



Minimizing the Pain of Local Anesthesia Administration in Interventional Radiology with an Anesthetic Portal Technique

Dylan Suttle¹ Virpal Gill² Daniel Sheeran³ Nicole Keefe⁴ Claire Davis⁵ James Patrie⁶
John F. Angle³

¹Greensboro Radiology, Vascular and Interventional Radiology Specialists, Greensboro, North Carolina, United States

²School of Medicine, University of Virginia, Charlottesville, Virginia, United States

³Division of Interventional Radiology, Department of Radiology, University of Virginia, Charlottesville, Virginia, United States

⁴Department of Radiology, University of North Carolina, Chapel Hill, North Carolina, United States

Address for correspondence Daniel Sheeran, MD, University of Virginia, Division of Interventional Radiology, Department of Radiology, 1215 Lee Street, Charlottesville, VA 22903, United States (e-mail: uuv3wp@virginia.edu).

⁵Division of Pulmonary and Critical Care, Department of Internal Medicine, University of Virginia, Charlottesville, Virginia, United States

⁶Department of Public Health Science, School of Medicine, University of Virginia, Charlottesville, Virginia, United States

Arab J Intervent Radiol 2024;8:36–42.

Abstract

Objective This article assesses the effectiveness of a standardized local anesthetic (LA) technique designed to minimize the pain of local anesthesia administration in interventional radiology (IR).

Materials and Methods A prospective study compared participants' experience in a control group ($n = 63$) of random LA administration techniques to a separate experimental group ($n = 60$) with a standardized technique based on known methods to minimize the pain of LA. Participants in each group were surveyed after LA administration to assess perceived pain and number of times a painful stick was felt. Participants were also asked to compare LA pain to prior experiences with LA, and to compare the overall pain experienced during the procedure to expected pain.

Statistical Analysis Ordinal variable distribution analyses were performed using the Wilcoxon rank sum test. Categorical variable analyses were performed with the Pearson's global exact chi-square test.

Results Pain of LA (mean 1.1 vs. 3.3 on a 0–10 scale, $p < 0.001$), number of times a painful stick was felt (mean 0.8 vs. 1.9 times, $p < 0.001$), and overall pain during the procedure (mean 1.5 vs. 3.4 on 0–10 scale, $p < 0.001$) were significantly less using the standardized versus random techniques. Compared with prior experiences of LA, pain using the standardized technique was less in 77.6%, the same in 22.4%, and more in 0% of patients while pain using the random technique was less in 46.4%, the same in 39.3%, and more in 14.3% of patients ($p < 0.05$).

Conclusion Severity and frequency of pain from LA administration in IR procedures is minimized using a standardized anesthetic portal technique. This technique may also decrease overall pain experienced during IR procedures as well.

Keywords

- ▶ anesthesia
- ▶ local
- ▶ pain
- ▶ procedural
- ▶ radiology
- ▶ interventional

article published online
February 29, 2024

DOI <https://doi.org/10.1055/s-0044-1781452>.
ISSN 2542-7075.

© 2024. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution License, permitting unrestricted use, distribution, and reproduction so long as the original work is properly cited. (<https://creativecommons.org/licenses/by/4.0/>)

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Administration of local anesthesia occurs nearly ubiquitously during procedures performed in interventional radiology (IR). A multitude of studies illustrate specific technical and pharmacologic details on minimizing the pain of local anesthesia, yet these details have not permeated into IR clinical practice. Paradoxically, administration of local anesthesia remains the most painful part of many minimally invasive procedures.^{1,2} While the pain caused by local anesthesia administration is often a temporary discomfort, it is easily reduced if the correct techniques are employed.³

Many surgical specialties have shifted to outpatient-based, minimally invasive procedures using only local anesthesia which then demands mastery of techniques to increase anesthetic effect and make the administration of local anesthesia tolerable to patients. Moreover, as the case complexity increases in the field of IR, so does the potential for pain experienced during procedures. There is a need for interventional radiologists to perfect techniques to minimize the pain associated with local anesthesia.

The purpose of this study was to develop a standardized technique to minimize the pain of local anesthesia administration in IR procedures and compare it to patient perceptions of pain with a less-structured approach to local anesthetic (LA). We hypothesized that patients will experience significantly less pain from local anesthesia administration, the primary outcome, when using the standardized technique compared to the less-structured approach.

