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XC: Main contribution in analysing the data, writing the paper, sending the manuscript and editing the final draft (corresponding author).

Abstract

Background: Nerve damage can occur after ultrasound guided peripheral nerve block (PNB). Injection pressure monitoring could improve the safety of PNB. The aim was to analyse parameters affecting pressure measurements during PNB.

Methods: The flow characteristics of needles connected to a pressure-sensing device were evaluated. Needles were placed under ultrasound guidance extra or epineurally in nerves/plexus of fresh cadavers. Using three flow rates, 4 mL of saline was injected and plateau pressure was measured. Finally, orthopaedic surgery patients receiving PNB were enrolled for an observational real-time pressure monitoring study. During PNB periods with pressure > 50 mmHg were noted (high pressure ≥ 750 mmHg). A blinded investigator recorded injection pressure curves and peak pressure.

Results: The needle diameter influenced the injection pressure (β = 66.8; $P < 0.0001$). Non-echogenic needles increased the injection pressure (β = 82; $P = 0.0009$) compared with echogenic needles. Cadaver injection pressure was higher for intraneural (255 [122.5–555] mmHg) *versus* extraneural needle tip location (90 [50–158] mmHg; $P < 0001$); for high flow (9.6 mL/min; 470 [265; 900] mmHg) *versus* low flow (1.2 mL/min; 120 [71–250] mmHg) ($P < 0.001$) and for cervical roots (900 mmHg, intraneurally) compared with nerves (300 mmHg, intraneurally). In 37 patients and 61 procedures, there were 7 [1–18] peaks of injection pressure per procedure. Pressure was noted > 750 mmHg during 13.80% of the procedural time.

Conclusions: Needle diameter, needle tip location, type of nerve/plexus, flow rates, and the anaesthetist can have a significant effect on injection pressure values and monitoring.

Introduction

Nerve damage after peripheral nerve block (PNB) is one of the most feared complications. The risk of neuropathy remains at 0.04% for a persistent neuropathy[1] to 1.9% for transient neurologic adverse events[2]. The addition of ultrasound technology and guidance for PNB contribute to improvement in needle tip location accuracy. However, ultrasound guidance does not eliminate the risk of intraneural injection[3–5] because adequate images of the needle-nerve interface are not obtained consistently[6]. The incidence of unintentional intraneural injection is estimated to be between 15% and 17% for ultrasound-guided blocks in expert hands[4,5]. On the other hand, intentional intraneural sciatic nerve injection of 1% ropivacaine promoted persistent electrophysiologic changes suggesting possible neuropathy[7]. A recent editorial claimed that intraneural injections are unnecessary and may be prohibitively dangerous in less qualified hands[8]. Neuropathy can be related to direct needle tip trauma or to an increase in intraneural pressure after injection of local anaesthetics in a low-compliance structure. In animals, injection pressure > 75 kPa (11 psi, 570 mmHg) during PNB increases the risk of nerve injury[9,10]. The increase in pressure generates a more or less prolonged neural ischaemia of the neurovascular structures (occlusion at 50 mmHg for capillaries and 145 mmHg for arteries)[11,12]. Feedback on the pressure generated during injection might provide an alert on intraneural needle tip placement because intra-epineural or inter-fascicular injections promote high pressure. However, the subjective detection of high (intraneural) injection pressure by the anaesthesiologist's hand has been shown to be inaccurate[13]. An easy way to use injection pressure monitoring system could improve the safety of PNB procedures[14,15]. Recently, a pressure-sensing device has been reported to detect intraneural location[16] or at least

needle-nerve contact with a sensitivity of 97% at a cut-off of 15 psi[17], providing an alert for high injection pressure. Several elements should be taken into account when using this type of monitoring; they can independently monitor the injection pressure; the needle (diameter, length, brand, echogenicity); the injection rate; the type of nerve and the injection technique[18]. Injection rates ≤ 15 mL/min are recommended to reduce the effect of factors upstream from the needle tip as a cause of false high-pressure readings. There are few data on the impact of new needles (echogenic and non-echogenic), needle tip/nerve contact and intraneural injection for different PNB approaches, and measurements of real-time pressure sensing during ultrasound-guided PNB. Previous studies used constant flows during injection, which is not the case in clinical practice when physicians inject the local anaesthetic solution. The aim of this study was to provide measurements and compare injection pressure characteristics on the bench to evaluate new needle systems for a variety of clinically relevant flow rates, different PNB approaches in fresh cadavers, and, as an end point to describe the values of injection pressures in a prospective observational study, during ultrasound-guided PNB in clinical practice.

Methods

The protocol for the in vitro part of the study was reviewed by the Montpellier University Hospital Research Ethics Committee as a non-human or animal study. We evaluated the flow characteristics in ambient air of 38 commonly used regional anaesthesia needles from four different brands: B. Braun (B. Braun, Melsungen, Germany), Pajunk (Pajunk, Geisingen, Germany), Vygon (Vygon Ecouen, France), Temena (Temena, Felsberg-Gensungen, Germany), corresponding to echogenic and non-echogenic needles from 18 G to 25 G and from 25 to 150 mm (Table 1). The needle was connected to a computerised pressure-

sensing device (CompuFlo®, Dynamic Pressure Sensor Technology, Computer Controlled Anesthesia System, Milestone Scientific, Livingston, NJ) via extension non-distensible tubing to the proximal port of the needle. The CompuFlo® device utilises a proprietary algorithm to measure exit-pressure at the tip of the needle in-situ. It is capable of providing real-time, continuous pressure monitoring as well as setting a maximum pressure, which controls the injection pressure. CompuFlo® digitally records flow-rate, pressure and fluid volume at four time per second and has this data available for analysis after the injection is completed. The system was calibrated and set to zero before connection. The computerised pressure-sensing instrument was set to deliver normal saline at a rate of 10 mL/min with a 20-mL syringe. Three measurements were done for three needles in every category of needles tested. All measurements were analysed. The measurements done for the four needle sets were done the same day with the same calibration, same tool and same physicians.

