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Ultrasound-Guided Continuous Brachial Plexus Block for Ambulatory Analgesia after Shoulder Surgery

Part II

Michael John Fredrickson

A thesis submitted in fulfilment of the requirements for the degree of
Doctor of Philosophy,
The University of Auckland, 2013
Abstract

Systematic literature review of the regional anaesthetic techniques used for analgesia following shoulder surgery concluded continuous interscalene block as the most effective analgesic technique for shoulder surgery, while subacromial local anaesthetic infiltration performed only marginally better than placebo. The review also identified knowledge deficiencies in continuous interscalene block pharmacology, and unresolved technical issues around interscalene catheter placement. Thus, six interventional studies on 798 patients receiving ultrasound-guided continuous brachial plexus block were conducted. A dose-finding study determined the optimal primary local anaesthetic bolus to prevent recovery room pain and minimise motor block, which was subsequently validated with a randomised trial. The impact of mandatory local anaesthetic boluses relative to a background infusion, the anterolateral and posterior interscalene catheter placement approaches and the effect of catheter threading distance and catheter orifice configuration were studied.

To prevent recovery room pain, the ropivacaine 0.5% ED(volume)\textsubscript{95} (95% CI) estimate was 20.5 mL (17.3-25.8). The ropivacaine 20 mL ED(concentration)\textsubscript{95} (95% CI) estimate was 0.34% (0.29-0.43). Compared to a traditional higher dose, satisfaction was modestly higher for this new/lower dose. Pooled data regression analysis showed that increasing ropivacaine concentration increased grip weakness but not block duration. Both local anaesthetic volume and concentration were found to influence block duration.
Postoperative pain, night awakenings and tramadol consumption were similar in patients receiving mandatory boluses at a lower background infusion rate compared to patients receiving PRN only boluses at a higher infusion rate. However, more patients receiving the higher infusion required a temporary infusion cessation due to side effects (p=0.02).

Compared with interscalene catheters placed via a posterior approach, anterolateral approach interscalene catheters resulted in less pain in the recovery room, reduced tramadol consumption during the first 24 postoperative hours, reduced catheter threading difficulty and reduced catheter placement time.

Patients who received a multi-orifice anterolateral catheter advanced 2.5 and 5 cm beyond needle tip were more frequently pain free in the recovery room compared with patients receiving an end-hole catheter advanced 0.5 cm. During the first 24 hours, the end-hole catheters were associated with an earlier time to first pain, higher “average pain”, and more ropivacaine bolus and tramadol consumption. Groups 2.5 and 5 cm did not significantly differ in any outcomes. Catheter orifice configuration was subsequently shown to not significantly affect the quality of continuous interscalene block. This work conducted in this thesis has further added to our knowledge of, while also improving the effectiveness/side effect balance of ultrasound-guided continuous brachial plexus block for analgesia after shoulder surgery.
Preface

Statement of Work

Acknowledgements

Publications and presentations

Statement of Work

The work in this thesis was conducted at the Southern Cross Brightside and North Harbour Hospitals, Auckland, New Zealand in my capacity as visiting specialist and Honorary Clinical Senior Lecturer, Department of Anaesthesiology, University of Auckland. The work contained in the thesis is exclusively my own, with the exception of the contributions made by my co-investigators, as listed under ‘publications and presentations’.

This thesis has not been accepted in whole or in part for any other degree or diploma.
Acknowledgements

I wish to acknowledge my supervisor, Associate Professor Simon Mitchell who assisted me during the writing of this thesis, our research assistants Margaret Watkin and Linda White, in addition to Lorraine Scott for their help in proof reading and formatting the final document. I would like to acknowledge the contribution made by my co-authors, in particular two of my surgical colleagues, Mr Adam Dalgleish and Mr Craig Ball. Without their support a number of studies would not have been conducted. I would also like to thank the three statisticians who assisted with the statistical analyses: Katherine Smith (M Biostat) from the University of Melbourne, Mathangi Santhakumar (B. Math) from the University of Auckland and Richard White (B. Math [Advanced] Honors) from Harvard University.

Finally, I would like to acknowledge the encouragement and support provided by my wife Andrea.

I would like to acknowledge the following organisations for providing financial support during the course of this work:

1. Auckland Medical Research Foundation
2. I-Flow International*

* This company had no involvement in any aspect of the conceptualisation, design, data collection, analysis or preparation of the work contained in this thesis or of the resulting publications.
Publications and Presentations

The following publications arose from this work (chronologically):

Editorials


Original Articles


The following selected presentations arose from this work:

1. ASRA Spring Meeting 2010, Toronto, Canada (Abstract of Chapter 4)

2. ASA ASM 2010, Melbourne, Australia (Abstract of Chapter 6)

3. ANZCA ASM 2011, Hong Kong, China ‘Free Paper Session’ (Abstract of Chapter 8)
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<tr>
<td>ASA</td>
<td>American Society of Anesthesiologists</td>
</tr>
<tr>
<td>CISB</td>
<td>Continuous Interscalene Block</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CONSORT</td>
<td>Consolidated Standards of Reporting Trials</td>
</tr>
<tr>
<td>ED(vol)</td>
<td>Estimated local anaesthetic volume</td>
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<tr>
<td>ED(conc)</td>
<td>Estimated local anaesthetic concentration</td>
</tr>
<tr>
<td>ETMAC</td>
<td>End-tidal minimum alveolar concentration</td>
</tr>
<tr>
<td>IA</td>
<td>Intra-articular</td>
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<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>kgf</td>
<td>kilogram-force</td>
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<tr>
<td>mcg</td>
<td>microgram</td>
</tr>
<tr>
<td>mA</td>
<td>milliampere</td>
</tr>
<tr>
<td>MF</td>
<td>The author of this thesis</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>N</td>
<td>Newton</td>
</tr>
<tr>
<td>NRPS</td>
<td>Numerical rating pain score</td>
</tr>
<tr>
<td>NRS</td>
<td>Numerical rating score</td>
</tr>
<tr>
<td>NS</td>
<td>Nerve stimulation</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>Nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>PACU</td>
<td>Post anaesthesia care unit</td>
</tr>
<tr>
<td>PRN</td>
<td>pro re nata (&quot;as needed&quot;)</td>
</tr>
<tr>
<td>SCPB</td>
<td>Superficial cervical plexus block</td>
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<tr>
<td>SBB</td>
<td>Subacromialbursal block</td>
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<td>SSISB</td>
<td>Single shot interscalene block</td>
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<td>SD</td>
<td>Standard deviation</td>
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<tr>
<td>SS</td>
<td>Single shot (single injection)</td>
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<td>US</td>
<td>Ultrasound</td>
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<td>VAS</td>
<td>Visual analogue score</td>
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Part I. Introduction

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Chapter 2  Postoperative analgesia for shoulder surgery
Chapter 1. Objective and plan of research

1.1. Objective

The objective of the work described in this thesis was to further evaluate and advance the technique of ultrasound-guided continuous brachial plexus block for ambulatory analgesia after shoulder surgery. A literature review was undertaken to identify relevant research questions, which were addressed in a series of clinical studies. The work is a continuation of my first thesis, which investigated other procedural aspects of the same treatment (Fredrickson MJ. Ultrasound guided continuous brachial plexus block for ambulatory analgesia after shoulder surgery)^A.

1.2. Plan of research

This work was conducted with the aim of further advancing the postoperative pain management of patients receiving ambulatory continuous brachial plexus blockade after shoulder surgery. A review of the relevant literature was followed by a series of investigative studies. A literature review of the regional anaesthetic techniques used for postoperative analgesia following shoulder surgery had not been previously conducted. This was essential to objectively establish and consolidate the state of knowledge in the literature from which gaps in knowledge might be inferred and future research directions pursued. The plan was to systematically search the literature using specific search criteria, and to systematically grade this evidence using accepted methodology.

Six investigative studies were then conducted. The first study involved determining the optimal primary bolus dose of ropivacaine to administer via an interscalene catheter to prevent recovery room pain and minimise motor block. The second study was designed to validate the dose findings from the first study, and to specifically investigate the role of local anaesthetic volume and concentration on block duration. The third study was directed at the postoperative local anaesthetic infusion: the effect of mandatory local anaesthetic boluses compared with PRN only boluses on the analgesic effectiveness of the technique during the first two postoperative days.

The plan was to then focus the enquiry on procedural aspects of the technique. First was the intended evaluation of the relative merits of the posterior (in-plane) and anterolateral (out-of-plane) approaches to interscalene catheter placement. These two approaches had been in common use for over a decade; both had been advocated as
the approach of choice, but no study had compared the two in a prospective randomised manner. The effect of catheter threading distance on the effectiveness of the technique was then investigated. The investigation raised questions about the influence of catheter orifice configuration. Although catheter orifice configuration had been studied in the setting of epidural analgesia, no studies had investigated the effect of catheter orifice design in the context of continuous peripheral nerve blockade. Therefore, a further study designed to evaluate the effect of catheter orifice configuration was conducted. Finally, in the interests of presenting a balanced view of interscalene catheter techniques, any related complications or unanticipated patient outcomes arising during the conduct of these studies were described and discussed.
Chapter 2. Postoperative analgesia for shoulder surgery: A critical appraisal and review of current techniques

2.1. Shoulder surgery

The last decade has seen a substantial increase in elective shoulder surgery. A recent database review found that in 2006, the incidence of acromioplasty surgeries had increased 250% over the 1996 figure, which compared with only a 78% increase for other ambulatory orthopaedic procedures. The 2006 rate equated to a population incidence of over 100 per 100,000 – a significant burden to any healthcare system. The most commonly performed shoulder surgeries include rotator cuff repair, stabilisation, subacromial decompression (“acromioplasty”) with or without excision of the lateral clavicle and total shoulder joint replacement. Rotator cuff repair and shoulder replacement are often coined “major” shoulder surgery based on the anticipated postoperative pain, while arthroscopic stabilisation and decompressive surgeries are often referred to as “minor” surgery. The late 1990s witnessed an increase in the popularity of minimally invasive arthroscopic techniques for shoulder surgery. By avoiding surgical trauma to the deltoid and pectoral muscles, arthroscopic techniques should theoretically reduce early postoperative pain, however, these benefits are typically only seen after the first few days. Consequently, analgesic requirements during the first 48 hours are often similar to open surgery; following arthroscopic shoulder surgery, one third of patients will report severe pain on the first postoperative day, despite multimodal analgesia.