Materials and Methods

We performed this study as a single-center prospective trial with equal allocation ratios between the experimental and control group. The trial was approved by the local Institutional Review Board. We recruited patients between March 2018 and January 2019 in the IR preprocedure area. All participants gave verbal consent after the trial was explained by a trained study volunteer prior to the procedure. All participants were eligible for the study if they were over the age of 18, were English-speaking, were not pregnant or imprisoned, and the procedure required LA.

Subjects in the control group underwent procedures with local anesthesia administration performed by five different physicians at our institution who were blinded to the nature of the study beyond the survey questions that were asked to the subjects. There is currently no standardized technique implemented at our institution and there are technical variances between providers. Trained observers monitored local anesthesia administration techniques of the control arm to account for providers who may have integrated intervention arm techniques by nature of their own practice. Observers then qualified the overlap and differences in technique variables between the control and intervention arms.

Once all control group data was complete, one of two physicians (distinct from the physicians in the control group) performed the standardized technique for LA administration

in the intervention arm. We synthesized individual technical and pharmacologic techniques to reduce pain of local anesthesia found in the literature into a single, standardized technique that included using warmed (37°C) 1% lidocaine with 1:100,000 epinephrine, using a 30-gauge needle, marking the site prior to initiating LA to define the portal, informing participants of local anesthesia prior to administration, tactile distraction by pressing on the injection site with a fingertip or needle cap, inserting the needle perpendicular to the skin surface with a subdermal injection, and injecting an initial amount of 2.5 mL at a slow rate (more than 15 seconds) to create the anesthetic portal (—Fig. 1). After creating the anesthetized portal, the proceduralist could proceed with the procedure as planned, including administering additional local anesthesia with a larger needle (e.g., subcutaneous tract anesthesia for tunneled catheter placement), making a skin nick, or navigating a needle under ultrasound guidance (e.g., deeper anesthesia administration to the peritoneum for paracentesis or insertion for vascular access). If additional local anesthesia was needed, the

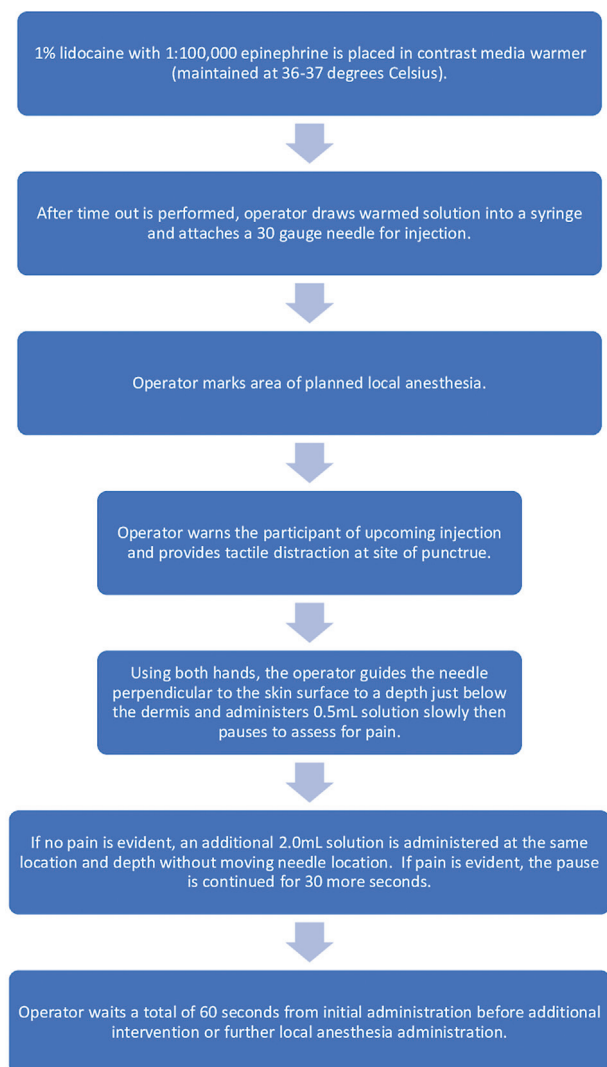


Fig. 1 A standardized technique for the creation of the anesthetic portal.