The cadaver trial consisted of a prospective, controlled, single-blind study conducted by anaesthesiologists and anatomists in the anaesthesiology and anatomy departments of Montpellier University Hospital. Five fresh cadavers of men who had given their written informed consent pre-mortem to use their bodies after death for educational purposes were obtained from the Laboratory of Clinical Anatomy of Montpellier University of Medicine donation program. All injections using a 22 G 80-mm Sonoplex echogenic needle (Pajunk, Geisingen, Germany) and the CompuFlo® device were performed under real-time ultrasound guidance (Logic E, General Electric, USA) and ultrasound-guided transverse views by three senior anaesthesiologists with several years of experience in ultrasound regional anaesthesia. Needle tips were placed in-plane in two different positions: either 1–2 mm from the nerve or within the nerve (into the epineurium). Each nerve received a perineural

(doughnut sign) and an intraneural (nerve swelling) injection. Bilateral injections were not realised in all five cadavers. The following locations were chosen from proximal to distal parts of the nerves: femoral, subgluteal sciatic, tibial, common peroneal nerve for the lower limb and C5, C6, C7 roots, interscalenic, infra-clavicular approaches and median and ulnar nerves in the arm for the upper limb. Four millilitres of saline using three different constant flow rates (1.2 mL/min, 4.8 mL/min and 9.6 mL/min, 15 s for every flow rate to reach a plateau pressure) were injected after calibration with the CompuFlo® when the operator considered the needle tip location appropriate according to the ultrasound image. Only the values of the plateau pressure were considered. A second investigator, blinded with respect to the needle tip position, was in charge of the recordings of the injection pressure curves and peak pressures.

In the final phase of the study, after institutional ethical committee approval (CPP Sud Mediterranée IV, Montpellier, France), clinical trial registration (DGRICCTIRS no. 12.355; ClinicalTrials.gov ID NCT03430453) and written informed consent, patients scheduled for orthopaedic surgery with nerve block were prospectively enrolled in the clinical prospective study for recording the real-time pressure obtained during PNB procedures. Exclusion criteria were a bleeding disorder, peripheral neuropathy or chronic pain syndrome, infection or injury at the needle entry point, allergy to local anaesthetic, patients less than 18 years of age, pregnancy, cognitive impairment, patient refusal, or participation in another clinical trial. On the day of surgery, patients were not premedicated. Standard monitoring was applied, including non-invasive arterial blood pressure, heart rate, and pulse oximetry. The skin was prepared with an alcoholic povidone-iodine solution. Ten experienced anaesthetists with more than one year of experience in regional anaesthesia performed the

ultrasound-guided blocks. The same ultrasonography system (Logic E, General Electric, USA) was used for all blocks. A three-way valve was connected between the CompuFlo® device and the 20-mL syringe manually controlled by the anaesthetist and the Sonoplex echogenic needle. It was calibrated before each procedure. An in-plane approach of the needle was applied for each nerve block. The needle tip was located extraneurally in the closest location to the nerve, sometimes indenting the nerve's paraneurium. A free injection flow was always obtained. Mepivacaine 10 mg/mL was injected to a maximal volume of 0.4 mL/kg. During the PNB procedure, every injection time was noted, specifically taking into account all periods with a pressure greater than 50 mmHg. High pressure was defined as a pressure greater than 750 mmHg (100 kPa or 15 psi). Two experts on ultrasound-guided PNB stored videos of the PNB procedures and were asked to analyse the films and CompuFlo® recordings (injection pressure curves and peak pressures) during the real-time procedure. Sensory blockade was assessed every 5 minutes after injection as loss of cold, pinprick, and light touch sensations in the selected nerve areas. Sensory blockade was classified as follows: 0, anaesthesia; 1, hypoesthesia; 2, normal sensation. A block was considered successful when a score of 0 was obtained for sensory blockade within 30 minutes after injection of local anaesthetic. Adverse events related to PNB were noted in the 24 hours postoperatively.

Statistical analysis

Categorical variables were expressed as number and percentage, and quantitative variables were expressed as median and range. The Shapiro-Wilk test was used to test the normality of continuous variables. Univariate analysis was performed between continuous variables and categorical data with the Student t test or the Mann-Whitney test for the non-

Gaussian variables. A linear regression was performed in a univariate analyse to measure the relation between pressure and quantitative variables (diameter needle or needle length). The results were presented as R squared (R^2). A multivariate analysis was performed in order to study the respective influence of co-variates on plateau injection pressure (the dependant variable). Variables were included according to significance level ($P < 0.20$) in the univariate analysis and clinical coherence.

In the Bench study, we applied linear mixed models analysis to investigate repeated measures of pressure including as independent variables: needle diameter, needle length (≤ 50;] 50-100 [; ≥ 100), needle brand (Vygon; BBraun; Pajunk; Temena) and needle echogenicity (or non-echogenic needle).

In the cadaver study, linear mixed models analysis was performed in order to study the respective influence of co-variates: nerve, injection flow (1.2; 4.8 or 9.6 mL/min) and the needle tip location (extraneural or intraneural) on plateau injection.

In the clinical study, multiple linear regression was applied including the technique and the nerves.

A test was considered significant for a $p < 0.05\%$. Statistical analysis was performed using SAS Enterprise Guide 7.1 (SAS Institute, Cary, North Carolina).

Results

Bench Study

Thirty-eight needles were assessed and 342 measurements were performed for the bench evaluation at a flow rate of 10 mL/min in the same environment. The most important determinant for pressure increase during constant flow appeared to be the diameter of the needle ($R^2 = 0.49$, $P < 0.0001$) (fig. 1A). The association between injection pressure and

needle length was lower (R^2 = 0.18; P < 0.0001). The needles selected for PNB and the values of injection pressure are reported in table 1. The injection pressure varied from 0 to 355 mmHg. The mixed model analysis shows that the diameter influenced the pressure (β = 66.8; P < 0.0001) but the length did not (β = 0.18; P = 0.70) (table 2). More surprisingly, for the same gauge and the same length, injection pressure values for Pajunk needles were significantly lower (β = −113.67; P = 0.002) compared with B. Braun, Temena and Vygon needles (fig. 1B4). The analysis also shows that the injection pressure with non-echogenic needles was significantly higher (β = 8.2; P = 0.0009) compared to echogenic needles, apart from Pajunk needles (fig. 1C).