Shoulder surgery is associated with a level of postoperative pain that may necessitate opioid use for several days. Opioid requirements may be similar to those seen
following gastrectomy or thoracotomy,° 10 and opioid only analgesic techniques for 
shoulder surgery are commonly associated with opioid related adverse effects such as 
nausea and vomiting, pruritis, sleep disturbance and constipation.° ‘Multi-modal’ 
analgesic approaches incorporating paracetamol, non-steroidal anti-inflammatory 
 drugs and tramadol can reduce opioid requirements, however, opioid consumption 
remains significant, particularly after rotator cuff surgery.° 11, 12 Recently, further 
evidence has emerged of the adverse effects of both poorly treated acute 
postoperative pain° 13 and acute postoperative opioid use.° 14 These adverse effects 
include nociception induced central sensitisation and opioid induced secondary 
hyperalgesia. Both mechanisms may be involved in the pathogenesis of persistent 
post-surgical pain.° 13 This highlights the potential value of developing opioid sparing 
regional anaesthetic techniques.

2.2. Anatomy and neural innervation of the shoulder joint° 15

The shoulder comprises three bones: the clavicle, scapula and humerus in addition to 
the associated muscles, ligaments and tendons. The articulations between the bones 
of the shoulder make up the shoulder joints. The glenohumeral joint is the main joint 
of the shoulder, articulating the humerus and scapula, but the acromioclavicular joint 
(between the acromial aspect of the scapula and clavicle) has relevance as it is 
frequently involved in shoulder pathology.

Knowledge of the neural innervation of the shoulder and associated structures is 
essential for successful regional anaesthetic techniques. Specifically, the supply of 
the shoulder structures by multiple nerves presents a significant challenge for 
achieving complete anaesthesia and analgesia. Indeed, a proximal approach to the
brachial plexus is required for surgical anaesthesia or complete analgesia. The shoulder joint is innervated by the 5th, 6th and 7th cervical nerve roots via the suprascapular, axillary, lateral pectoral, subscapular and musculocutaneous nerves. These nerves ultimately supply the ligaments, capsule and synovial membrane as well as the acromioclavicular joint. The glenohumeral joint is innervated predominantly by the suprascapular nerve, and to a lesser extent the axillary (circumflex) and lateral pectoral nerves. The suprascapular nerve provides sensory contributions to 70% of the joint capsule in addition to the subacromial bursa, the acromioclavicular joint and the coracoclavicular ligament. Wide interpatient variability exists in shoulder joint innervation. For example, in some patients the axillary nerve can predominate in its innervation of the shoulder, while the musculocutaneous nerve can predominate in other patients. Like all joints, the nerves follow small vessels into the joint itself.

In addition to the cutaneous axillary nerve terminations of the brachial plexus (C5-7), the skin of the shoulder is innervated by the superficial cervical plexus (C3-4), predominantly via the supraclavicular nerves. The supraclavicular nerves also supply the acromioclavicular joint.

The intercostobrachial nerve derived from the 2nd thoracic nerve root innervates the medial side of the axilla. Thus, a brachial plexus block alone may not cover incisions involving this site.

Analgesia for shoulder surgery thus requires blockade of the 3rd, 4th, 5th, 6th and 7th cervical nerve roots, and if the incision involves the axilla, the 2nd thoracic root.
The course of the cervical phrenic nerve has particular relevance to interscalene analgesia. The phrenic nerve arises from the ventral rami of the 3rd, 4th and 5th cervical nerve roots, passing through the neck and thorax to supply the diaphragm. In the neck it travels deep to the sternomastoid muscle, anterior to the anterior scalene muscle but immediately deep to the prevertebral fascia (the fascia surrounding the scalene muscles). More caudally, the phrenic nerve passes in front of the first part of the subclavian artery. The phrenic nerve is therefore frequently blocked as a result of local anaesthetic injected close to the interscalene brachial plexus (either at the interscalene level or by proximal local anaesthetic spread to the C3-5 nerve roots). 

2.3. Approaches to analgesia after shoulder surgery

2.3.1. Oral and intravenous analgesia

Standard perioperative oral and intravenous analgesia is used following shoulder surgery similar to other surgeries. Paracetamol, NSAIDs and strong opioid (oral and intravenous) all have a place either on their own, or in combination with regional anaesthetic techniques (see below), although it has been suggested that NSAIDs are relatively contraindicated after shoulder surgery because of the potential for delayed soft tissue healing. As previously stated, opioid analgesic techniques on their own (oral or intravenous) are often inadequate for shoulder surgery with a significant proportion of patients reporting moderately severe postoperative pain in the first few days.
2.3.2. Regional anaesthetic techniques

The recognition that shoulder surgery is associated with severe postoperative pain despite oral and intravenous opioid analgesia has led to the search for opioid sparing techniques. These include:

1. Subacromial (bursal) or intra-articular infiltration of local anaesthetic (SBB).
2. Suprascapular with or without axillary (circumflex) nerve block
3. Single injection (‘single shot’) interscalene nerve block (SSISB)
4. Continuous interscalene nerve block (CISB)

As stated for interscalene block, these regional techniques may be performed as either single injection (“single shot”) or continuous techniques. Interscalene block can be performed with nerve stimulator guidance, or as outlined in part one of the theses, through ultrasound guidance (see later section of this Chapter). With respect to ultrasound guided interscalene block, the out-of-plane approach refers to block needle orientation perpendicular to the long axis (or "plane") of the ultrasound beam. Needle tip approximation is through observation of tissue displacement and/or injectate spread. With the in-plane technique, block needle orientation is parallel to the long axis (or "plane") of the ultrasound beam. Short axis imaging refers to orientation of the ultrasound beam perpendicular to the long axis of the nerve. Most ultrasound guided regional anaesthesia is conducted using the short axis approach. Long axis imaging refers to orientation of the ultrasound beam parallel to the long axis of the nerve. These concepts are further elaborated in the discussion section of this Chapter and the preface of Chapter 7. What follows is a short introduction to each regional technique.
2.3.2.1. Subacromial (bursal)/intra-articular infiltration analgesia (SBB)

SBB is usually performed by the surgeon at the end of the surgical procedure just prior to wound closure. The joint space and/or subacromial space is filled with 20-50 mL of local anaesthetic and this may be followed by placement of a catheter. The technique gained popularity during the early part of the current decade, because it was seen as a simple and effective alternative to interscalene analgesia, but without the risks.

2.3.2.2. Suprascapular and/or axillary (circumflex) nerve block

The suprascapular nerve is readily blocked in the suprascapular fossa either with a landmark only technique or with the assistance of a nerve stimulator or ultrasound device. Concomitant blockade of the axillary (circumflex) nerve has been recently used to provide more complete perioperative shoulder joint analgesia. Descriptions of the techniques used to block each nerve can be found in the cited references.

2.3.2.3. Single injection (‘single shot’) interscalene block (SSISB)

SSISB is a widely used regional technique for postoperative analgesia following shoulder surgery. The block is performed at the root/trunk level of the brachial plexus (approx. C6/7 vertebral level, corresponding to the cricoid cartilage level). At this level, the roots/trunks lie wedged between the scalene muscles. The block was traditionally performed by palpation of the sternomastoid muscle and then more
posterior, the groove between the anterior and middle scalene muscles. The interscalene brachial plexus lies between these two muscles. The original description recommended the elicitation of a 'paraesthesia' around the area of the shoulder joint as an end-point for appropriate needle tip placement, but peripheral nerve stimulation became an attractive alternative for correctly identifying appropriate proximity between needle tip and plexus. The most commonly accepted motor responses for correct needle tip position at this level are a deltoid, lateral pectoralis, biceps or triceps response. Further description of the neurostimulation technique can be found in the previous thesis (Part 1).

