Research Protocol

**Scientific Title:** Distribution pattern and area of sensory overlap of the posterior antebrachial, medial antebrachial and lateral antebrachial cutaneous nerves of the forearm detected by ultrasound guided local anaesthetic nerve block in volunteers.

**Simplified Title:** Sensory innervation of the forearm detected by ultrasound-guided local anaesthetic block

**Investigators:** Dr Philip Corke (Chief Investigator), Senior Staff Specialist Anaesthetist and Director of Acute Pain, Concord Repatriation General Hospital and Dr James Chan Hee Kim (Co-investigator), Resident Medical Officer, Concord Repatriation General Hospital.

**Aim:** The primary aim of this study is to map the sensory distribution pattern and area of sensory overlap of the posterior antebrachial, medial antebrachial and lateral antebrachial cutaneous nerves (PABCN, MABCN, LABCN) of the forearm following an ultrasound-guided local anaesthetic block. The secondary aim is to map any sensory block that occurs in the hand.

**Hypothesis:** The hypothesis is that there is a high degree of individual variability in the sensory-distribution pattern and overlap in the innervation of the forearm from the PABCN, MABCN and LABCNs. The PABCN, MABCN and LABCN may provide a variable degree of sensory cutaneous innervation to the hand.

**Background:** The skin and subcutaneous tissues of the forearm receive their innervation from three nerves: the medial, lateral and posterior antebrachial cutaneous nerves of the forearm. The sensory distribution pattern of the cutaneous nerves of the forearm is primarily based on historical cadaver dissection studies. Standard anatomical texts depict these distribution patterns as discrete homogenous areas covering the lateral, medial and posterior aspects of the forearm with no overlap between individual nerves. The hand is depicted as receiving its innervation from branches of the median (MN), ulna (UN) and superficial radial nerve (SRN) with no contribution from the forearm antebrachial nerves (1-2). Recent studies using local anaesthetic nerve block techniques have demonstrated a greater variability in the sensory distribution pattern of cutaneous nerves than classically described. Keplinger *et al* (3) reported that large areas of the hand were not innervated as expected by the MN, UN, SRNs. Variant innervation in the hand may be derived from the LABCN and PABCN (4-6). In the lower limb, Riegler *et al* found variability and overlap of the anterior femoral cutaneous nerves and the infrapatellar branch of the saphenous nerve (7).

 Iatrogenic injury to the cutaneous nerves of the forearm may result from phlebotomy, steroid injection and elbow surgery (8-10). These nerves may also be injured by trauma, inflammation, compression and infection (11-12). Neuropathic pain in the forearm commonly occurs after these injuries. Current anatomical descriptions of the cutaneous sensory nerve distribution of the forearm have well defined boundaries (1-2). Variations in cutaneous nerve distribution have been reported but these are rarely reported in standard textbooks (4-7). Reliance on the “standard anatomical” model of cutaneous innervation may result in incorrect diagnosis, inappropriate investigation and interventions (13).

This study is designed to precisely map the distribution pattern, area of sensory overlap and any proximal extension into the hand of the three antebrachial cutaneous nerves of the forearm. The distribution pattern, area of sensory overlap and any proximal extension has not been previously reported. The PABCN, MABCN and LABCN will be located with ultrasound and separately blocked with local anaesthetic (lignocaine 2%). Lignocaine 2% is commonly used for subcutaneous anaesthesia prior to venous cannulation. It will be sourced from the supply in the operating theatres at CRGH. The manufacturer of lignocaine 2% does not have any interests in the study, will not be providing the drug or receive any data from the study. An up to date Australian Register of Therapeutic Goods (ARTG) certificate will be provided for lignocaine 2%. This information will be provided in the PISCF.

The total cutaneous sensory block area (CSBA) for each individual nerve will be mapped by testing for loss of sharpness sensation. Overlapping areas of innervation in the forearm and hand will be reported as a percentage of the total CSBA. Areas of the forearm that remain unblocked will be reported as a percentage of the total CSBA. Information from the study will be helpful to anaesthetists who use regional anaesthetic techniques to provide analgesia for surgery of the forearm and hand. It may help explain why some local anaesthetic cutaneous nerve blocks fail to provide the predicted area of analgesia. It will benefit pain physicians investigating the cause of symptoms of injury to the cutaneous nerves of the forearm and ensure proper local anaesthetic deposition is used for treatment. Forearm flaps are often used by plastic surgeons to repair soft tissue defects especially in sensitive regions such as the hands, mouth and penis (14). Sensory deficits often occur over the skin at the donor site. The results of this study will help with sensory matching when designing forearm flaps for reconstructive surgery (15).

**Research Plan:**

 Study Type Device and drug administration

##  Setting/Location Anaesthetic bay or recovery area within the operating theatre complex of Concord Repatriation General Hospital (CRGH). In order not to impact on patients receiving clinical care these areas will be only be used when normal theatre operating times have concluded (after 1630pm on weekdays)

 Duration of Study: 4 days for ultrasound-guided blockade of the three forearm nerves and follow-up. One month for data analysis.