Cadaver Study

Figure 2A presents the plateau injection pressure for extraneural and intraneural injections and nerves. The univariate analysis shows that the plateau injection pressure (median [quartiles]) was significantly higher for intraneural (255 [122.5-555] mmHg) than for extraneural injections (90 [50-158] mmHg; P < 0.001). With intraneural injections, the pressure differed significantly between low flow (1.2 mL/min, 120 [71-250] mmHg) and highest flows (4.8 mL/ min, 305 [190; 640] mmHg; 9.6 mL/min, 470 [265; 900] mmHg; P < 0.001). Figure 2B presents the plateau injection pressure between flow rates for the different nerves. Injection pressure ranged from 10 mmHg (tibial nerve, extraneural location at 1.2 mL/min) to 900 mmHg, which is the maximum allowed by the CompuFlo® device before it stops the infusion (C7 root, intraneural location at 9.6 mL/min). Twenty-five intraneural injections (15%) showed an injection plateau pressure above 15 psi. There were significant differences for intraneural injection pressure between nerves: from a median (quartiles) value at 180 [110–190] mmHg for the ulnar nerve to 900 [760–850] mmHg for

the C7 root. The mixed model analysis shows a positive independent association between injection pressure value and intraneural needle tip location ($P < 0.001$), type of nerve ($P < 0.001$) and flow ($P < 0.001$) but not extraneural tip location and cadaver number (table 2).

Clinical Study

Sixty-one ultrasound-guided PNBs have been done in 37 patients and 103 individual nerves or plexus were blocked (15 axillary, 9 sciatic, 7 femoral, 7 obturator, 7 interscalene, 5 infraclavicular, 5 supraclavicular, 2 lateral cutaneous nerve of the thigh, 3 cervical plexus blocks and 1 transverse abdominis plane block) were done and 103 nerves were anaesthetised. The mean duration of the PNB procedure was 81.7 [36–111] s, with 7 [1–18] peaks of injection pressure per procedure (fig. 3). The mean (standard deviation [SD]) maximum injection pressure was 812 (313) mmHg. High pressures (>v750 mmHg) were noted in 58 of the 103 nerves injected (56%). The median (quartiles) procedural time with injection pressures > 15 psi was 13.80% [1%–45%] of the total procedural time. The type of nerve anaesthetised was significantly associated with the injection pressure with negative estimation for musculocutaneous, ulnar and median nerves when the femoral nerve was the reference in the model (table 2). Two inadvertent intra-epineural injections were noted (swelling of the nerve). No block failure or postoperative neurologic complication was observed. Univariate and multivariate analyses of plateau injection pressure variables are summarised in table 2.

Discussion

The results of this study highlight the different parameters that can distort actual pressure monitoring during PNB. Some of these factors were already reported in the

literature, such as some needle features (diameter and brand)[18] or contact with a muscular fascia[19], which lead to high injection pressures that can be confounded with nerve contact. Other important parameters are described here for the first time: the difference between echogenic and non-echogenic needles, intraneural injection pressure value depending on type of nerve/plexus approach and different flow rates. This study shows for the first time in clinical practice that during ultrasound-guided PNB, the anaesthetist injects the local anaesthetic discontinuously, with high compartmental pressure peaks.

The injection pressure detected by a sensor placed at the proximal part of the needle tip to the injection tubing is influenced by the injection system, the speed of injection, the size of the needle and the size of the connection tubes[18]. Assuming that the pressure drop across the line proximal to the needle and in the three-way valve was found to be negligible compared with the needle shaft, and that flow through all needles was laminar at 10 mL/min[18], our results confirm with commonly used needles that brand and internal diameter, but surprisingly not length, have a major impact on peak injection pressures. This is related to the Poiseuille equation and Bernoulli principle. In standard fluid dynamics notation, $\Delta P = 8\mu LQ/\pi R4$, where ΔP is the pressure difference between the two ends, L the length of the pipe, μ the dynamic viscosity, Q the volumetric flow rate, and R the pipe radius. The injection pressure required to overcome the internal resistance of a small diameter tube can be notably high with B. Braun, Vygon and Temena needles. Therefore, standardisation of the tubing set selected becomes another variable when performing an injection, and should be controlled. It is also interesting to note that echogenic needles from B. Braun and Temena generated less injection plateau pressure than non-echogenic needles of the same brand and the same gauge. The only explanation is that the internal

diameter of the needle increases. We can suppose that Pajunk needles have the greatest internal diameters. During clinical practice, anaesthetists may assume that pressures measured in the injection line are equal to pressures at the needle tip. This is only true if there is no flow through the needle. Previous literature[15,20] reported that the opening injection pressure is the pressure at the beginning of injection necessary to counteract the resistance of the needle and the flow of local anaesthetic out of the needle into relatively non-compliant nerve tissue or fascia[17,19,20]. The opening pressure is a dynamic phenomenon in the 60-s interval during which the injection is initiated. Authors agree that 10 mL/min continuous injection is not a realistic imitation of a clinical injection. In a daily clinical setting, local anaesthetic is often injected in aliquots of 3-5 mL with an injection flow rate higher than 10 mL/min. However, all studied needles received the same flow rate and the results for a 10mL/min flow can be extrapolated to higher flows. Furthermore, the physician should be aware that at flow rates exceeding 15 mL/min, the pressure values upstream could be at and above those of intraneural injection. This results from the flow resistance in the needle shaft and in the connection tube. In clinical practice, anaesthetists might identify a false-positive high pressure wrongly interpreted as an intraneural injection. So, any injection pressure monitor in the injection line would need to be calibrated and validated for specific needles[21]. In addition, the flow rate that is used during an injection has been shown in this study to impact the opening pressure of an injection, therefore flow rate becomes a critical parameter and should be controlled at all phases of the injection.

We reported in cadavers that plateau injection pressures were higher for intraneural than for extraneural injections and that intraneural injection pressure levels depended on the injection flow rate and the different nerve locations. There is evidence that intraneural injection associated with high injection pressures leads to nerve damage[9,10], because high