More recently, ultrasound guidance has increasingly been used to perform this block. Significant variability exists in the position and visibility of the respective nerve roots (1-4 roots/1-3 trunks may be visible). The roots/trunks appear hypoechoic compared to the surrounding scalene muscles. The superficial-most scalene muscle fascia often appears as a “flying seagull sign”: the most superficial root represents the bird’s trunk with the scalene fascia appearing as its wings. The target for local anaesthetic placement is often directly lateral to the two most superficial structures: C5/6 or superior/middle trunks that innervate the shoulder area. The phrenic nerve lies on the surface of the anterior scalene muscle, while the long thoracic and dorsal scapular nerves lie approx. 0.7 cm lateral (posterior) to the C6 root, which itself is approx. 1 cm deep to the skin. Contact with all three nerves is best avoided by use of an "anterolateral" needle approach (see below). SSISB may not provide a sufficient duration of potent analgesia following shoulder surgery and is therefore often combined with either adjuvants or a continuous infusion.
To this end, anaesthesiologists have added multiple adjuvant drugs to local anaesthetic in an attempt to prolong block duration. These include adrenaline, opioid, midazolam, bicarbonate, neostigmine, magnesium and clonidine. Although statistically significant block prolonging effects have been demonstrated, results have been generally disappointing. 38 39-42

Recent studies have shown that when used as a local anaesthetic adjuvant for brachial plexus block, dexamethasone may prolong block duration defined as time to first pain after upper limb surgery, and ultimately improve postoperative analgesia. 43, 44 45 44, 46-48 Postulated dexamethasone mechanisms include a direct effect on c-fiber glucocorticoid receptors, 49 up-regulation of potassium channels, 50,51 disruption to c-fiber lipid membrane equilibrium, 49 or vasoconstriction. However, because systemic dexamethasone also causes dose dependent analgesia,52 a limitation of previous studies is the absence of systemic dexamethasone in controls, thus it is unclear whether the demonstrated increase in time to first pain and improved analgesia reflects a systemically mediated effect. Multiple studies have shown that intravenous dexamethasone at doses ≥ 8mg has an analgesic effect, increasing the time to first analgesic request and reducing postoperative pain and analgesic requirements. 52 Time to first analgesic request is often used as a surrogate indicator for block duration, therefore, it is unclear whether the previously demonstrated prolongation of block duration represents a systemically mediated dexamethasone effect rather than a specific perineural effect.
2.3.2.4. Continuous interscalene block (CISB)

Continuous blocks are achieved by the placement of a catheter in proximity to the target nerves with the subsequent infusion of local anaesthetic. Before the turn of the century, prolonging nerve blockade through the use of continuous techniques was considered challenging because of the limitations of the equipment available at the time and limited understanding of the approaches required for successful catheter placement. Of all the peripheral nerve block techniques, the interscalene approach is possibly the most suited to a continuous technique. This is because of the prolonged severe pain associated with shoulder surgery; the anatomical advantage that a single catheter can block the shoulder joint, and that any resulting motor block is generally well tolerated.

The aim of this review was to systematically search and assess the evidence for effectiveness of the commonly used regional anaesthesia techniques for postoperative analgesia following shoulder surgery. Conclusions about management of postoperative pain after shoulder surgery were drawn based on the present state of the literature. More importantly, a series of relevant research questions were generated, some of which formed the basis for the studies described in this thesis.

2.4. Relative effectiveness of regional anaesthetic techniques

2.4.1. Methods

Two independent investigators (Satish Krishnan, Chao-Yuan Chen) systematically searched the Medline, Embase, Google Scholar and Cochrane Central Register of Controlled Trials databases for relevant articles relating to pain, regional anaesthetic
interventions and shoulder surgery published between January 1, 1990 and October 1, 2009. The authors selected keywords for the search: shoulder, rotator cuff repair, acromioplasty, subacromial decompression, intra-articular, suprascapular, interscalene, subacromial and cervical paravertebral. The reference lists of eligible articles were also searched. Only prospective randomised controlled trials that included objective measures of postoperative pain (visual analogue or numerical rating scales) were considered for the assessment of analgesic effectiveness. For trials involving both shoulder and non-shoulder surgery, there had to be a defined shoulder surgery group, which could be analysed independently of the non-shoulder group. Non-English language reports were excluded.

The methodological quality of the selected trials was rated using the scoring system advocated by Jadad et al. 54 The Jadad scoring system is the most commonly used tool for assessing the methodological quality of randomised trials, 55 and as of 2008, the original description had been referenced in over 3000 scientific analyses. The tool is sometimes referred to as the Oxford quality scoring system as it was first described by Columbian physician, Alejandro Jadad-Bechara while working at the Oxford Pain Relief Unit, a division of the Nuffield Department of Anaesthesia of Oxford University. The initial impetus for development of the tool was based on recognition of the importance of the randomised controlled trial in advancing medical science. The scale was originally described in the appendix to the seminal publication, rating trials on a scale of one to five, with one being of low quality and five being the highest quality. 54

The scale incorporates the quality of randomisation, blinding, and handling of subject withdrawals and dropouts. These factors can significantly skew the results of a
randomised trial irrespective of the treatment being tested. For example, subjects who dropped out, but are not accounted for in the analysis can be the cause of significant bias.

The Jadad scale is based on the following assessments, each attracting a score of zero or one: 54

1. Is the study described as randomised?
2. Is the study described as double-blind?
3. Is there a description of withdrawals and dropouts?

Additional points are given if:

1. The randomisation method was appropriate.
2. The blinding method was appropriate.

Points are, however, deducted if:

- The method of randomisation was described, but was inappropriate.
- The method of blinding was described, but was inappropriate.

The combined score is between zero and five. Jadad scores are used to assess the quality of medical research in a particular subject area; to specify a minimum quality for trials to be included in a meta-analysis; or for critical analysis of an individual paper. Criticisms of the scale include it being too simplistic and placing overemphasis on the level of blinding. 56 Critics also claim it is subject to interobserver inconsistency. 56
Each investigator (SK and CYC) independently assessed each trial according to the Jadad score and where disagreement occurred, these were resolved by round table discussion. Authors of the original studies were not contacted as part of the assessment. The studies were stratified according to the block techniques as follows: subacromial bursal/intra-articular block, suprascapular block, interscalene block and within these groups, according to whether these were single injection or catheter based techniques. Catheter techniques were further stratified according to whether they were intermittent bolus or a continuous infusion. In order to enable comparison between studies, pain score data recorded on 0-10 numerical rating pain score scale were converted to a 0-100 scale by simple multiplication, which was uniformly described as the VAS (visual analogue score). Studies were evaluated by assessment of the analgesic effectiveness reported in each individual study (i.e. differences in VAS scores between treatment groups), and in addition, for each block group, the plan was to perform a meta-analysis if that group contained three studies reporting mean (SD) VAS data at comparable time points e.g. 0-24 or 24-48 postoperative hours.

Non-randomised controlled trials were included in this review if they were relevant to the resulting recommendations for each treatment (most commonly complications or safety issues); however, they were not used when assessing the relative effectiveness of each technique.

2.4.2. Results

Thirty-six studies fulfilled the inclusion criteria and all were included regardless of methodological quality (Table 1). For each stratified group, there were at most, two
studies reporting mean (SD) VAS data at specific time points. Therefore, meta-analysis was not conducted.
Table 2.1: Randomised Controlled Trials Evaluating Acute Post-operative Pain According to Regional Anaesthetic Technique