Table 1 Standardized survey questions

| Question | Answer (circle one) |
|---|---|
| How many times did you feel pain from the local anesthesia? | 0, 1, 2, 3, 4, or > 4 times |
| How would you rate the pain of the local anesthesia? (visual analog scale) | 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 |
| How would you rate the pain of the overall procedure? (visual analog scale) | 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 |
| How would you compare the pain of the local anesthesia with other times receiving local anesthesia? <i>The pain you experienced during this procedure was:</i> | More painful Same painfulness Less painful N/A |
| How would you compare the pain of the local anesthesia during this procedure to the pain of local anesthesia during other procedures you've had in radiology, specifically? <i>The pain you experienced during this procedure was:</i> | More painful Same painfulness Less painful N/A |
| How would you compare the pain you actually experienced during this procedure to the pain you expected during this procedure? <i>The pain you experienced during this procedure was:</i> | More painful Same painfulness Less painful N/A |

Abbreviation: N/A, nonapplicable.

anesthetic portal was used for the entry site of the needle through which additional local anesthesia was delivered. If the anesthetic area was enlarged, for example, with the planned incision site for a port placement, the needle was advanced by leading with at least 1 cm of subdermal LA. The trained observers surveyed all study participants immediately after local anesthesia administration and after the completion of the participant's procedure (►Table 1).

The primary outcome measured was pain associated with the local anesthesia administration (visual analog scale [VAS] 0–10). Secondary outcomes measured included the number of times pain was felt from local anesthesia administration (0, 1, 2, 3, 4, or 4+ times), pain associated with the overall procedure (VAS 0–10), pain experienced versus pain expected (less, same, or more) during the entire procedure, and comparison to pain associated with local anesthesia in prior experiences both in general and specifically during radiology procedures (less, same, or more), if applicable.

We abstracted additional variables from the electronic medical record based on their plausible association with

pain and our outcomes of interest. These included age at procedure, sex, ethnicity as identified by the participant, procedure performed, and anatomic region of the procedure. In order to characterize the association between the methods of LA administration, we limited our analysis to immediately after the LA and at the termination of the procedure.

Ordinal variable distribution analyses were performed using the Wilcoxon rank sum test. Categorical variable analyses were performed with the Pearson's global exact chi-square test. Sample size was determined by the number of trained study volunteers and by the availability of the two physicians who performed the standardized technique.

Results

There were 123 patients who participated in the study. Of the participants, 67 (54.5%) were male, 107 (87%) were white, and mean age at procedure was 56 years (± 17) (►Table 2). Each group consisted of an assortment of cases, with the

Table 2 Characteristics of study population

| Variable | All N = 123 | Control group N = 63 | Experimental group N = 60 |
|-------------------------------|----------------|-------------------------|------------------------------|
| Age, y, mean \pm SD | 56 \pm 17 | 55 (16) | 57 (18) |
| Sex: male, n (%) | 67 (54.5) | 35 (56) | 32 (53) |
| Race: white, n (%) | 107 (87) | 52 (83) | 55 (92) |
| Ethnicity, n (%) ^a | | | |
| Caucasian | 107 (87) | 52 (83) | 55 (92) |
| African American | 13 (10.6) | 10 (16) | 3 (5) |
| Hispanic/Latino | 3 (2.4) | 1 (2) | 2 (3) |
| Declined | 0 | 0 | 0 |

Abbreviation: SD, standard deviation.

^aEthnicity was recorded as the ethnicity self-identified by participants.