injection pressures may indicate that the needle tip is intraneural. In our study, all measurements obtained during intraneural placement of the needle tip were higher than those obtained extraneurally. None of the injection pressure values measured intraneurally at any location was lower than those measured in the extraneural space. Only high intraneural injection pressures are responsible for neurologic symptoms[10]. Without high pressure, histologic nerve damage may occur, but no clinical nerve injury. There is a specific pathophysiology that explains the damage from high injection pressure. Microcirculatory ischaemia can occur (occlusion at 50 mmHg for capillaries, 145 mmHg for the vasa nervorum)[11,12,22], which can lead to the axonal degeneration and myelin fragmentation responsible for neurologic symptoms.[22] Previous literature concluded that acute compression of a nerve may cause long-term impairment of intraneural microcirculation due to mechanical injury to blood vessels[22]. Intraneural injection of local anaesthetic and 0.9% saline both resulted in a similar extent of nerve injury when both were associated with significantly high injection pressure resulting in severe histologic damage of the nerve fiber[23]. On the other hand, intraneural plateau injection pressure values differed for the different nerves studied. This may be related to differences in neural architecture (ratio of neural/non-neural tissue), which changes significantly from proximal to distal parts of the nerve. This reflects injection of a liquid in a compartment with lower compliance. Compliance with a high ratio of nerve component tissue is low. This suggests a higher vulnerability to high injection pressure with the needle tip in an intraneural location and of neurologic sequelae in proximal nerve approaches[24,25]. The difference in injection pressure between extraneural and intraneural injections may open new perspectives in defining pressure thresholds for extraneural and intraneural needle tip positioning during PNB procedures. Currently, there is no reliable method of detecting and avoiding an

intraneural/intrafascicular injection. The only commercially available devices for the measurement of injection pressure during PNB procedures are pressure valves placed at the connection between the syringe and the injection line: the BSmart (B. Braun Melsungen AG, Melsungen, Germany) and the NerveGuard (Pajunk, Geisingen, Germany)[21]. Our results highlight that, depending on the approach, nerve location and injection flow rate during injection of local anaesthetic solution, a proximal device is not a perfect monitoring system[26], but at least stopping a high pressure injection might be a safe vision in regional anaesthesia. The use of a high injection pressure sensor or a pressure limiter could be included in modern multimodal injection monitoring for PNBs[27]. However, extrapolation of our results to clinical practice may have limitations. First, in cadavers, pressures could be even greater that those measured by the anaesthesiologists because of the resistance of cadaver body tissues. Second, the flows used are constant flows, which are not reproducible in clinical practice with hand injection.

Our results demonstrate for the first time in clinical practice that injection of local anaesthetic solution during a PNB procedure does not occur at the recommended constant flow of 15 mL/min[18]; multiple injection pressure peaks related to different injection flow rates and movements of the needle are generated during ultrasound-guided procedures. These peaks of pressure are related to injection, hydro-dissection and repositioning of the needle tip to optimise the spread of the local anaesthetic. High pressures (> 750 mmHg) occurred in 56% of the procedures for 14% of the total procedural time. These results confirm those of Claudio et al.[28] who reported in a bench trial that 14.7% of injection pressures ranged from 20 to 29.9 psi and that 70% of the physicians exerted a force greater that 20 psi at some time during the injection. These authors also reported that the force

with which anaesthesiologists injected local anaesthetic solutions varied widely. The same results were noted among the different physicians but also within the same PNB procedure. We can also consider that anaesthesiologists would have injected more carefully than they did in their clinical practice simply because they were participating in a study. Interestingly, the values for the mean maximal pressure reached did not differ between residents and consultants. This is related to the fact that the syringe-feel method cannot predict the actual injection pressure and that the physicians, whatever the category, have divergent perceptions of what is a normal or abnormal pressure[13,28]. These results reinforce the interest in pressure monitoring with in-line devices during PNB procedures with the knowledge that parameters which can have an impact on measurements[29].

Conclusions

Pressure monitoring should be sensitive and easy to use to improve the safety of PNB. The results of this three-way study show that parameters such as needle diameter, manufacturer, echogenicity, intraneural/extraneural needle tip location depending on the type of nerve/plexus approach, different flow rates and the anaesthetist injecting the local anaesthetic discontinuously, with high compartmental pressure peaks can modify the injection pressure values. All these parameters should be taken into account to avoid high injection pressure during PNB procedures.

ACKNOWLEDGEMENTS:

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References

1. Sites BD, Taenzer AH, Herrick MD, Gilloon C, Antonakakis J, Richins J, Beach ML. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. Reg Anesth Pain Med 2012; 37:478–82.

2. Widmer B, Lustig S, Scholes CJ, Molloy A, Leo SPM, Coolican MRJ, Parker DA. Incidence and severity of complications due to femoral nerve blocks performed for knee surgery. Knee 2013; 20:181–5.

3. Brull R, Hadzic A, Reina MA, Barrington MJ. pathophysiology and etiology of nerve injury following peripheral nerve blockade. Reg Anesth Pain Med 2015; 40:479–90.

4. Liu SS, YaDeau JT, Shaw PM, Wilfred S, Shetty T, Gordon M. Incidence of unintentional intraneural injection and postoperative neurological complications with ultrasound-guided interscalene and supraclavicular nerve blocks: incidence of unintentional intraneural injection. Anaesthesia 2011; 66:168–74.

5. Hara K, Sakura S, Yokokawa N, Tadenuma S. Incidence and effects of unintentional intraneural injection during ultrasound-guided subgluteal sciatic nerve block. Reg Anesth Pain Med 2012; 37:289–93.

6. Sites B, Spence B, Gallagher J, Wiley C, Bertrand M, Blike G. characterizing novice behavior associated with learning ultrasound-guided peripheral regional anesthesia. Reg Anesth Pain Med 2007; 32:107–15.

7. Cappelleri G, Ambrosoli AL, Gemma M, Cedrati VLE, Bizzarri F, Danelli GF. Intraneural ultrasound-guided sciatic nerve block: minimum effective volume and electrophysiologic effects. Anesthesiology 2018; 129:241–8.

8. Vlassakov K, Lirk P, Rathmell JP. Intraneural injection: is the jury still out? Anesthesiology 2018; 129:221–4.

9. Lupu CM, Kiehl T-R, Chan VWS, El-Beheiry H, Madden M, Brull R. Nerve expansion seen on ultrasound predicts histologic but not functional nerve injury after intraneural injection in pigs. Reg Anesth Pain Med 2010;35:132–9.

10. Hadzic A, Dilberovic F, Shah S, Kulenovic A, Kapur E, Zaciragic A, Cosovic E, Vuckovic I, Divanovic KA, Mornjakovic Z, Thys DM, Santos AC. Combination of intraneural injection and high injection pressure leads to fascicular injury and neurologic deficits in dogs. Reg Anesth Pain Med 2004; 29:417–23.

11. Rydevik B, Lundborg G, Bagge U. Effects of graded compression on intraneural blood blow. An in vivo study on rabbit tibial nerve. J Hand Surg Am 1981; 6:3–12.