<table>
<thead>
<tr>
<th>Author</th>
<th>Surgical procedures</th>
<th>N</th>
<th>Results</th>
<th>Pain Scores</th>
<th>Jadad score (max=5)</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muittari</td>
<td>Neer acromioplasty +/- RCR</td>
<td>Enrolled=42  SSSBB (bupivacaine)=14  SSSBB (oxycodeone)=14  Control (no block)=14</td>
<td>Pain scores were lowest in the bupivacaine group and highest in the control group, but the differences did not reach statistical significance at any time points. Perioperative opioid consumption was higher in the control group.</td>
<td>VAS mean(SEM) at 6h/24h  Intrabursal bupivacaine 40(40-48)/31(31-35)  Intrabursal oxycodeine 32(25-32)/32(32-42)  Intramuscular oxycodeine 41(35-41)/29(24-29)</td>
<td>4</td>
<td>None reported</td>
</tr>
<tr>
<td>Boss (2004)</td>
<td>RCR Acromioplasty</td>
<td>Enrolled=50  CSBB (bupivacaine)=20  Control (saline)=22  Eliminated=7  Excluded=1</td>
<td>There was no statistically significant difference either in total cumulative morphine consumption or in subjective pain perception between the two groups.</td>
<td>VAS mean (SD) in the first 48 hr (time not specified).  Rest:  CSBB 32 (14)  Control 31 (15)  Movement  CSBB 39 (16)  Control 41 (30)</td>
<td>4</td>
<td>None reported</td>
</tr>
<tr>
<td>Eroglu (2006)</td>
<td>Acromioplasty</td>
<td>Enrolled=48  PCA subacromial ropivacaine=16  PCA subacromial fentanyl=16  PCA IV fentanyl=16</td>
<td>The postoperative pain scores at 2, 4, 6 and 12 h were higher in the Group PCA subacromial fentanyl compared with the other 2 groups. However, the pain scores at the other time points were similar between the three groups. PCA subacromial fentanyl was not as effective as either PCA subacromial ropivacaine or PCA IV fentanyl.</td>
<td>VAS mean(SD) at 12h/24h/48h  PCA subacromial ropivacaine 40 (20)/50 (20)/10 (10)  PCA subacromial fentanyl 20 (10)/40 (10)/10 (10)  PCA IV fentanyl 10 (10)/10 (10)/10 (10)</td>
<td>4</td>
<td>None reported</td>
</tr>
<tr>
<td>Savoie (2000)</td>
<td>ASD</td>
<td>Enrolled=62  CSBB (bupivacaine)=31  Control (saline)=31</td>
<td>There was a statistically significant difference in pain in all parameters tested in the CSBB group as compared with the control group.</td>
<td>VAS (mean-nil SD reported) at 24h/48h  CSBB 32 06  Control 39 49</td>
<td>3</td>
<td>None reported</td>
</tr>
<tr>
<td>Harvey (2004)</td>
<td>ASD Arthroscopic RCR Distal clavicle resection</td>
<td>Enrolled=24  CSBB (ropivacaine)=10  Control (saline)=9  Excluded=5</td>
<td>Subacromial infusions of ropivacaine were associated with an overall significant reduction of 34% in pain scores (46% on day 1 and 22% on day 2). Opioid consumption similar between groups.</td>
<td>VAS at 24h/48h  CSBB/glensohumeral 23/34</td>
<td>5</td>
<td>None reported</td>
</tr>
<tr>
<td>Barber (2002)</td>
<td>Arthroscopic surgery</td>
<td>Enrolled=50  CSBB+/+glensohumeral joint infusions (bupivacaine)=25  Control (saline)=25</td>
<td>Lower pain scores were observed in the CSBB/glensohumeral group at all recorded times throughout the 7 days of data collection.</td>
<td>VAS mean at 24h/48h  CSBB/glensohumeral 23/34</td>
<td>5</td>
<td>None reported</td>
</tr>
<tr>
<td>Author</td>
<td>Surgical procedures</td>
<td>N</td>
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<tr>
<td>Banerjee (2008)</td>
<td>Arthroscopic RCR</td>
<td>Enrolled=60</td>
<td>Marginal difference in pain and opioid consumption between groups.</td>
<td>VAS mean (SD not reported) at 12h/24h/48 h CSBB(2ml group) 20/22/21 CSBB(5ml group) 34/32/26 Control 34/36/12</td>
<td>4</td>
<td>None reported</td>
</tr>
<tr>
<td>Coghlan (2009)</td>
<td>RCR (A) ASD (B)</td>
<td>Enrolled=158</td>
<td>Continuous subacromial ropivacaine infusion resulted in a significant,</td>
<td>VAS mean(SD) 12h/24h CSBB(A)(ropivacaine) 21.2 (10.7)/20.4 (17.4) CSBB(B)(ropivacaine) 16.2 (11.4)/13.4 (11.9) SSSBB (A)(control) 28.2 (17.2)/25.0 (17.2) SSSBB (B)(control) 21.6 (10.8)/15.8 (10.3)</td>
<td>5</td>
<td>Slightly greater proportion of patients with nausea and vomiting in the ropivacaine arm (not significant)</td>
</tr>
<tr>
<td>Axelsson (2003)</td>
<td>ASD</td>
<td>Enrolled=30 (3 groups of 10): 1. Prilocaine preoperatively and ropivacaine infusion postoperatively (PR) 2. Saline+epinephrine preoperatively and ropivacaine infusion postoperatively (SR) 3. Saline+epinephrine preoperatively and saline infusion postoperatively (SS)</td>
<td>Postoperative pain at rest was significantly lower in group PR than in group SS during the first 30 min postoperatively. After 1 h the pain decreased in all three groups, so that from the 4th postoperative hour, the VAS was between 10 and 20 in all groups.</td>
<td>VAS median(IQR) at 12h/24h/48h Rest: PR=5(0-35)/5(0-25)/5(0-20) SR=20(0-35)/5(0-20)/5(0-25) SS=20(0-45)/10(0-25)/15(0-10) Movement: PR=50(0-100)/40(0-70)/40(0-80) SR=50(0-80)/50(0-75)/50(0-90) SS=60(0-85)/60(0-75)/60(0-95)</td>
<td>5</td>
<td>3 patients had a positive isolated culture of coagulase negative staphylococcus. None developed infection</td>
</tr>
<tr>
<td>Bain (2001)</td>
<td>Digitally assisted acromioplasty</td>
<td>Enrolled=40</td>
<td>Shoulder pain was significantly less in the SSISB group on day 1. The difference in pain scores between the block and nonblock groups was not significant beyond day 1.</td>
<td>VAS presumed mean(SD reported) at 24h/48h SSISB 25(30) Control 55/38</td>
<td>1</td>
<td>None reported</td>
</tr>
<tr>
<td>Al-Kawy (1998)</td>
<td>ASD Arthroscopic stabilisation, RCR, capsule shift.</td>
<td>Enrolled=30</td>
<td>VAS scores were significantly less in the SSISB group compared with control at 20 min, 30 min, 60 min and 240 min. Reduced opioid consumption (and side effects) with SSISB.</td>
<td>VAS mean(SD) at 0.5h/1h/2h SSISB 34(29)/25(13)/22(10) Control 68(7)/50(12)/56(12)</td>
<td>4</td>
<td>None reported</td>
</tr>
<tr>
<td>Hadzi (2003)</td>
<td>RCR</td>
<td>Enrolled=55</td>
<td>Moderate/severe pain (VAS 30) was not reported by any of the SSISB patients, whereas 80% of all GA patients requested treatment with analgesics in the PACU. No significant difference between groups in pain scores at 24h, 48h and 72 h</td>
<td>VAS mean/median (SD/IQR) not reported</td>
<td>2</td>
<td>None reported</td>
</tr>
<tr>
<td>Kimura (1994)</td>
<td>Acromioplasty</td>
<td>Enrolled=30</td>
<td>Highly statistical difference in pain scores during the first postoperative day between the two groups in favour of the SSISB group.</td>
<td>VAS mean(SD) at 24h SSISB 18(23) Control 35(28)</td>
<td>2</td>
<td>None reported</td>
</tr>
</tbody>
</table>