Table 3 Comparison of procedures performed

| Procedure | All N = 123 (%) | Control group N = 63 (%) | Experimental group N = 60 (%) | p-Value ^a |
|---|------------------------|-----------------------------|----------------------------------|----------------------|
| Arteriogram, abdominal | 12 (10) | 11 (17) | 1 (2) | N/A |
| Biliary tube check, change | 2 (1) | 1 (2) | 1 (2) | N/A |
| Fistulogram | 10 (8) | 8 (13) | 2 (3) | N/A |
| IVC filter removal | 4 (3) | 2 (3) | 2 (3) | N/A |
| Midline placement | 3 (2) | 1 (2) | 2 (3) | N/A |
| Nephrostomy tube change | 3 (2) | 1 (2) | 2 (3) | N/A |
| Non-tunneled central venous line | 2 (1) | 2 (3) | 0 (0) | N/A |
| Percutaneous nephrostomy tube placement | 1 (0.8) | 1 (2) | 0 (0) | N/A |
| PICC placement | 42 (34) | 17 (30) | 25 (42) | N/A |
| PICC rewire | 2 (1) | 0 (0) | 2 (3) | N/A |
| Central venous port placement | 23 (19) | 10 (16) | 13 (22) | N/A |
| Central venous port removal | 6 (5) | 1 (2) | 5 (8) | N/A |
| Transjugular liver biopsy | 4 (3) | 4 (6) | 0 (0) | N/A |
| Tunneled central line | 7 (6) | 2 (3) | 5 (8) | N/A |
| Tunneled line exchange | 1 (0.8) | 1 (2) | 0 (0) | N/A |
| Tunneled line removal | 1 (0.8) | 0 (0) | 1 (2) | N/A |
| Venogram, pelvis | 1 (0.8) | 1 (2) | 0 (0) | N/A |
| Femoral | 13 (57) | 12 (19) | 1 (2) | N/A |
| Flank, trunk | 14 (11) | 5 (8) | 9 (20) | N/A |
| Jugular | 41 (33) | 21 (33) | 20 (33) | N/A |
| Upper extremity | 56 (46) | 26 (41) | 30 (50) | N/A |
| Pain medication within 24 hours prior to procedure | 53 (43) | 36 (57.1) | 27 (42.9) | < 0.01 |
| Sedation during procedure | 75 (70) | 45 (71.5) | 30 (50) | 0.02 |
| Mean procedure time, min [SD], (minimum, maximum min) | 52.3 [39.5], (14, 301) | 65.7 [52.7], (14, 301) | 38.9 [26.3], (15, 100) | 0.001 |

Abbreviations: IVC, inferior vena cava; N/A, nonapplicable; PICC, peripherally inserted central catheter; SD, standard deviation.

^aWilcoxon rank sum test used to calculate *p*-values.

majority of cases being performed at upper extremity or neck access sites in both cohorts (► **Table 3**).

In the control group, 36 participants (57.1%) received pain medication (any pain medication including acetaminophen, nonsteroidal anti-inflammatory, opiates, etc.) in the 24 hours prior to the procedure compared to 17 participants (28.3%) in the experimental group ($p < 0.01$). The majority of participants in the control group underwent procedures with conscious sedation (45 patients, 71.5%), while half of the participants (30 patients, 50%) in the experimental group received conscious sedation ($p = 0.02$). Total procedure time was significantly longer in the control group (mean 65.7 [standard deviation [SD] 52.7] minutes) than the experimental group (mean 38.9 [SD 26.3] minutes) ($p = 0.001$) (► **Table 3**). There were no documented complications related to the LA administration in either group.

No instance of LA administration in the control group utilized every aspect of the standardized technique (► **Table 4**). The most utilized aspect of the standardized technique employed in the control group was informing

participants of local anesthesia prior to administration (59 participants, 93.4%) and the least utilized aspects were warmed LA solution (0 participants, 0%) and tactile distraction (0 participants, 0%).

The primary outcome, pain rating of local anesthesia administration, was significantly lower in the experimental group (mean 1.1 out of 10 on VAS, SD 1.2, minimum 0 and maximum 4) compared to the control group (mean 3.3 out of 10 on VAS, SD 2.4, minimum 0 and maximum 9) ($p < 0.001$). The experimental group also reported a significantly lower overall pain rating of the entire procedure (mean 1.5 out of 10 on VAS, SD 1.2, minimum 0 and maximum 6) compared to the control group (mean 3.4 out of 10 on VAS, SD 2.4, minimum 0 and maximum 10) ($p < 0.001$). The experimental group reported decreased number of times pain was felt from local anesthesia when compared to the control arm. Over 70% of the experimental group also reported less pain than they anticipated during the entire procedure and less pain during LA administration when compared to local anesthesia from another time in their life. No participants in the experimental

Table 4 Elements of standardized local anesthetic administration performed in the control group

| Technique | Number of times performed, (%) |
|--|--------------------------------|
| Inform subject of injection | 59 (93) |
| Remove ultrasound probe prior to injection | 25 (40) |
| Mark skin at planned injection site | 22 (35) |
| Inject perpendicular to skin surface | 17 (27) |
| Two hands for injection | 16 (26) |
| 30 ga needle (vs. 25 ga needle) | 13 (21) |
| Distract subject (verbal) | 5 (8) |
| Pause and assess subject pain after 0.5 mL initial injection | 3 (5) |
| 1% lidocaine with 1:100,000 epinephrine | 1 (2) |
| Distract subject (tactile) | 0 (0) |
| Warmed local anesthetic | 0 (0) |
| Employ all elements of standardized injection technique | 0 (0) |

