; LG, lateral head of gastrocnemius muscle; MG, medial head of gastrocnemius muscle; ON, obturator nerve; S, sartorius muscle; SM, semimembranosus muscle; ST, semitendinosus muscle; TN, main trunk of tibial nerve.

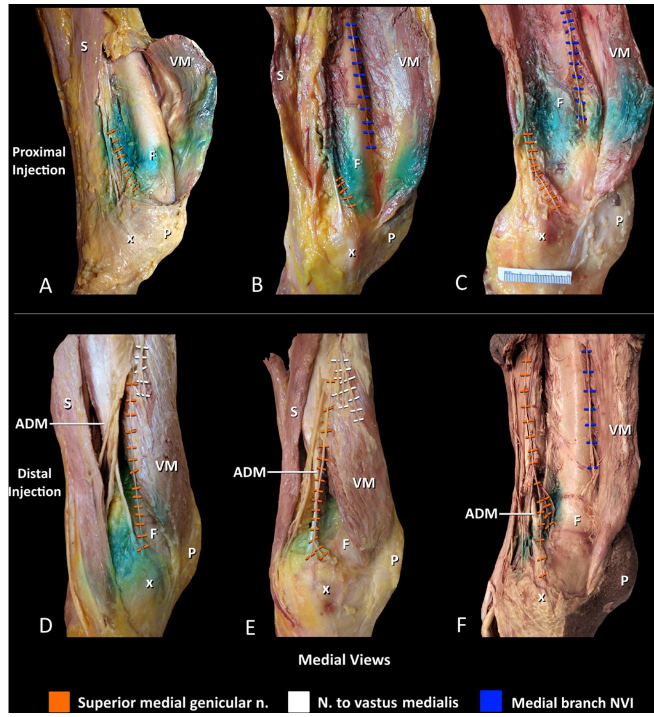

Figure 6 Medial dye spread through the adductor hiatus following proximal and distal infiltration of the interspace between the popliteal artery and capsule of the knee (iPACK) injections. (A–C) Proximal iPACK injection. (D–F) Distal iPACK injection. ADM, adductor magnus tendon; F, femur; P, patella; S, sartorius muscle; VM, vastus medialis muscle; X (white), medial epicondyle.

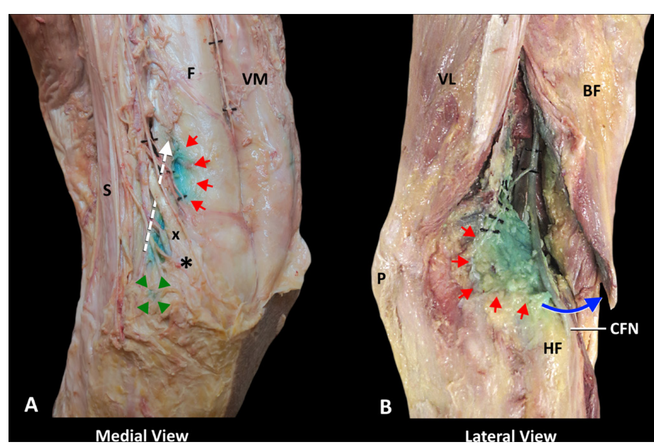

Figure 7 Anterior spread of dye using distal injection technique. (A) Anteromedial dye spread through adductor hiatus. (B) Anterolateral dye spread deep to biceps femoris. Arrow (blue) indicates the reflection of biceps femoris; arrow (red), margin of dye spread in anterior compartment of thigh; arrowheads (green), injection needle entry/exit point; asterisk, adductor tubercle; dashed arrow (white), direction of dye spread through adductor hiatus. BF, biceps femoris; CFN, main trunk of common fibular nerve; F, femur; HF, head of fibula; P, patella; S, sartorius muscle; VL, vastus lateralis; VM, vastus medialis (reflected); X, adductor magnus tendon.