Single shot interscalene block vs. Control

<table>
<thead>
<tr>
<th>Author</th>
<th>Surgical procedures</th>
<th>N</th>
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<th>Jadad score (max=5)</th>
<th>Complications</th>
</tr>
</thead>
</table>
| Bain (2001)     | Digitally assisted acromioplasty | Enrolled=40       | Should...
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<th>Jadad score (max=5)</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singelyn (2004)</td>
<td>ASD</td>
<td>120</td>
<td>Groups SSISB and SBB had significantly lower pain scores at rest at 4h compared to SBB and controls. No significant difference was observed between the SBB and control groups.</td>
<td>VAS mean(SD) at 4h/24h: Rest: SSISB 7(14)/16(14), SBB 40(20)/30(24), SSB 19(18)/11(13), Control 34(20)/25(16). Movement: SSISB 1(24)/3(22), SBB 54(23)/81(23), SSB 15(25)/35(19), Control 55(21)/53(19).</td>
<td>2</td>
<td>Postoperative sedation more in control group. Local tenderness (no difference between the 3 block groups), nausea and vomiting (more in the control group).</td>
</tr>
<tr>
<td>Nisar (2008)</td>
<td>ASD +/- Mumford procedure Co-planing</td>
<td>60</td>
<td>No significant differences in pain between the SBB and SSISB groups during the first 12 hours postoperatively, although the values for the SSISB and SBB groups were significantly lower than those in the control group.</td>
<td>Mean VAS at 12h/24h: SSISB 12/8, SBB 15/12, Control 25/15.</td>
<td>3</td>
<td>None reported</td>
</tr>
<tr>
<td>Laurila (2002)</td>
<td>ASD Arthroscopic RCR, stabilization</td>
<td>45</td>
<td>Pain scores during the first 4h at rest and during the first 6h on movement were lower in the SSISB group compared with the SBB and control groups. No statistical difference was found in the pain scores at rest or on movement between the SBB and control groups at any measurement point.</td>
<td>VAS median (IQR) at 6h/8h/20h: Rest: SSISB 10(0-15)/10(0-20)/12(0-20), SBB 10(0-20)/10(0-20)/12(0-20), SBB 20(15-30)/20(15-30)/20(15-30)/20(15-30)/20(15-30), Control 40(10-65)/40(10-50)/30(15-50).</td>
<td>3</td>
<td>Respiratory rate less than 10 (3 patients in control group and one patient in SBB group). The lowest measured oxygen saturation was 89 in the ISB group (two patients), 93 in the SBB group, and 90 in the control group.</td>
</tr>
<tr>
<td>Author</td>
<td>Surgical procedures</td>
<td>N</td>
<td>Results</td>
<td>Pain Scores</td>
<td>Jadad score (max=5)</td>
<td>Complications</td>
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<tr>
<td>Chao (2006)</td>
<td>ASD</td>
<td>Enrolled=41</td>
<td>Single shot interscalene block vs. Continuous subacromial bursal block</td>
<td>No difference in pain, analgesic consumption between groups.</td>
<td>VAS mean(3D) at 24h/48h Daytime: SSISB 43 (19)/47(20) CSBB 58 (27)/64(25) Night SSISB 41(21)/47(25) CSBB 57(27)/58(26)</td>
<td>1</td>
</tr>
<tr>
<td>Klein (2001)</td>
<td>Shoulder arthroscopy</td>
<td>Enrolled=40</td>
<td></td>
<td>The mean VAS scores at rest for SSISB+CSBB group at 12h, 24h and 48h were significantly lower than the SSISB group.</td>
<td>VAS mean(3D) at 12h/24h/48h Rest: SSISB+CSBB 25(30)/29(27)/35(25) SSISB 45(37)/50(29)/30(17) Movement SSISB+CSBB 29(31)/30(29)/20(25) SSISB 48(37)/56(26)/36(19)</td>
<td>5</td>
</tr>
<tr>
<td>Webb (2007)</td>
<td>All shoulder procedures</td>
<td>Enrolled=56</td>
<td>No statistically significant differences were identified between the 2 groups with regard to visual analog scale pain scores.</td>
<td></td>
<td>VAS mean (no SD reported) at 12h/24h/48h SSISB 51/49/47 CSBB 51/49/44</td>
<td>3</td>
</tr>
<tr>
<td>Ciccone (2008)</td>
<td>ASD ± RCR</td>
<td>Enrolled=128</td>
<td></td>
<td>CSBB only group had significantly higher scores than all other groups for the first 2 hours. The percentage of patients who required oral opioid or intravenous pain medication was significantly higher for the CSBB only group than for the other groups.</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Author</th>
<th>Surgical procedures</th>
<th>N</th>
<th>Results</th>
<th>Pain Scores</th>
<th>Jadad score (max=5)</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chao (2006)</td>
<td>ASD</td>
<td>Enrolled=41</td>
<td>Single shot interscalene block vs. Continuous subacromial bursal block</td>
<td>No difference in pain, analgesic consumption between groups.</td>
<td>VAS mean(3D) at 24h/48h Daytime: SSISB 43 (19)/47(20) CSBB 58 (27)/64(25) Night SSISB 41(21)/47(25) CSBB 57(27)/58(26)</td>
<td>1</td>
</tr>
<tr>
<td>Klein (2001)</td>
<td>Shoulder arthroscopy</td>
<td>Enrolled=40</td>
<td></td>
<td>The mean VAS scores at rest for SSISB+CSBB group at 12h, 24h and 48h were significantly lower than the SSISB group.</td>
<td>VAS mean(3D) at 12h/24h/48h Rest: SSISB+CSBB 25(30)/29(27)/35(25) SSISB 45(37)/50(29)/30(17) Movement SSISB+CSBB 29(31)/30(29)/20(25) SSISB 48(37)/56(26)/36(19)</td>
<td>5</td>
</tr>
<tr>
<td>Webb (2007)</td>
<td>All shoulder procedures</td>
<td>Enrolled=56</td>
<td>No statistically significant differences were identified between the 2 groups with regard to visual analog scale pain scores.</td>
<td></td>
<td>VAS mean (no SD reported) at 12h/24h/48h SSISB 51/49/47 CSBB 51/49/44</td>
<td>3</td>
</tr>
<tr>
<td>Ciccone (2008)</td>
<td>ASD ± RCR</td>
<td>Enrolled=128</td>
<td></td>
<td>CSBB only group had significantly higher scores than all other groups for the first 2 hours. The percentage of patients who required oral opioid or intravenous pain medication was significantly higher for the CSBB only group than for the other groups.</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Author</td>
<td>Surgical procedures</td>
<td>N</td>
<td>Results</td>
<td>Pain Scores</td>
<td>Jadad score (max=5)</td>
<td>Complications</td>
</tr>
<tr>
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<td>-------------------------------------------------------------------------</td>
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<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Hofmann-Kiefer</td>
<td>RCR Acromio-clavicular procedures</td>
<td>Enrolled=87 CISB=36 PCA (IV opioid)=34 Excluded=17</td>
<td>In the CISB group, pain scores were significantly lower at rest at 6h, 24h, 72 h and during physiotherapy on day 2.</td>
<td>VAS median(IQR) at 6h/24h/CISB 10(0-25)/20(10-35)/20(10-40) PCA 35(30-40)/30(20-45)/30(20-42)</td>
<td>3</td>
<td>Mild dyspnoea; horner’s syndrome; catheter dislodgement (all CISB group)</td>
</tr>
<tr>
<td>Lehtipalo</td>
<td>Acromioplasty</td>
<td>Enrolled=30 CISB (ropivacaine)=7 PCA (IV morphine)=10 IM or IV Morphine=10 Excluded=3</td>
<td>Pain scores in the CISB group were significantly lower than in groups IM Morphine and PCA.</td>
<td>VAS mean(SEM) at 12h/24h/CISB 10(5)/9(7) PCA 35(8)/30(7) IM/IV Morphine 55(7)/35(3)</td>
<td>2</td>
<td>Respiratory depression in one patient in PCA group; CISB group patients - ptosis(5), horner’s syndrome(4), hematoma(1)</td>
</tr>
<tr>
<td>Beaudet</td>
<td>All shoulder procedures</td>
<td>Enrolled=60 CISB (ropivacaine)=29 CSBB (bupivacaine)=30 Excluded=1</td>
<td>Pain when patients arrived in the PACU were significantly lower in group CISB.</td>
<td>VAS mean(SD) at 24h CISB 57 (25) CSBB 50 (25)</td>
<td>2</td>
<td>One patient in group CSBB reported persistent paresthesia in the first, second, and fifth fingers of the operated limb, which had diminished in intensity after 9 months of follow-up but not completely resolved.</td>
</tr>
<tr>
<td>Delaunay</td>
<td>Arthroscopic RCR</td>
<td>Enrolled=30 CISB (ropivacaine)=14 CSBB (ropivacaine)=15 No follow up</td>
<td>Pain in PACU, oral morphine and local anaesthetic consumption at 24 hours was lower in the CISB group.</td>
<td>VAS median(IQR) at 24h/48h Rest: CISB 0(0-25)/0(0-30) CSBB 20(0-45)/10(0-60) Movement: CISB 100(0-60)/150(0-60) CSBB 45(20-100)/50(0-60)</td>
<td>3</td>
<td>Three patients in the interscalene group experienced a Horner’s syndrome</td>
</tr>
<tr>
<td>Author</td>
<td>Surgical procedures</td>
<td>N</td>
<td>Results</td>
<td>Pain Scores</td>
<td>Jadad score (max=5 )</td>
<td>Complications</td>
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</tr>
<tr>
<td>Winkler (2009) 81</td>
<td>ASD</td>
<td>Enrolled=40</td>
<td>The CISB patients had significantly lower pain levels at rest and</td>
<td>VAS mean(SD) at 12h/24h</td>
<td>3</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CISB (ropivacaine)=20</td>
<td>movement at 8h and 12h. Night pain was reported in 22.2% of the CISB</td>
<td>Rest: CISB 25/25/20(15) CSBB 40/30/30(20) Movement: CISB 30(0)/40(15) CSBB= 60(25)/90(10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CSBB (ropivacaine)=20</td>
<td>group vs. 60% in the CSBB group.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mariano (2009) 82</td>
<td>Arthroscopic and open</td>
<td>Enrolled=32</td>
<td>Ropivacaine infusion group had significantly less pain, less opioid</td>
<td>’Average’ VAS (over previous 24h) median(IQR) at 24/48h</td>
<td>5</td>
<td>Mild dyspnorea (CISB), catheter site pain (saline), catheter dislodgement</td>
</tr>
<tr>
<td></td>
<td>shoulder surgery</td>
<td>CISB (ropivacaine infusion)=15</td>
<td>consumption and less sleep disturbance than the control group</td>
<td>CISB 20-30/20-30 Control 50(30-65)/40(20-50).</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control (SSISB)=15</td>
<td>(SSISB only).</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Not included=2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ilfeld (2003) 83</td>
<td>Arthroscopic and open</td>
<td>Enrolled=25</td>
<td>Pain reduced in CISB group. 80% of patients receiving CISB</td>
<td>’Average’ VAS median(IQR) at 24/48h</td>
<td>5</td>
<td>Catheter dislodgement</td>
</tr>
<tr>
<td></td>
<td>shoulder surgery</td>
<td>CISB (ropivacaine infusion)=10</td>
<td>required less than or equal to 1 opioid tablet per day during their</td>
<td>CISB 00-20/150-20 Control 45(40-50)/40(35-50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control (SSISB)=10</td>
<td>infusion vs. more than or equal to 4 opioid tablets in controls.</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Not included=5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kean (2006) 84</td>
<td>All shoulder procedures</td>
<td>Enrolled=16</td>
<td>The CISB group had lower pain scores at each assessment. Morphine</td>
<td>VAS mean(range) at 12/24h</td>
<td>5</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CISB (levobupivacaine)=8</td>
<td>consumption was also lower in the CISB group.</td>
<td>CISB 1.3(0-10)/17(0-60) SSISB=27(0-70)/44(0-80)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SSISB=8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borgeat (1997) 85</td>
<td>Shoulder arthroplasty</td>
<td>Enrolled=43</td>
<td>Pain score was similar in both groups when CISB and PCA were started</td>
<td>VAS mean(SD) at 12/24/48h</td>
<td>3</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td>RCR</td>
<td>CISB (ropivacaine)=20</td>
<td>(t=0) and 6 h later (t=6). Significantly better pain control was</td>
<td>CISB 2.5(0.1/1.9)/17(1.1/19) SSISB+PCA= 24(0)/32(0/16)19)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Control (SSISB+IV PCA)=20</td>
<td>observed in the CISB group at 12 h and 38 h. At 24h, 30h, 36h, 42h, and</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Excluded=3</td>
<td>48 h, no significant difference in pain score between the two groups was</td>
<td></td>
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</tr>
</tbody>
</table>