Table 5 Summary of survey results

| Survey question | Control group | Experimental group | p-Value ^a |
|---|------------------------------|--------------------|----------------------|
| | Mean, SD (min, max score) | | |
| Number of times pain was felt from the local anesthesia | 2 ± 1 (0, 5) | 1 ± 1 (0, 3) | < 0.001 |
| Pain rating of local anesthesia injection (VAS) | 3 ± 2 (0, 9) | 1 ± 1 (0, 4) | < 0.001 |
| Pain rating of overall procedure | 3 ± 2 (0,10) | 2 ± 1 (0, 6) | < 0.001 |
| | N (%) | | |
| Comparison of expected pain during procedure to pain experienced | More painful | 8 (13) | 0.05 |
| | Same as expected | 12 (19) | |
| | Less painful | 43 (68) | |
| Comparison of pain of local anesthesia to other times receiving local anesthesia | More painful | 8 (14) | < 0.001 |
| | Same pain | 22 (39) | |
| | Less painful | 26 (46) | |
| | N/A | 7 (11) | |
| Comparison of pain of local anesthesia during procedure to pain of local anesthesia during other radiology procedures | More painful | 4 (10) | 0.04 |
| | Same pain | 16 (38) | |
| | Less painful | 22 (52) | |
| | N/A | 21 (33) | |

Abbreviations: N/A, nonapplicable; SD, standard deviation; VAS, visual analog scale.

^aWilcoxon rank sum test used to calculate p-values.

group reported more pain when compared to local anesthesia from another time in their life. In the control group, 8 participants (14.3%) reported more pain compared to local anesthesia from other life experiences (→ **Table 5**).

Discussion

Lalonde and colleagues describe most technical aspects of our standardized technique as the “Hole in One Technique”—tar-

geted for use in superficial plastic surgery.¹ Our standardized technique tailors the “Hole in One Technique” to minimally invasive image-guided procedures with a focus on creating an anesthetic portal. This technique can be applied to nearly every procedure in IR, from venous and arterial access to paracentesis, by creating a small regional cutaneous nerve block through which a procedure may be carried out or additional deeper or lateral anesthetic may be administered.

Skin is a richly innervated organ comprised of two basic layers, the superficial epidermis and the deeper dermis. The nociceptor-free nerve endings are located in the epidermis, which coalesce deeper in the dermis and subcutaneous tissues.⁴ The free nerve endings are in general oriented parallel to one another and perpendicular to the skin surface. Once a threshold number of nociceptors are activated, an action potential and an efferent signal is sent to the brain generating the sensation of pain.⁵ For an action potential to be propagated, sodium must enter the neuron's axon at the node of Ranvier. LAs reversibly block these sodium channels at an intracellular location. Thus, LAs must traverse the axon's cell membrane in a nonionized form, reequilibrate with the ionized form once within the axon, and then bind and block the sodium channel.^{3,6}

Older LA administration techniques still prevail as dogma. The most durable of these is creating a "skin wheal" upon initial injection, which constitutes inserting the needle at a shallow angle relative to the skin surface and infiltrating LA into the epidermis to create a raised bump with an "orange peel appearance." Some use this technique just to mark the LA, but a skin marker appears to be a much less painful way to identify the LA portal. Thus, we argue that a less painful and more effective technique is perpendicular injection into the subdermis to avoid stretching the epidermis nociceptors and injecting at 90 degrees to the skin surface versus 45 degrees, which significantly reduces pain^{5,7,8} and requires less force.⁸ Once the needle is in the subdermal location, a slow injection rate decreases the rate of pain.^{1,7,9,10} Smaller needle diameter also results in less pain by minimizing the traumatization of direct encounters with nerve fibers upon entering the skin.^{1,5}

Use of one hand to administer LA is also a typical practice. The three holed "control syringes" for local administration allow for the ability to aspirate or inject with a single hand; however, they are designed with the needle positioned farthest from the operator's hand. This can magnify small hand movements, which translate to wobbling and oscillation of the needle that may irritate nerve fibers near the needle tip. Our protocol called for holding the syringe with two hands to eliminate the oscillating motion and allow for fine depth control.