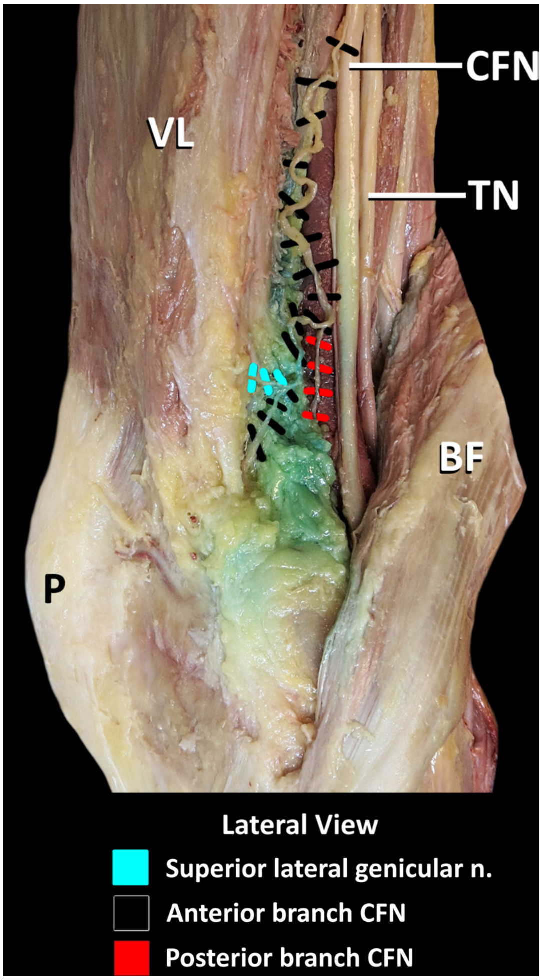

Figure 8 Lateral dye spread following distal infiltration of the interspace between the popliteal artery and capsule of the knee (iPACK) injection. BF, biceps femoris muscle; CFN, main trunk of common fibular nerve; P, patella; TN, main trunk of tibial nerve; VL, vastus lateralis muscle.

Overall staining percentage of the 12 articular branches did not differ between the two injection techniques (mean 49.4%±12.9%, proximal vs 50.9%±9.3%, distal) (table 1). Nerves most consistently stained were the GBPON (100%), SBTN (≥75%), as well as ABCFN and PBCFN (≥50% of specimens) (table 2).

To compare the percentage of nerves stained with each technique, the knee joint capsule was divided into three regions: posterior, anterolateral, and anteromedial. The distal injection resulted in higher capture percentage of nerves supplying the posterior (>13%) and anterolateral (>10%) regions, whereas the proximal injection had greater capture percentage of the nerves supplying anteromedial (>25%) region (table 2). Of the four articular branches supplying the posterior knee joint capsule, the IBTN was the least likely to be stained with either technique (table 2). Of the four articular branches that supplied the anterolateral knee capsule, the NVL and LBNVI were not stained by either technique. The ABCFN and SLGN were both consistently stained with the distal injection technique (100%) as compared with 71% with the proximal technique. Of the four nerves that supplied the anteromedial knee joint capsule, the NVM was not stained with either technique while the SMGN was stained in 100% of specimens with the proximal technique. The MBNVI and main trunk of SPN had variable staining percentages. It is interesting to note that the TN was stained in 43% (both techniques), whereas the CFN was stained in 57% (proximal technique) and 71% (distal technique).

Table 2 Comparison of articular nerve staining between iPACK injection techniques

	Proximal injection		Distal injection	
Articular branches of knee joint	**Identified**	**Stained**	**Identified**	**Stained**
	n/7 SP	n (%)	n/7 SP	n (%)
Posterior capsule				
Superior branch tibial nerve	4/7	3/4 (75)	7/7	6/7 (85)
Inferior branch tibial nerve	7/7	2/7 (29)	7/7	3/7 (42)
Posterior branch CFN	4/7	2/4 (50)	5/7	4/5 (80)
Genicular branch PON	7/7	7/7 (100)	7/7	7/7 (100)
		14/22 (64)		20/26 (77)
Anterolateral capsule				
Anterior branch CFN	7/7	5/7 (71)	7/7	7/7 (100)
Lateral branch NVI	7/7	0/7 (0)	7/7	0/7 (0)
Nerve to vastus lateralis	7/7	0/7 (0)	7/7	0/7 (0)
Superior lateral genicular nerve	7/7	5/7 (71)	7/7	7/7 (100)
		10/28 (40)		14/28 (50)
Anteromedial capsule				
Nerve to vastus medialis	7/7	0/7 (0)	7/7	0/7 (0)
Medial branch NVI	7/7	5/7 (71)	7/7	0/7 (0)
Superior medial genicular nerve	7/7	7/7 (100)	7/7	4/7 (57)
Saphenous nerve*	7/7	3/7 (43)	7/7	4/7 (57)
		15/28 (54)		8/28 (29)

*Indicates main trunk staining.
CFN, common fibular nerve; NVI, nerve to vastus intermedius; PON, posterior division of obturator nerve; SP, specimen; iPACK, infiltration of the interspace between the popliteal artery and capsule of the knee.