12. Lundborg G, Myers R, Powell H. Nerve compression injury and increased endoneurial fluid pressure: a "miniature compartment syndrome". J Neurol Neurosurg Psychiatry 1983; 46:1119–24.

13. Theron PS, Mackay Z, Gonzalez JG, Donaldson N, Blanco R. An animal model of “syringe feel” during peripheral nerve block. Reg Anesth Pain Med 2009; 34:330–2.

14. Gadsden J, McCally C, Hadzic A. Monitoring during peripheral nerve blockade. Curr Opin Anaesth 2010; 23:656–61.

15. Patil J, Ankireddy H, Wilkes A, Williams D, Lim M. An improvised pressure gauge for regional nerve blockade/anesthesia injections: an initial study. J Clin Monit Comput 2015; 29:673–9.

16. Ross S, Edwards K, MacFadden K, Bigeleisein PE, Orebaugh SL. Pressures of injection in a cadaver model of peripheral nerve blockade. J Anesth Clin Res 2014; 5:445.

17. Gadsden JC, Choi JJ, Lin E, Robinson A. Opening injection pressure consistently detects needle–nerve contact during ultrasound-guided interscalene brachial plexus block. Anesthesiology 2014;120:1246–53.

18. Patil JJ, Ford S, Egeler C, Williams DJ. The effect of needle dimensions and infusion rates on injection pressures in regional anaesthesia needles: a bench-top study. Anaesthesia 2015; 70:183–9.

19. Gadsden J, Latmore M, Levine DM, Robinson A. High opening injection pressure is associated with needle-nerve and needle-fascia contact during femoral nerve block. Reg Anesth Pain Med 2016; 41:50–5.

20. Vermeylen K, Hermans M, Soetens F, Vereecke E, Steinfeldt T, Groen G, Hadzic A, Van de Velde M. Opening injection pressure is higher in intraneural compared with perineural injections during simulated nerve blocks of the lower limb in fresh human cadavers. Reg Anesth Pain Med 2017; 42:362–7.

21. Gadsden J. Current devices used for the monitoring of injection pressure during peripheral nerve blocks. Expert Rev Med Devices 2018; 15:571–8.

22. Gao Y, Weng C, Wang X. Changes in nerve microcirculation following peripheral nerve compression. Neural Regen Res 2013; 8:1041–7.

23. Ilvana Hasanbegović, Eldan Kapur, Lejla Dervišević, Amela Džubur-Alić, Alen Džubur. Intrafascicular application of Lidocaine 2% or 0.9% NaCl into median nerve of the rat. Folia Med 2016; 51:55–61.

24. Moayeri N, Bigeleisen PE, Groen GJ. Quantitative architecture of the brachial plexus and surrounding compartments, and their possible significance for plexus blocks. Anesthesiology 2008; 108:299–304.

25. Moayeri N, Groen GJ. Differences in quantitative architecture of sciatic nerve may explain differences in potential vulnerability to nerve injury, onset time, and minimum effective anesthetic volume. Anesthesiology 2009; 111:1128–34.

26. Saporito A, Quadri C, Kloth N, Capdevila X. The effect of rate of injection on injection pressure profiles measured using in-line and needle-tip sensors: an in-vitro study. Anaesthesia 2018; doi:10.1111/anae.14415.

27. Neal JM, Barrington MJ, Brull R, Hadzic A, Hebl JR, Horlocker TT, Huntoon MA, Kopp SL, Rathmell JP, Watson JC. The Second ASRA Practice Advisory on neurologic complications associated with regional anesthesia and pain medicine: executive summary 2015. Reg Anesth Pain Med 2015; 40:401–30.

28. Claudio R, Hadzic A, Shih H, Vloka JD, Castro J, Koscielniak-Nielsen Z, Thys DM, Santos AC. Injection pressures by anesthesiologists during simulated peripheral nerve block. Reg Anesth Pain Med 2004; 29:201–5.

29. Gadsden J. Injection pressure monitoring: no more excuses. J Clin Monit Comput 2015; 29:671–2.

Figure Legends

Fig. 1. (A) Injection pressure values according to needle diameter. The diameter influences the injection pressure values. (B) Injection pressure values according to needle diameter for different brands. For the same gauge and the same length, Pajunk needles promoted a significantly decreased injection pressure compared with B. Braun, Temena and Vygon needles. (C) Injection pressure values according to needle echogenicity. The use of non-echogenic needles significantly increased the injection pressure values compared with echogenic needles, apart from Pajunk needles.

Fig. 2. (A) Plateau injection pressure at 9.6 mL/min in all perineural and intraneural locations studied and (B) intraneural plateau injection pressures related to different constant injection flows. For all nerve or plexus locations studied, there was a statistically significant difference when the needle tip was located in an intraneural location compared with an extraneural location ($P < 0.05$). In an intraneural location, increase in injection flow significantly increased the plateau pressure in all nerves studied ($P < 0.05$) apart from flows of 4.8 mL/min and 9.6 mL/min in C6 and C7 roots.

Fig. 3. Graphs from the Compuflo® device highlighting manual injection peaks in pressure above 750 mmHg during an axillary block procedure.