**Continuous interscalene block vs. Single shot interscalene block**
<table>
<thead>
<tr>
<th>Author</th>
<th>Surgical procedures</th>
<th>N</th>
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<th>Pain Scores</th>
<th>Jadad score (max=5)</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borgeat (1998)</td>
<td>Shoulder arthroplasty</td>
<td>Enrolled=65</td>
<td>Except for 42 h after surgery, pain was less in the CISB group at all times.</td>
<td>VAS scores not reported</td>
<td>3</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td>RCR</td>
<td>CISB (ropivacaine)=30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SSISB (IV PCA)=30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Excluded=5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capdevila (2006)</td>
<td>Acromioplasty</td>
<td>Enrolled=40 (subgroup)</td>
<td>The control group had higher pain scores and higher consumption of morphine and ketoprofen compared with both ropivacaine groups.</td>
<td>VAS scores for shoulder subgroup not reported</td>
<td>3</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CISB (ropivacaine infusion)=15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SSISB (IV PCA)=10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamosiuna (2004)</td>
<td>ASD</td>
<td>Enrolled=80</td>
<td>The CISB group had less pain at rest and on movement than the control group (p=0.0001). The requirement for supplemental analgesia was also lower.</td>
<td>VAS median(IQR) at 12h/24h/48h</td>
<td>5</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CISB (bupivacaine)=35</td>
<td></td>
<td>Rest: CISB 4(0-39)/6(0-27)/4(0-31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control (SSISB)=38</td>
<td></td>
<td>Control 21(2-42)/35(17-44)/31(19-42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ASD</td>
<td>Not included=7</td>
<td></td>
<td>Movement: CISB 8(0-45)/11(4-51)/10(2-52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klein (2000)</td>
<td>Open RCR, Biceps tendonesis</td>
<td>Enrolled=40</td>
<td>Reduced pain in CISB group</td>
<td>VAS mean(SD) at 12h/24h</td>
<td>5</td>
<td>Mild dyspnoea, catheter site pain, catheter dislodgement (all CISB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CISB (ropivacaine)=22</td>
<td></td>
<td>Rest: CISB 10(5)/15(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SSISB=18</td>
<td></td>
<td>Control 29(5-70)/47(36-75)/47(36-75)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borgeat (2000)</td>
<td>Shoulder arthroplasty</td>
<td>Enrolled=55</td>
<td>Pain score was similar in both groups when CISB and SSISB were started (6 h after the ISB). Significantly better pain control was observed in the CISB group at 12h and 24 h.</td>
<td>VAS median (IQR) at 12h/24h/48h/PCA 6(0-15)/4(5-10)/0(0-5)/SSISB 30(0-40)/20(0-29)/0(0-22.5)</td>
<td>3</td>
<td>None reported</td>
</tr>
<tr>
<td></td>
<td>RCR</td>
<td>CISB (ropivacaine)=18</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SSISB=15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Excluded=2</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Patients in SSISB, IA + SBB and SBB groups had less pain than those of the control group at all time points. Pain in IA + SBB group was statistically comparable with those in SSISB and SBB groups at each time interval.

<table>
<thead>
<tr>
<th>Author</th>
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<th>Pain Scores</th>
<th>Jadad score (max=5)</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fontana (2009) 39</td>
<td>Acromioplasty RCR</td>
<td>Enrolled=120 IA=19, SBB=21, IA+SBB=23, SSISB=20, Control=20 Excluded=17</td>
<td>Patients in SSISB, IA + SBB and SBB groups had less pain than those of the control group at all time points. Pain in IA + SBB group was statistically comparable with those in SSISB and SBB groups at each time interval.</td>
<td>VAS (area under the curve) mean (SD) at 24h: IA=118(5.6), SBB=87(4.6), IA+SBB=63(3), SSISB=37(2.6), Control=147(6.5)</td>
<td>3</td>
<td>Four cases of mild dyspnøea and two occurrences of dysphonia were observed in the SSISB group.</td>
</tr>
</tbody>
</table>

ASD = arthroscopic subacromial decompression; CISB = continuous interscalene block; CSBB = continuous subacromial bursa block; GA = general anaesthesia; IA = intraarticular; IM = intramuscular; IQR = interquartile range; ISB = interscalene block; IV = intravenous; PACU = post anaesthetic care unit; PCA = patient controlled analgesia; PCIA = patient controlled interscalene analgesia; PR = prilocaine-ropivacaine; RCR = rotator cuff repair; RCT = randomised controlled trial; SBB = subacromial bursa block; SR = saline-ropivacaine; SS = saline-saline; SSB = suprascapular nerve block; SSISB = single shot interscalene block; SSSBB = single shot sub acromial bursa block; VAS = Visual analogue pain score.

If not specifically stated, “control” groups all received opioid rescue analgesia.
2.4.3. Evidence for the effectiveness of each technique

The key comparisons and findings of the studies described in Table 2.1 are summarised below.

2.4.3.1. Subacromial (bursal)/intra-articular infiltration analgesia (SBB)

Three studies compared single injection SBB with controls (subacromial saline or no block); all failed to show any clinically significant reduction in postoperative pain. 58, 70, 72 Eight studies compared continuous SBB with controls (subacromial saline). 11, 59-65 The four earliest studies (n=206), 61-63, 65 demonstrated a reduction in pain of between 7-20 points in the continuous SBB groups. The subsequent four studies (n=444) (including a recent study involving 158 patients and having the maximum Jadad score of 5) 11 failed to demonstrate any clinically significant reduction in pain compared with controls (subacromial saline). Two additional studies compared continuous SBB with controls, with both groups first receiving a SSISB; one showing clinical benefit with continuous SBB, 74 the other showing no benefit. 76

Of the five studies (n=206) demonstrating a clinical benefit from continuous SBB over controls (subacromial saline), none involved open procedures and only one study included rotator cuff repair. On the other hand, of the five studies (n=444) failing to show clinical benefit from continuous SBB over controls, three involved open procedures and four included rotator cuff repair. The two groups of five studies (effective vs. ineffective) did not significantly differ with respect to the dose and volume of local anaesthetic administered.
2.4.3.2. Suprascapular and/or axillary (circumflex) nerve block

The suprascapular and axillary (circumflex) nerves provide the predominant sensory innervation to the shoulder joint. Compared with placebo, suprascapular nerve block reduced postoperative pain, morphine consumption and nausea following arthroscopic shoulder surgery. Suprascapular nerve block also provided better postoperative analgesia compared with intra-articular infiltration, but inferior analgesia compared with SSISB. Suprascapular nerve block added little clinical benefit when added to a general anaesthesia-interscalene block technique.

2.4.3.3. Single injection (‘single shot’) interscalene block (SSISB)

Four studies compared SSISB with controls; all showed reduced pain in the SSISB groups; albeit, only up to 24 postoperative hours. Only one of these studies had a Jadad score of more than two. Three studies compared SSISB with single injection SBB, but all had low Jadad scores. Two of these favoured SSISB, while one showed comparable pain scores with each technique. One study compared SSISB with continuous SBB, with better analgesia achieved in the SSISB group. Three studies evaluated the effect of adding a continuous SBB to a SSISB; one demonstrated improved analgesia with continuous SBB, the other two failed to show any benefit from continuous SBB once the SSISB had resolved.

2.4.3.4. Continuous interscalene block (CISB)

Two studies compared CISB with controls (no block). Both demonstrated reduced pain with CISB. Three studies compared CISB with continuous SBB; two
demonstrated reduced pain in the CISB group $^{80, 81}$ while the other study (Jadad score=2) showed no difference. $^{79}$ Nine studies compared CISB with SSISB and all demonstrated a reduction in pain in the CISB group. $^{7, 8, 82-88}$ In six of these studies, the treatment effect continued for the 48 hours of follow up (in two studies, pain scores were only measured until 24 hours). More importantly, in all but one of these nine studies, the Jadad scores were four or more.

2.5. Review limitations

The inability to perform metanalysis rendering the account a narrative systematic review is the most obvious limitation. Secondly, previous investigators have specified a 2-point shift on the 11 point numerically rated pain scale as being clinically significant for acute postoperative pain. $^{91}$ A minimum threshold VAS shift was not specified for each trial, but rather, statistical significance was used when assessing whether a treatment effect had been demonstrated. This was based on the fact that what constitutes a clinically relevant shift in VAS depends on the intervention required to produce that effect. In other words, any demonstrated treatment effect, regardless of how small, should be interpreted in the context of the downside to the intervention required to achieve that outcome benefit. In the studies evaluated, a wide range of interventions were trialled; some invasive (e.g. interscalene block), and some logistically straight forward (e.g. local anaesthetic infiltration), so an arbitrary VAS threshold figure is inappropriate.

Pain assessment in the constituent studies was either by a simple numerical rating scale or visual analogue scale. Although these instruments are methodologically different, a recent systematic review found overall good concordance between the
two scales. There is little reason, therefore, that this confounder would have influenced the findings between trials.

A potential limitation of systematic reviews including the present review is the equal weight given to negative studies with high power versus negative studies with low power. Many studies did not report standard deviation, which makes posthoc assessment of study power challenging. However, where possible, greater emphasis was placed on negative studies with high power.

2.6. Implications

2.6.1. Subacromial/intra-articular infiltration analgesia

The discrepancy in the findings between the early studies of this technique and the more recent studies could be explained, as stated, by the surgical procedures included in each study. The initial studies demonstrating clinical benefit from continuous SBB tended to be simple, arthroscopic, non-rotator cuff procedures. However, the lower number of patients included in these earlier ‘positive’ studies always raises the possibility of publication bias, as the risk of a positive finding arising as a result of statistical chance alone (Type I errors) is reduced as sample size is increased. On balance, it appears that at best, the technique is only effective for arthroscopic non-rotator cuff procedures; for open and/or rotator cuff (and other major) procedures it appears to perform only marginally better than placebo. Consequently, the use of this technique has declined over the last five years as a result of this uncertainty over effectiveness and a rise in popularity of peripheral nerve blockade.
Adverse effects: More recently, concern has been raised over the possibility of iatrogenic chondrolysis associated with intra-articular local anaesthetic. 94 These concerns were highlighted in a recent editorial. 95 Essentially, there is convincing animal evidence for local anaesthetic induced chondrotoxicity, especially for bupivacaine when used in high doses. 96-99 These data have coincided with several reports of catastrophic glenohumeral chondrolysis occurring in healthy young patients, all having received high and prolonged doses of intra-articular bupivacaine. 94 The condition had been rarely reported prior to the introduction of intra-articular local anaesthetic infusions. Consequently, some ambulatory pump manufacturers are now actively advising against the use of their pumps for the intra-articular route of administration. 100

2.6.2. Suprascapular and/or axillary (circumflex) nerve block

On its own, suprascapular nerve block provides clinically significant improvements in postoperative pain control compared with placebo but provides inferior analgesia compared with interscalene block. 70 When combined with an axillary (circumflex) nerve block, prospective observational data suggests that it will often achieve complete shoulder joint analgesia. 28, 29 The main advantage of this approach over brachial plexus blockade is the avoidance of motor block to those parts of the upper limb innervated by the more inferior roots of the brachial plexus (eighth cervical root or first thoracic root). It also eliminates the risk of phrenic nerve blockade. Thus, patients with moderate-to-severe respiratory disease who might be expected to be intolerant of both ipsilateral phrenic nerve block (associated with interscalene block) and high doses of perioperative opioid represent prime candidates for this technique. The disadvantage of this approach for perioperative analgesia is the requirement for
two separate nerve block procedures, incomplete blockade of all nerves innervating the shoulder joint (in particular the lateral pectoral nerves) and a limited duration of action. Placing perineural catheters adjacent to the suprascapular and/or axillary (circumflex) nerves are possible, but few data exist to support this practice.  