DISCUSSION

This cadaveric study provides insight into the mechanism of analgesia of an iPACK block. With a 10 mL injection, the injectate reaches many of the articular branches in the popliteal region, and spreads anteriorly to reach some of the articular branches supplying the anterolateral and anteromedial knee joint capsule. Previous clinical reports and cadaveric injection studies have reported injectate spread from the adductor canal into the popliteal fossa.[6–9] We observed the reverse phenomenon using both injection techniques. Although the extent of anterior spread with the proximal injection technique was greater due to possible anteromedial injection during needle withdrawal, anterior spread can also be seen with the distal injection technique that cannot be explained by direct or inadvertent anteromedial injection while withdrawing the needle. Therefore, the findings of this current study suggest that an iPACK block has the potential to relieve pain originating from both the posterior and anterior aspects of the knee.

In a recent anatomical study, articular branches of the TN were found to be the main source of innervation to the entire posterior knee joint capsule.[10] Superiorly, the posterior capsule also received additional innervation from the GBPON and PBCFN. Conceivably, neural blockade of these articular branches is essential to control posterior knee pain following TKA. Results of the current study showed that although the mean area of dye spread was comparable with the two injection techniques, staining frequency of the four articular branches in the posterior knee compartment differed (table 2). For example, while the SBTN and GBPON were most consistently stained irrespective of the injection technique, staining of the IBTN and PBCFN was more likely with the distal technique. Such nerve staining pattern may suggest that distal injection is the preferred technique for relief of posterior knee pain pending clinical confirmation.

Dye spread into the anteromedial and anterolateral compartment of the thigh following an iPACK block injection suggests that this block may also relieve anterior knee pain in varying degrees. We observed extensive anteromedial dye spread and high frequency of staining the SMGN and MBNVI with the proximal injection. This is likely due to the trajectory of needle advancement (from anteromedial to posterolateral) and anteromedial dye spread through the adductor hiatus. Anterolateral dye spread, on the other hand, was more extensive with distal injection resulting in greater staining of the ABCFN, and its branch, the SLGN. This staining pattern may be attributed to the spread of dye along the lateral femoral condyle into the lateral epicondylar region following the distal injection. A preliminary clinical study supports the concept that SMGN and SLGN are important targets as ultrasound-guided genicular nerve blocks were reported to provide effective analgesia following TKA.[11]

Preliminary clinical analgesic data of iPACK block are encouraging when it is combined with ACB,[3–5 12] FNB,[4] or periarticular local anesthetic infiltration (PAI).[13] These combined procedures have been reported to improve post-TKA pain relief,[4 5 12 13] decrease opioid consumption,[3 12] improve postoperative rehabilitation,[3 5 12] and shorten hospital length of stay.[3] Furthermore, combining an iPACK block with ACB and PAI significantly reduced dynamic pain on ambulation and physical therapy when compared with PAI alone.[13] Although ropivacaine 0.2% and 0.25% has been used in past clinical studies in varying volumes, 15 mL,[12] 20 mL,[5] 25 mL,[13] and 30 mL,[3] the optimal volume and concentration (dose) of local anesthetic administration has not been determined pending future dose–response and pharmacokinetic studies.

Similar to ACB, the iPACK block is a motor-sparing analgesic modality that targets distal sensory articular branches to the knee joint.[3 12] In this cadaver study, staining of the TN and CFN was noted proximally following both injection techniques. In the clinical setting, we have occasionally observed unintentional CFN blockade causing foot drop after an iPACK block injection (personal observation). It is therefore important to first identify the location of the TN and CFN prior to injection. Noting the location of the TN and CFN before injection is paramount as this influences the choice of site and depth of final needle tip position before injection. Conceivably, a needle tip placed close to the TN and particularly the CFN will increase the chance of inadvertent local anesthetic spread to these nerves leading to neural blockade and motor paralysis. Nerve staining in the cadaveric specimens is not necessarily interpreted as neural blockade in the clinical setting because local anesthetic of sufficient quantity must penetrate the paraneural sheath before reaching these nerves.

Limitations of the current study include small sample size thus a lack of power to analyze sex and age differences. Meticulous nerve dissection and digitization of dye spread is time consuming and labor intensive thus precludes larger sample sizes. In addition, the spread of injectate, as in all cadaveric studies, may not exactly replicate local anesthetic spread patterns in vivo. However, lightly embalmed specimens have been reported to have tissue qualities similar to that of live subjects with minimal structural distortion.[14–16]

In conclusion, the two iPACK injection techniques provided similar area of dye spread in the popliteal region and extensive staining of the articular branches supplying the posterior capsule of the knee joint. However, the proximal injection technique promoted greater anteromedial dye spread while the distal injection had more anterolateral spread. Future clinical studies are required to confirm our cadaveric study findings.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement All data relevant to the study are included in the article or uploaded as supplementary information.

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