 Methods

* Recruitment of 12 healthy volunteers. This is a convenience sample which has been used in previous studies of cutaneous nerve block (3,4,6,16).
* All blocks will be performed in the anaesthetic bay or recovery area of the operating theatres at Concord Repatriation General Hospital.
* Monitoring of the ECG (electrocardiography), non-invasive blood pressure, pulse oximetry and resuscitation equipment will be available in the anaesthetic bay if needed.
* This equipment is readily available in the anaesthetic bays and recovery area of the operating theatres.
* The current Covid-19 pandemic will not impact on the study.
* No funding has been received for the study.
* Volunteers will be in supine position. The right side will be used in all participants to maintain consistency
* The medial and lateral epicondyles will be identified at the elbow. A marker pen will be used to draw a line circumferentially around the forearm between each epicondyle. This line (the intercondylar line) will define the proximal border of the forearm.
* The radial and ulna styloid will be identified at the wrist. A marker pen will be used to draw a line circumferentially around the wrist between each styloid. This line (the inter-styloid line) will define the distal border of the forearm.
* Sensory loss distal to the inter-styloid line will be considered anatomically to be within the hand region.
* Scanning of neural structures in the upper limb will be performed with a 15- to 6-MHz linear ultrasound probe and a transportable ultrasound machine (Sonosite, X-Porte).
* A Sonosite, X-Porte ultrasound machine is available in the operating theatre complex of CRGH. It is owned by the hospital. The company (Sonosite) have no interest in the study.
* The ultrasound probe and its cable will be covered with a sterile disposable sleeve.
* The LABCN, MABCN and PABCN will be located with ultrasound in accordance with previously described techniques (4,6,14).
* An individual nerve will be randomly blocked on three successive days.
* Volunteers will come from medical and nursing staff who are employed at the hospital on the three days of the study.
* There will be no reimbursement for participation in the study
* The site of injection will be disinfected with a wipe containing 70% isopropyl alcohol and 2% chlorhexidine digluconate (SoluPrep Antiseptic Wipe, 3M).
* An insulin syringe (BD-Ultra-fine) will be used to deliver a subcutaneous injection of 0.3-0.5mL 2% lignocaine prior to insertion of a 22G x 50mm echogenic needle (SonoPlex STIM, Pajunk)
* The target nerve will then be blocked by injecting 1ml 2% lignocaine (20mg) to achieve circumferential spread of the local anaesthetic around the nerve
* Sensation to light touch and sharpness will be assessed 15 minutes later using a commercially available tool widely used for testing peripheral neuropathy in diabetic patients (Neuropen, Owen Mumford).
* This device (Neuropen) has been purchased by the principle investigator (Dr P Corke)
* The unblocked forearm will be tested first to ensure the volunteer understands what sensation to expect.
* Volunteers will be asked to state “Sharp” or “Not Sharp” when the monofilament is pressed onto the skin.
* Volunteers will be asked not to look at the monofilament when it is pressed on the skin to avoid bias.
* Testing of the blocked forearm will start in an area of normal sensation and repeated in approximately 1cm incremental movements until loss of sensation (“Not Sharp”) is reported.
* The blocked area will be outlined on the skin with a surgical marker pen and traced on to a paper transparency.
* A photograph will be taken of the blocked area.
* The same paper transparency will be used to trace each individual nerve using the intercondylar and inter-styloid line as anchor points.
* The total CSBA (cm2) for each individual nerve will then be calculated from photographs of the transparency using the software SketchAndCalc.
* The software SketchAndCalc will only be used for measurement. Data will be stored within RedCaps.
* Areas of sensory overlap between two nerves will be reported as a percentage of the total CSBA for each individual nerve using the software SketchAndCalc.
* Area of sensory block in the hand will be reported as a percentage for each individual nerve using the software SketchAndCalc.
* Areas of the forearm that remain unblocked will be reported as a percentage of the total CSBA for all nerves.
* If no area of sensory block can be elicited within 15 minutes this will be recorded as a failed block.
* Block failure will be managed by repeating the block 15 minutes later as previously described.
* A repeated block will occur once only.
* If a repeat block fails, this will be managed by recruitment of another volunteer.
* This may result in an increase in the anticipated number of volunteers recruited.
* On day 3 the CSBA for each individual nerve will be drawn on the volunteer’s skin using a coloured marker pen.
* Each nerve will be identified by a different colour (red, green and blue)
* Areas of sensory overlap will be marked on the skin using a hatched pattern.
* Photographs will be taken.
* Any volunteers with tattoos, scars, birthmarks or moles in the area that is photographed are excluded from the study to prevent inadvertent identification.
* Photographs of the CSBA showing individual variability, sensory overlap and any extension to the hand and will be used in any future publication.
* All drugs and devices including 2% lignocaine and the Neuropen will be used according to their listed and approved indication on the Australian Register of Therapeutic Goods (ARTG). A copy of the certificate will be provided.
* All interventions will be done by Dr Philip J Corke, Senior Staff Specialist Anaesthetist who has 20 years experience in regional anaesthesia
* Volunteers will only be recruited to the study if they are going to be at CRGH on four consecutive days.
* All volunteers will be reviewed the following day to assess the skin for signs of local infection and to assess for any residual sensory changes.