Adverse effects: Experience with both of these blocks is still relatively limited; therefore, data concerning safety is also limited. Both procedures carry a risk of nerve damage and intravascular injection while suprascapular nerve block also carries a risk of pneumothorax.

### 2.6.3. Single injection interscalene block

The posterior approach to the brachial plexus was first described by Pippa and more recently popularised by Boezaart. It has been claimed that more selective sensory-motor differential blockade can be achieved with this approach compared with the anterior approach as blockade occurs proximal to the point of fusion of the sensory and motor fibres. Despite these claims, data supporting reduced motor block with this approach are lacking.

The main limitation of both anterior and posterior needle approach SSISB is the limited duration of action, which for most shoulder surgery is shorter than the requirement for potent postoperative analgesia. Many practitioners have tried to address this by way of combining the block with subacromial infusions of local anaesthetic, but these approaches have been limited in their effectiveness. Following more major procedures, SSISB provides better analgesia and reduced opioid related side effects relative to local anaesthetic infiltration techniques.
Despite the limited duration of potent analgesia provided by SSISB, it is still a very useful technique, particularly where the expertise and logistics required for continuous interscalene analgesia are unavailable. SSISB arguably provides a sufficient duration of potent analgesia following minor arthroscopic surgery. 105

Adverse effects: In addition to the common risks associated with peripheral nerve blocks (nerve damage, local anaesthetic toxicity), interscalene block is also associated with a risk of pleural puncture. More importantly, it has been associated with central neuraxial needle placement, cervical spinal cord damage and permanent paralysis. 106 To prevent this potentially devastating complication, it is essential to limit needle depth and maintain the needle in a caudad direction thereby minimising the risk of entering an intervertebral foramen (see Chapter X) 107, 108. Finally, of note, needle placement in the spinal cord can occur with the posterior approach to the interscalene brachial plexus. 109 Phrenic nerve block is discussed in the complications section of this thesis.

2.6.4. Continuous interscalene block (CISB)

Of all the techniques assessed in this review, the strongest evidence for effectiveness exists for CISB. Therefore, the technique will be discussed in detail.
2.7. Evolution of continuous interscalene block

CISB was first described in 1987, using an approach similar to that described by Winnie for interscalene block, however these early reports were associated with failure rates as high as 25%. Between 1990 and 1997 reports of the technique were infrequent, but improvements in equipment and a description of a new approach by Meier resulted in a rise in its popularity and with it, increasing reports of its effectiveness. The technique is similar to SSISB, but with the essential modification that the needle insertion point is at a point cephalad of the 6th cervical vertebral level. This enables the needle to approach the interscalene brachial plexus along its long axis, which facilitates catheter threading in close proximity to the nerves and enables the placement of sufficient catheter beneath the skin thereby facilitating catheter fixation.

Early descriptions of the technique involved non-stimulating catheters, which were threaded at least 5 cm beyond needle tip. ‘Secondary’ catheter failure rates were high (i.e. primary block using local anaesthetic injected through the needle successful, but the catheter itself ineffective), which resulted in editorial commentary remaining sceptical of the technique. As late as 2002 these went so far as to state, “interscalene catheters will never become routine because of high failure rates and long insertion times”. A subsequent report described less catheter advancement beyond the needle tip and was associated with a lower failure rate. The technique originally described by Meier underwent a very minor modification by Borgeat and colleagues who termed it a ‘lateral’ approach, even though the needle is essentially directed in a caudal/medial direction. Electrical catheter stimulation was promoted as a way of precisely confirming appropriate catheter positioning and reducing the
previously reported high secondary failure rates.\textsuperscript{114} However, subsequent prospective randomised studies have failed to demonstrate the superiority of stimulating over non-stimulating catheters.\textsuperscript{115-117} This, however, does assume that non-stimulating catheters are advanced no further than 3-5 cm beyond the target needle tip position.\textsuperscript{34} (the exact threading distance < 5 cm beyond the needle tip of a non-stimulating catheter has not been evaluated). Finally, interscalene catheter placement utilising a posterior approach analogous to that used for posterior approach SSISB has been shown to be an effective analgesic technique following painful shoulder surgery.\textsuperscript{114} To date, this approach has not been formally compared with the anterolateral approach and this certainly represents an area of needed research.

\subsection*{2.7.1. Ultrasound guidance for interscalene catheter placement}

The neurostimulation technique for plexus localisation specific for interscalene catheter placement has been shown to be associated with a false negative motor response rate of over 50%, and this is higher than that reported for single injection techniques.\textsuperscript{36} This high false negative motor response rate was the likely reason for a subsequent study which showed that use of ultrasound for determination of the target needle tip position (rather than that determined by neurostimulation) results in a reduction in both needle passes and procedural pain.\textsuperscript{118} Furthermore, the incorporation of ultrasound guidance for this procedure, by facilitating catheter positioning adjacent to the most appropriate elements of the brachial plexus (5\textsuperscript{th} and 6\textsuperscript{th} cervical roots/superior trunk) has been recently shown to improve indices of interscalene catheter performance, in particular local anaesthetic and supplemental oral analgesic adjuvant consumption.\textsuperscript{119} However, a subset of patients exists in
whom the use of nerve stimulation is essential for accurate catheter placement. The size of this subset is dependent on the operator’s level of experience with ultrasound.

The choice of out-of-plane vs. in-plane techniques for ultrasound guided perineural catheter placement remains controversial. The exact definitions of these terms is important and will be repeated for clarity. The out-of-plane approach refers to block needle orientation perpendicular to the long axis (or "plane") of the ultrasound beam. Needle tip approximation is through observation of tissue displacement and/or injectate spread. With the in-plane technique, block needle orientation is parallel to the long axis (or "plane") of the ultrasound beam. The entire needle shaft and tip may be visualised with this orientation. Short axis imaging refers to orientation of the ultrasound beam perpendicular to the long axis of the nerve. Most ultrasound guided regional anaesthesia is conducted using this approach. Long axis imaging refers to orientation of the ultrasound beam parallel to the long axis of the nerve. Nerve imaging can be challenging using this approach, and therefore, it is rarely used.

The out-of-plane approach has been the most frequently described and is popular for a number of reasons. Many anaesthetists are already familiar with this approach for venous cannulation. From an anatomical perspective, out-of-plane needle-probe alignment places the needle and therefore the catheter along the long axis of the plexus, potentially promoting catheter advancement along it. Catheter alignment along the long axis of the nerve would therefore maximise the surface area of catheter in contact with the nerve, which may be important for multi-orifice catheters where orifices are positioned up to 1.5 cm from the catheter tip. Finally, and arguably the most important, orientation of a short bevelled or Tuohy tipped needle along the long axis of a nerve or plexus theoretically eliminates the possibility
of intraneural needle placement. Intraneural needle placement has yet to be reported with a Tuohy needle and this needle-to-nerve orientation. The main problem with the out-of-plane approach is the inability to visualise the needle tip, and therefore, a lack of needle tip precision. Out-of-plane assessment of needle tip position requires the operator generate a 3 dimensional image, which can be conceptually challenging. However, with superficial blocks, such as interscalene block, the needle can be orientated more in line with (along the long axis of) the nerve; therefore, inadvertent needle advancement beyond the ultrasound beam should not significantly compromise needle-nerve proximity. Finally, it is important to note that during out-of-plane needle advancement, puncturing important structures (e.g. vessels) is possible as needle advancement is, to a large extent, "blind".

Theoretically, by facilitating needle tip visualisation, in-plane needle-probe alignment might facilitate catheter positioning adjacent to the most appropriate roots and/or trunks. However, the main drawback of the in-plane approach is that the needle can deviate from the ultrasound beam, and thus be lost from view. This can place the nerve at risk of needle impalement. In-plane needle-probe alignment with consequent orientation of needle perpendicular to the plexus in theory renders the catheter-past-needle distance more critical with respect to the resultant proximity of catheter and plexus. Therefore, when using the in-plane short-axis technique (needle perpendicular to nerve/plexus), it may be prudent to limit the advancement of a non-stimulating interscalene catheter no further than 1-2 cm past the needle tip. Obstructions to the needle path may necessitate the use of a particular approach. For example, access to the interscalene brachial plexus without crossing the path taken by the dorsal scapular and long thoracic nerves necessitates the out-of-plane approach. Both nerves pass approximately 1 cm posterior and lateral to the 5th and
6th nerve cervical nerve roots – directly in the path of a needle inserted in-plane from posterior. 37 With the out-of-plane approach, use of a blunt needle is advantageous, as a blunt needle facilitates the assessment of needle tip position by causing tissue displacement (a sharp needle will cut through the tissues and cause minimal tissue displacement).