Another common teaching is avoiding epinephrine in local anesthesia solution. The myth was the result of direct epidermal injection of anesthetic, which historically was laced with substances such as cocaine¹¹; numerous sources have since disproven this lore.^{2,12-15} Instead, addition of epinephrine to LA solution results in vascular smooth muscle contraction, prolonging the presence of local anesthesia before being resorbed into systemic circulation. Furthermore, epinephrine nearly doubles the duration of action of lidocaine (60–240 vs. 30–60 minutes with lidocaine alone),¹⁶ and reduces the risk of LA toxicity, allowing for higher maximum doses.^{1,3,11,16,17} These authors strongly encourage use of LAs with epinephrine, particularly when there is high risk of bleeding from the puncture or incisional site (e.g., tunneled lines, ports, coagulopathy, etc.).

Similar to warming iodinated contrast for intravascular injection, warming LAs to body temperature reduces the

pain of injection.^{1,18,19} It is theorized that increased temperature of LA solution predisposes the solution to the uncharged state which allows the anesthetic to cross the cell membrane more easily.¹⁹ While shelf life has not shown to be affected by warming,¹⁸ our practice is placing the LA in the department's stand-alone contrast warmer (set to 37°C) during room preparation for a procedure, then drawing up the solution after the procedural "time out" just prior to administration.

Tactile distraction involves intentionally causing a mildly noxious stimulus near the site of forthcoming pain to "close the nerve gate" and reduce perceived pain. The Gate Control Theory involves complex interplay at the spinal level of nociceptor relay and is the basis behind scratching to cause local pain which decreases the sensation of itching.^{1,20,21} In our study, pressing the operator's fingernail or the back of a needle cap at the planned LA injection site just prior to injection was used. Tapping, pinching, vibrating, or stretching the skin are other described techniques of tactile distraction.¹

An unexpected finding of this study was that there was an association between participants experiencing less pain from local anesthesia and less pain during the overall procedure. This finding suggests that either LA administration is the most painful part of most procedures in IR, or that more pain caused from local anesthesia, typically performed at the beginning of procedures, predisposes patients to expect and experience more overall pain. Overall reduction in pain during procedures in IR implies less need for analgesia, specifically opioids, as part of moderate sedation. Decreasing use of opioids related to pain from IR procedures due to minimizing pain from local anesthesia could be examined in future iterations of this study.

There are several limitations inherent to this study. We would have liked to use buffered (sodium bicarbonate, 8.4%, 1:10) LA as part of our standardized protocol as buffering is one of the most widely known and studied methods to reduce the painful sting of acidic lidocaine,^{3,6,9,17,18,22-24} but this was unavailable for use during our study due to a national pharmacy shortage. This limitation could be addressed in future iterations of this study.

Another limitation was the heterogeneity between the experimental and control group. More participants in the control group received pain medications within 24 hours prior to the procedure, received sedation during the procedure, and had a longer procedure duration. The sedation given during the procedure and the longer procedure times in the control group could have affected their response to pain felt during the overall procedure but would not affect their pain levels during LA administration. Additionally, despite having been less likely to receive pain medications before the procedure, the experimental group still experienced less pain during their LA administration. Therefore, while creating a more homogenous sample through standardized eligibility criteria may be beneficial to further support the decreased pain rating of the overall procedure using the standardized technique, the effect of decreased pain felt during LA administration shows that this standardized method would be beneficial in IR clinical care.

Conclusion

Severity and frequency of pain from LA administration in IR procedures is minimized using a standardized anesthetic portal technique which synthesizes many individual pharmacological and technical aspects of local anesthesia administration that are known to reduce pain. This technique may also decrease overall pain experienced during IR procedures as well.

Ethical Approval Statement

The University of Virginia Institutional Review Board reviewed this study and approved it as a quality improvement study.

Authors' Contribution

The first author, D.S., led this study and authorship of the paper with each of the remaining authors contributing equally to the study design, data collection, data analysis, and/or manuscript edits and reviews.

Conflict of Interest

None declared.