Fig 1, Panel A

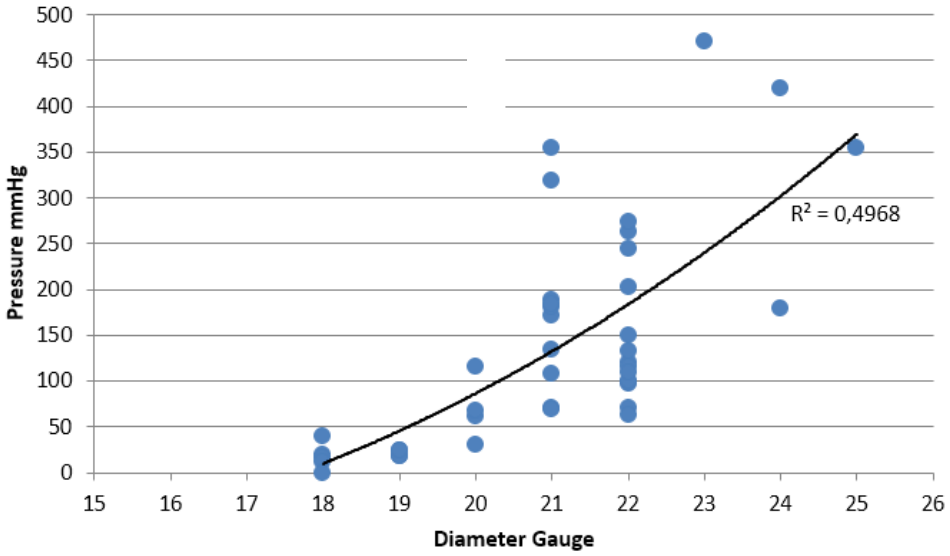

Fig 1, Panel B

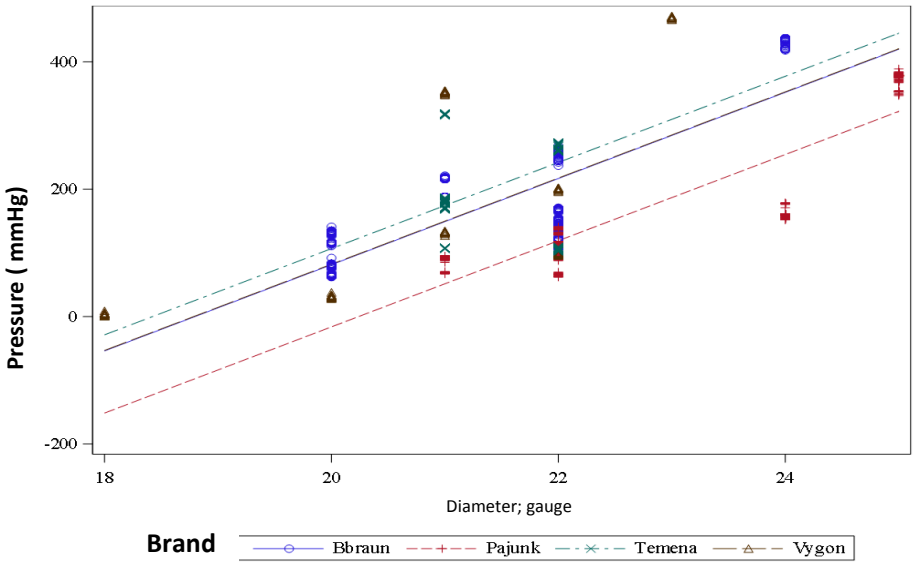

Fig 1, Panel C

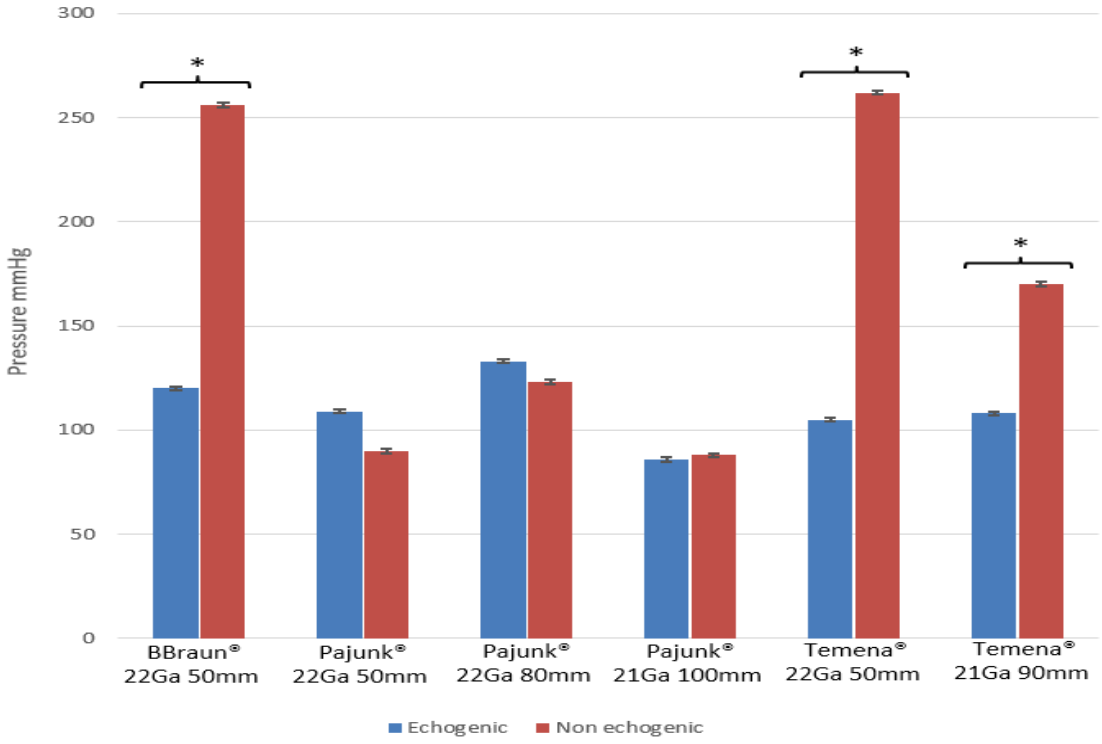
300
250
200
150
100
50
0
Pressure mmHg
*
*
*
BBraun®
22Ga 50mm
Pajunk®
22Ga 50mm
Pajunk®
22Ga 80mm
Pajunk®
21Ga 100mm
Temena®
22Ga 50mm
Temena®
21Ga 90mm
Echogenic
Non echogenic