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| Study Population | Healthy volunteers, male and female aged 18-65, BMI 18-35 kg/m2.  |
| Recruitment | Medical and nursing staff from CRGH will be invited to participate in the study via posters distributed throughout the operating theatres and doctor’s common room. The use of a poster will exclude the potential for coercion or pressure to participate in the study and acknowledges the HREC National Statement Section 2.2.9 on voluntary participation in research. |
| Number of volunteers | A convenience sample of 12 volunteers. This number is based on previous studies assessing sensory block in volunteers (3,4,6). Block failure will be managed by recruitment of another volunteer. This would increase the number of volunteers. |
| Key Inclusion Criteria | Healthy volunteers, male and female aged 18-65, BMI 18-35 kg/m2. |
| Key Exclusion Criteria | Known allergy to local anaesthetic drugs (direct questioning of volunteer); injury, deformity or previous surgery to the right arm or cutaneous nerves of the forearm; pain or pre-exiting neurological deficit of the right arm; identifying features on the arm such as tattoos, moles, scars or birthmarks. |
| Study Intervention | Mapping the area of cutaneous sensory loss following ultrasound-guided nerve block of posterior, lateral and medial cutaneous nerves of the forearm. |
| Control Group | There will be no control group |
| Randomization | Each volunteer will have a random nerve blocked on each day |
| Follow-up | Volunteers will be followed up the day following each nerve block and assessed for residual sensation or motor deficit, bruising and infection |
| Endpoints/Outcome MeasurementsPrimary endpointsSecondary endpointsConfounders | The main aim and secondary aim are outlined previously. |
| Statistical Considerations/Data analysis | We will be using a sample size of 12. This is consistent with prior studies which have explored cutaneous innervation and sensation in the hand and forearm. Gender, age and body mass index (BMI) of volunteers will be reported. These variables ensure that the volunteers are representative of the study population. The total cutaneous sensory block area (CSBA) for each individual nerve will be mapped. Overlapping areas of innervation in the forearm and hand will be reported as a percentage of the total CSBA. Areas of the forearm that remain unblocked will be reported as a percentage of the total CSBA. Any failed block will be reported. The area of sensory cutaneous loss and overlap will be depicted in diagrams and photographs. Any adverse events will be documented and reported. Statistical data will be reported as median and range |
| Ethical Considerations | A poster will be used to invite volunteers to participate in the study Written consent will be obtained for each participant. Each participant is able to withdraw from the study at any time. Verbal withdrawal is sufficient. Any data collected prior to withdrawal will not be used.  |
| Safety Considerations | All blocks will be performed in the anaesthetic bay or recovery area of the operating theatres at CRGH by Dr Philip Corke. Monitoring (ECG, NIBP, pulse oximetry) and resuscitation equipment will be available if needed. Adverse events to be monitored and documented. Bruising and local discomfort will be managed with simple analgesic medications. Any severe adverse events will be escalated to the chief investigator immediately for assessment and treatment pathways. Neuropathic pain will be referred to a pain physician for ongoing management. |
| Investigator obligations | Research data collected will be deidentified/coded and stored securely on a hospital computer, password protected, backed up to the hospital server and accessed by hospital staff only. Data will be stored for at least 5 years since the date of last publication as per NHMRC Guidelines. Safe storage of data on secure applications i.e. Research Electronic Data Capture (RedCap). Stored data will be in a re-identifiable format for auditing and monitoring purposes |
| Funding | N/A |
| Conflict of Interest | The investigators have a vested interest in the results of the study. |

**Outcomes and Significance:**

The primary aim of this study is to map the sensory distribution pattern and area of sensory overlap of the posterior antebrachial, medial antebrachial and lateral antebrachial cutaneous nerves (PABCN, MABCN, LABCN) of the forearm following an ultrasound-guided local anaesthetic block. The secondary aim is to map any sensory block that occurs in the hand.

Results from the study will enhance our current understanding of the variability of cutaneous sensory innervation. It may clarify why some local anaesthetic nerve blocks do not produce the expected area of cutaneous sensory anaesthesia. It will benefit pain physicians when investigating and managing the cause of symptoms of injury to the cutaneous nerves of the forearm. Forearm flaps are often used by plastic surgeons to repair soft tissue defects. Sensory deficits often occur over the skin at the donor site. The results of this study will help with sensory matching when designing forearm flaps for reconstructive surgery (15).

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