References

- Strazar AR, Leynes PG, Lalonde DH. Minimizing the pain of local anesthesia injection. *Plast Reconstr Surg* 2013;132(03):675–684
- Lalonde D, Bell M, Benoit P, Sparkes G, Denkler K, Chang P. A multicenter prospective study of 3,110 consecutive cases of elective epinephrine use in the fingers and hand: the Dalhousie Project clinical phase. *J Hand Surg Am* 2005;30(05):1061–1067
- Culp WC Jr, Culp WC. Practical application of local anesthetics. *J Vasc Interv Radiol* 2011;22(02):111–118, quiz 119
- Skin. In: Mescher AL, ed. *Junqueira's Basic Histology*, 14e. New York, NY: McGrawHill. Accessed May 8, 2018 at: <http://accessmedicine.mhmedical.com/content.aspx?bookid=1687§ionid=109633806>
- Egekvist H, Bjerring P, Arendt-Nielsen L. Pain and mechanical injury of human skin following needle insertions. *Eur J Pain* 1999;3(01):41–49
- Steele EA, Ng JD, Poissant TM, Campbell NM. Comparison of injection pain of articaine and lidocaine in eyelid surgery. *Ophthalmol Plast Reconstr Surg* 2009;25(01):13–15
- Mustoe TA, Buck DW II, Lalonde DH. The safe management of anesthesia, sedation, and pain in plastic surgery. *Plast Reconstr Surg* 2010;126(04):165e–176e
- Martires KJ, Malbasa CL, Bordeaux JS. A randomized controlled crossover trial: lidocaine injected at a 90-degree angle causes less pain than lidocaine injected at a 45-degree angle. *J Am Acad Dermatol* 2011;65(06):1231–1233
- Hanna MN, Elhassan A, Veloso PM, et al. Efficacy of bicarbonate in decreasing pain on intradermal injection of local anesthetics: a meta-analysis. *Reg Anesth Pain Med* 2009;34(02):122–125
- Scarfone RJ, Jasani M, Gracely EJ. Pain of local anesthetics: rate of administration and buffering. *Ann Emerg Med* 1998;31(01):36–40
- Thomson CJ, Lalonde DH, Denkler KA, Feicht AJ. A critical look at the evidence for and against elective epinephrine use in the finger. *Plast Reconstr Surg* 2007;119(01):260–266
- Thomson CJ, Lalonde DH. Randomized double-blind comparison of duration of anesthesia among three commonly used agents in digital nerve block. *Plast Reconstr Surg* 2006;118(02):429–432
- Fitzcharles-Bowe C, Denkler K, Lalonde D. Finger injection with high-dose (1:1,000) epinephrine: does it cause finger necrosis and should it be treated? *Hand (N Y)* 2007;2(01):5–11
- Mohan PP. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Epinephrine in digital nerve block. *Emerg Med J* 2007;24(11):789–790
- Denkler K. Dupuytren's fasciectomy in 60 consecutive digits using lidocaine with epinephrine and no tourniquet. *Plast Reconstr Surg* 2005;115(03):802–810
- Moran TC, Kaye AD, Mai AH, Bok LR. Sedation, analgesia, and local anesthesia: a review for general and interventional radiologists. *Radiographics* 2013;33(02):E47–E60
- Cepeda MS, Tzortzopoulou A, Thackrey M, Hudcova J, Arora Gandhi P, Schumann R. Adjusting the pH of lidocaine for reducing pain on injection. *Cochrane Database Syst Rev* 2010;(12):CD006581
- Colaric KB, Overton DT, Moore K. Pain reduction in lidocaine administration through buffering and warming. *Am J Emerg Med* 1998;16(04):353–356
- Hogan ME, vanderVaart S, Perampaladas K, Machado M, Einarson TR, Taddio A. Systematic review and meta-analysis of the effect of warming local anesthetics on injection pain. *Ann Emerg Med* 2011;58(01):86–98.e1
- Zilinsky I, Bar-Meir E, Zaslansky R, Mendes D, Winkler E, Orenstein A. Ten commandments for minimal pain during administration of local anesthetics. *J Drugs Dermatol* 2005;4(02):212–216
- Dickenson AH. Gate control theory of pain stands the test of time. *Br J Anaesth* 2002;88(06):755–757
- Pascuet E, Donnelly RF, Garceau D, Vaillancourt R. Buffered lidocaine hydrochloride solution with and without epinephrine: stability in polypropylene syringes. *Can J Hosp Pharm* 2009;62(05):375–380
- Burns CA, Ferris G, Feng C, Cooper JZ, Brown MD. Decreasing the pain of local anesthesia: a prospective, double-blind comparison of buffered, premixed 1% lidocaine with epinephrine versus 1% lidocaine freshly mixed with epinephrine. *J Am Acad Dermatol* 2006;54(01):128–131
- Xia Y, Chen E, Tibbits DL, Reilley TE, McSweeney TD. Comparison of effects of lidocaine hydrochloride, buffered lidocaine, diphenhydramine, and normal saline after intradermal injection. *J Clin Anesth* 2002;14(05):339–343