Fig 2, Panel A

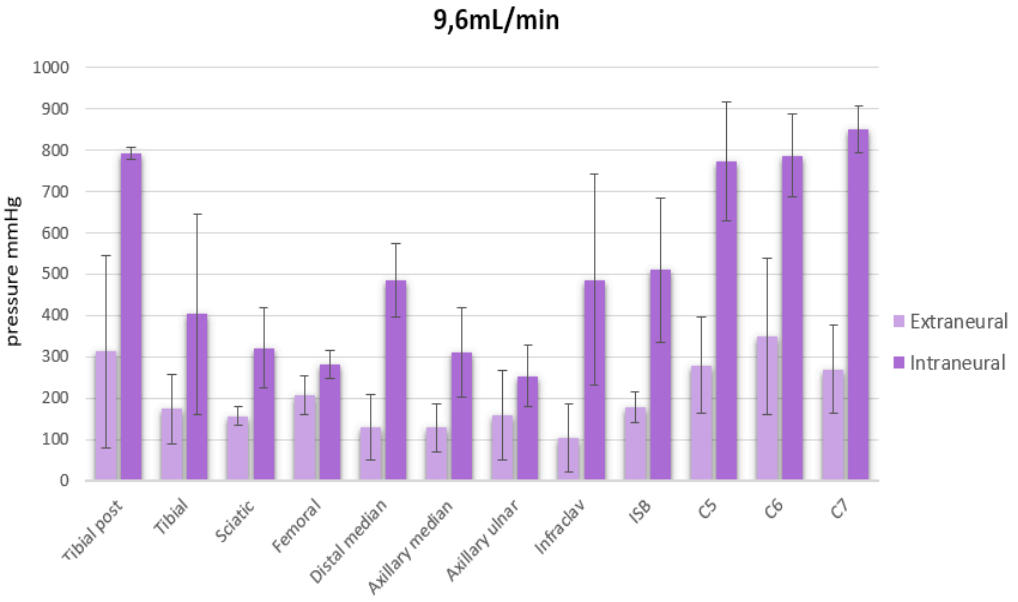

Fig 2, Panel B

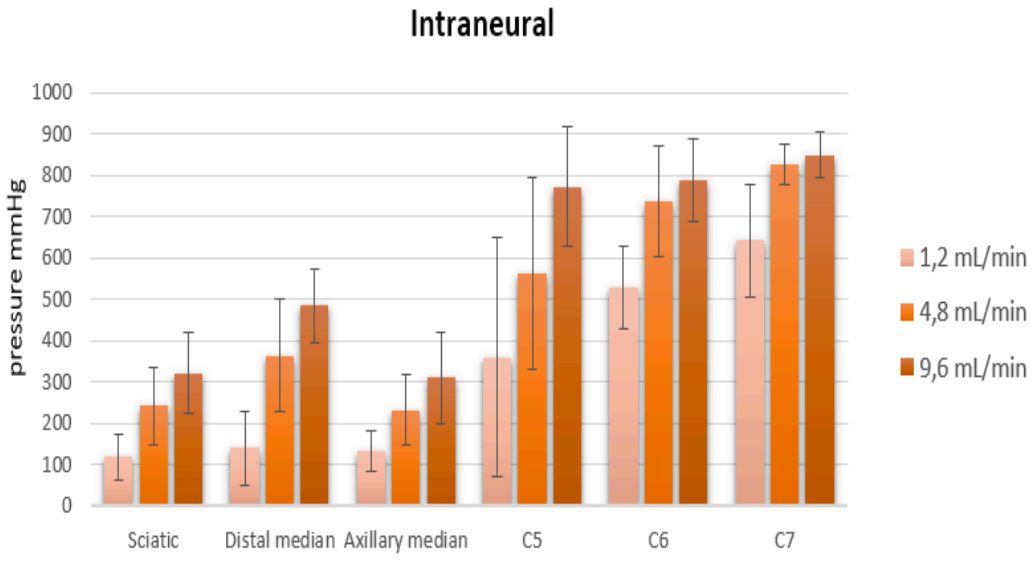

Fig 3

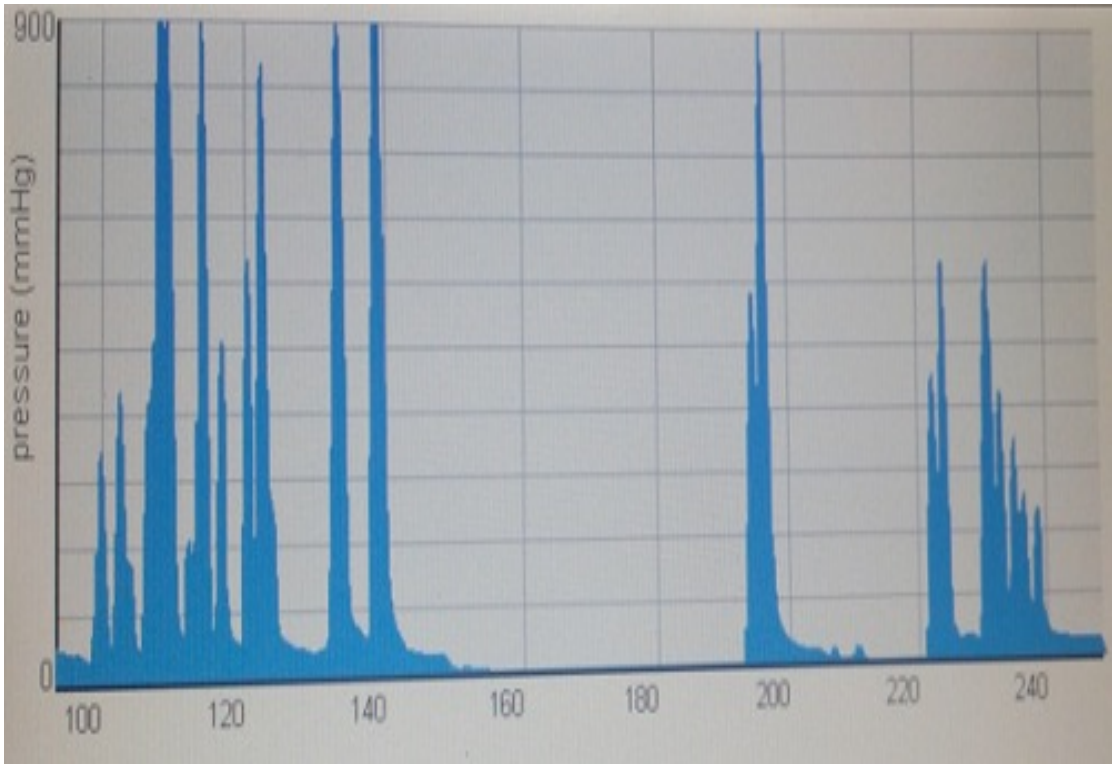

Table 1. Injection Pressure values in ambient air for a flow of normal saline delivered at a rate of 10 mL/min with a 20-mL syringe: 25 needles of different brands, diameter and gauge are reported

Needle Brand and Type		Injection Pressure in Ambient Air (mmHg) mean [IC95%]					
		Specific Echogenic Needle		Non-echogenic Needle			
Bbraun®		Stimuplex Ultra	Ultraplex	Stimuplex A			
	22Ga 50mm	132,3 [131,1-133,6]	108,9 [108,3-108,96]	255,7 [254,1-257,2]			
	22Ga 80mm	162,6 [160,9-164,4]	141,6 [141,1-142,1]				
	21Ga 100mm			209 [207,2-212,4]			
	20Ga 100mm	76,2 [75,2-77,1]					
Pajunk®		Sonoplex	SonoTAP	Uniplex			
	22Ga 50mm	108,8 [108,1-109,7]		90,9 [89,1-92,8]			
	22Ga 80mm	137,3 [136,8-137,8]	110 [107,8-112,2]	123,8 [121,8-125,9]			
	21Ga 100mm	85,8 [82,1-89,6]		87,6 [86,3-88,9]			
Vygon®		Visioplex		Echoplex	Silverstim	Locoplex	
	22Ga 50mm			200,1 [198,7-201,4]			
	22Ga 85mm	98,7 [98,2-99,3]					
	21Ga 85mm			132,4 [131,3-133,4]			
	21Ga 100mm					352,4 [351,1-353,6]	
	20Ga 100mm				30,8 [30,3-31,3]		
Temena®		USB Evolution		UPB		Hybrid needle	
	22Ga 50mm	105,5 [104,7-106,2]		261,6 [261,2-262]			
	22Ga 55mm					271,7 [271,1-272,3]	
	21Ga 90mm	107,7 [107,5-108]		170,3 [169,9-170,6]			
	21Ga 95mm					179,3 [178,8-179,7]	

	Univariate Analysis			Multivariate Analysis		
	estimate	CI (95%]	P	estimate	CI (95%]	P
BENCH STUDY (N=2183)						
Diameter	51.5	1.1	<0.0001	66.79	13.26	<0.0001
Lenght (ref = lenght ≤50)						
]50-100[	-81	[-91;-71]	<0.0001	10.5	[-48.5;69.5]	0.7
≥100	-101.6	[-110.7;-92.6]	<0.0001	56.6	[-12;125.3]	0.1
Brand (reference =Vygon)						
Bbraun	52.9	[35.2;70.5]	<0.0001	-22.5	[-89.7;44.6]	0.5
Pajunk	36.5	[19;54.1]	<0.0001	-127.1	[-195.4;-58.8]	<0.001
Temena	76.9	[56.5;97.4]	<0.0001	-3.7	[-67;59.6]	0.9
Echogenicity (in reference)						
Non echogenic needle	89.6	[81.5;97.7]	<0.0001	71.5	[22.9;120.1]	0.004
CADAVER STUDY (N=353)						
Nerve (reference = femoral)						
Sciatic nerve	47	164.46	0.9	11.6	[-44.9;68.5]	0.7
Tibial nerve	142.4	260.11	0.6	17.3	[-51;86]	0.6
Common peroneal nerve	-64.9	[-174.9;45]	0.2	-46.8	[-120;26.8]	0.2
Ulnar nerve	-93.8	[-476.2;288.6]	0.6	48.	[-205.5;308.5]	0.7
Median distal	14.5	[-86;114.9]	0.8	56.2	[-10.2;123.1]	0.09
Tibial nerve	268	[163.5;372.5]	<0.0001	252.7	[183.2;321.7]	<.0001
C5	227.3	[122.9;331.9]	<0.0001	212.1	[142.6;281.1]	<.0001
C6	300.8	[196.3;405.3]	<0.0001	285.5	[216.1;354.5]	<.0001
C7	326.8	[222.3;431.5]	<0.0001	311.6	[242.1;380.6]	<.0001
Interscalene block	101.1	[-3.4;205.7]	0.06	85.8854	[16.4;154.8]	0.01
Infraclavicular block	68.3	[-36.3;172.8]	0.2	53.01	[-16.5;122]	0.1
Median nerve axillary app	3.3	[-105.2;111.8]	0.9	8.5	[-63.7;81]	0.8
Ulnar nerve axillary app	-6.1	[-110.6;98.5]	0.9	10.75	[-58.9;79.8]	0.8
Inj Flow (ref=1.2 ml/min)						
4.8 ml/ min	126.5	[73.8;179.1]	<0.0001	105.74	[47;164.5]	<0.001
9.6 ml/min	220.7	[167.7;273.]	<0.0001	201.24	[142.4;260.1]	<.0001
Tip location (reference Ext N)						
Int N	228.8	[269.6;179.1]	<0.0001	228.93	[180.3;277.5]	<0.0001
CLINICAL STUDY (N=103)						
Physician grade (ref resident)						
Senior Physician	22.7	[-148;193.5]	0.8			
Nerve (reference = femoral)						
Musculocutaneous nerve	-359.2	[-573.9;-144.5]	0.001	-354.9	[-558.3;-151.4]	<0.001
Radial nerve axillary app	-26.2	[-229.4;177]	0.8	-33	[-225.7;159.5]	0.7
Ulnar nerve axillary app	-163.4	[-366.5;39.9]	0.1	-170.3	[-362.9;22.4]	0.08
Median nerve axillary app	54.2	[-197.2;305.6]	0.7	98.7	[-140.9;338.4]	0.4
Sciatic nerve	3.2	[-229.3;235.8]	0.9	51.3	[-170.8;273.4]	0.6
Obturator nerve	18.5	[-232.9;269.9]	0.9	63	[-176.64;302.4]	0.6
LFC nerve	373	[-34.4;780.3]	0.07	433.6	[46;821.2]	0.02
Interscalene block	89.3	[-162.1;340.7]	0.5	37.4	[-202.8;277.6]	0.7
Cervical plexus block	84.1	[-259.4;427.6]	0.6	32.2	[-294.7;359.1]	0.8
Supraclavicular block	5.5	[-276.8;287.7]	0.9	-46.5	[-315.6;222.6]	0.7
Infraclavicular block	46.7	[-235.5;328.9]	0.7	-5.3	[-274.4;263.8]	0.9
Median nerve forearm	-323.5	[-730.9;83.8]	0.1	-375.5	[-762.64;11.7]	0.05
Posterior TAP block	155.5	[-401;712]	0.6	103.5	[-424.7;631.7]	0.7

Table 2. Parameters that have an Impact on Injection Pressure Values and Measurements during the Three-Way Study

N= Number of Injection Pressure evaluations; App : approach ; Ref : reference ; LFC : Lateral Femoral Cutaneous nerve of the thigh. The regression coefficients for modelling pressure measurements: significant associations between covariates and pressure value $P<0.05$; positive estimates: increased value of pressure; negative estimates: decreased value of p