2.7.2. Other technical aspects of interscalene catheter placement

Catheter threading in the interscalene area can be challenging. 2 Expanding the perineural space with injectate has been shown to facilitate catheter advancement.128 Local anaesthetic, normal saline and dextrose 5% have all been used, but dextrose has advantages over both saline and local anaesthetic because an evoked muscle response is typically maintained after injection through the stimulating needle.129 With a neurostimulation-assisted technique, this is advantageous if catheter threading proves difficult, as the needle can be manipulated in an attempt to facilitate catheter threading often without losing the muscle response.129, 130 Placing all local anaesthetic via the catheter provides a simple (if not gross) method of confirming the functional proximity of catheter and plexus. 2, 5, 34, 36, 118, 119, 131

Catheter fixation in this area can be difficult because of the mobile nature of the surrounding area and adjacent hair follicles. Attention to this often-overlooked detail is crucial for effective management of continuous interscalene techniques especially in the ambulatory setting. Two or three drops of topical medical cyanoacrylate (e.g. Dermabond®, Ethicon, Berkshire, U.K or Glustitch®, Delta, BC, Canada) at the catheter entry site can reduce problematic postoperative catheter leakage to an acceptable 1% of patients. 2 Catheter tunnelling is popular in many centres but is not
essential for effective fixation. An effective non-tunnelled catheter fixation technique that facilitates both catheter retention and patient self-removal has involved the use of a simple epidural catheter securing device (Lockit-Plus®, Portex, UK) combined with a clear occlusive dressing (e.g. Tegaderm®, 3M, St Paul, MN, U.S.A) and non-woven fabric (e.g. Hypafix®, Smith & Nephew, Auckland, NZ). This system is efficient and well tolerated. Of note, no previous studies have evaluated the optimal distance to thread a non-stimulating interscalene catheter beyond the needle tip. Higher threading distances should theoretically reduce the risk of inadvertent catheter dislodgement, but may be associated with increased catheter deviation away from the plexus.

2.7.3. Ambulatory management

Ambulatory application of CISB was first described in 2000 and followed three years later with a small placebo controlled trial. A small feasibility study and later a large prospective study involving over 300 consecutive patients, performed by a single operator confirmed that the technique could also be safely and effectively applied in the private practice/community environment. The technique has also been shown to be feasible when performed by a mixed group of anaesthetists. However, successful and safe ambulatory management of this treatment, like all perineural catheters, requires careful patient selection, substantial preoperative education and close postoperative supervision. Preoperative education typically starts when the patient is booked for surgery. Postoperative instructions are ideally accompanied by explicit written instructions, which must provide a clear point of contact in the event of catheter related problems including inadequate analgesia. This
typically involves either the primary anaesthetist (e.g. private practice setting)\textsuperscript{2} or acute pain service (e.g. teaching hospital).\textsuperscript{121}

Ambulatory perineural catheter management – by promoting earlier home discharge – ensures the cost effectiveness of continuous peripheral nerve blockade.\textsuperscript{134} 22 An additional benefit of ambulatory catheters is that they suit patients who prefer to recuperate in their own home rather than in hospital.\textsuperscript{135} It has also been suggested that the earlier discharge enabled by ambulatory perineural catheters may theoretically reduce the perioperative nosocomial wound infection risk.

Depending on the surgery, individual patients’ pain tolerances, and the logistical setup of the hospital and ambulatory perineural catheter service, ambulatory perineural catheters can reduce hospital stay by 0.5-2 nights – an average of one night saving (approx. $600) has been quoted.\textsuperscript{22, 136} A $600 saving typically exceeds the ambulatory pump cost and extra professional fees required for safe management.

The main choice of infusion device is between elastomeric and electronic pumps. Electronic pumps have the advantage of being programmable and many have alarms, which will alert the patient to catheter obstruction. Elastomeric pumps are generally lighter, and do not run the risk of troublesome false alarms which can generate unnecessary patient concern and consequent phone calls to the ambulatory service. Regardless of a flow pressure alarm, an obstructed catheter will eventually manifest as uncontrolled pain. The obstruction can usually be readily diagnosed with a manual catheter bolus. Compared to electronic pumps, elastomeric pumps are preferred by patients.\textsuperscript{137} A low background infusion maximises patient control, minimises motor block, and maximises pump duration for a given reservoir volume.\textsuperscript{138}
All the currently available ambulatory pumps are limited by their relatively low bolus flow rates ($\leq 150 \text{ mL.hr}^{-1}$) – higher flow rates promote better multi orifice flow, which has been shown to improve epidural catheter effectiveness.

Despite the analgesia provided by CISB, NSAIDs, tramadol and/or opioid supplementation is generally still required, particularly in the ambulatory setting where the technique is limited by the use of low volume infusion pumps, which necessitate low background infusions in order to provide more than 1-2 days of blockade. 8, 131

### 2.8. CISB Pharmacology

The optimum combination of local anaesthetic type, volume and concentration for interscalene infusion rates is largely unknown. Initial reports of the technique used infusion rates as high as 10 mL.hr$^{-1}$, however, subsequent reports have been characterised by progressively lower background infusions and the incorporation of patient controlled boluses. 104, 141, 142 Lower background infusions have arisen because of an appreciation that high rates were not necessary, that high doses may increase unwanted motor block, because ambulatory pumps have limited reservoir volumes and possibly because interscalene catheter placement has become more precise. Ropivacaine 0.2% was shown to provide similar analgesia to bupivacaine 0.15% but with reduced motor block and has subsequently remained the most common local anaesthetic drug studied. Ilfeld et al showed that ropivacaine 0.2% infused continuously at 8 mL.hr$^{-1}$ with a 2 mL hourly bolus capability provided superior baseline analgesia compared to the same drug administered at 4 mL.hr$^{-1}$ with 6 mL boluses. 141 Le and colleagues using a neurostimulation catheter
placement technique based on a biceps or deltoid motor response, compared ropivacaine 0.2% and 0.4% administered at a constant total dose (8 mL infusion/4 ml bolus vs. 4 mL infusion/2 mL bolus). The secondary outcome, postoperative pain was reduced in the high volume/low concentration group. However, in another study, compared with ropivacaine 0.25%, ropivacaine 0.4% was associated with both reduced ropivacaine bolus demands and reduced supplemental ketoprofen administration. With ropivacaine 0.2% administered at 2 mL.hr⁻¹ by continuous infusion supplemented with on-demand patient controlled 5 mL boluses, rotator cuff surgery and arthroplasty surgeries were associated with a significant proportion of patients experiencing moderate-to-severe breakthrough pain, which was not improved by increasing the concentration to ropivacaine 0.4%. These studies suggest that a background infusion of at least 4 mL.hr⁻¹ is required for optimal analgesia, but equally important is the PRN bolus dose, the optimal volume of which appears to be at least 4 mL. There appears to be little benefit in administering concentrations of ropivacaine greater than 0.2%. These relatively high basal and bolus volumes will be difficult to administer in the ambulatory setting where the duration of treatment is limited by limited volume pumps. However, the small subset of patients who require more than 72 hours of potent analgesia can be safely and effectively managed by having their elastomeric pump refilled in order to provide extended brachial plexus blockade. Clearly, further research is required to identify the optimal combination of local anaesthetic infusion and bolus volume. Another unanswered issue is the optimal primary bolus dose to be administered via the catheter at the time of surgery.
2.9. CISB Surgical indications

Early prospective randomised trials comparing CISB with SSISB demonstrated profound analgesia following major shoulder surgery including rotator cuff repair and open procedures (Table 2.1). More recently, an ultrasound guided placement technique targeting the 5th and 6th cervical nerve roots and/or superior/middle trunks has also been shown to improve analgesia and reduce supplemental oral analgesic adjuvant consumption following minor arthroscopic procedures.  

2.10. CISB Training issues

Interscalene catheter placement has long been recognised as technically challenging, and this factor has been a likely reason for the slow uptake in the utilisation of the technique. Over the last decade, improvements have been made in the design features of the commonly available catheter kits. These improvements have been accompanied by a steady increase in the availability in the operating theatre of portable ultrasound equipment. There is some evidence to suggest that ultrasound guidance may accelerate proficiency with peripheral nerve block procedures; however, it remains to be seen whether this modality will affect the rates of perineural catheter utilisation. It is possible that the only solution to the current low utilisation rates will be the adoption of minimum training requirements and minimum levels of ongoing case exposure similar to that often seen with the cardiac, paediatric and obstetric anaesthesia subspecialties (see Chapter 16).

Adverse effects: Side effects are similar to SSISB, although those side-effects likely to be volume/dose related should theoretically be less frequent with a lower
‘primary’ local anaesthetic dose, as is often used when incorporating a continuous infusion. The most common side effects reported with the technique include mild dyspnoea related to phrenic block (7%), hoarseness (4%) and Horner’s syndrome (7%). More significant adverse effects include pneumothorax, intravascular injection (all approximately 0.2%) and local inflammation/infection (0.3-0.8%). Transient postoperative neurological symptoms associated with shoulder surgery and CISB combined are relatively frequent (8%) at day 10, but are infrequent (2-4%) after one month. Differentiating transient symptoms arising as a result of the block from other causes is difficult, however, block related neurological sequelae lasting more than 6 months are exceedingly rare.

2.11. Superficial cervical plexus block

The superficial cervical plexus innervates the skin on the side of the neck and shoulder joint principally via the supraclavicular nerves. Consequently, an isolated block of the brachial plexus or its terminal nerves will not provide cutaneous anaesthesia for shoulder surgery. It has been suggested that a conventional interscalene block will result in local anaesthetic spread to the cervical plexus and therefore the elimination of the requirement for a separate injection, but this notion is not supported by definitive data. Because CISB often involves large calibre needles (e.g. 18G Tuohy), it is likely that interscalene catheter placement involves greater procedural pain than single injection techniques that utilise smaller calibre needles (e.g. 22G short bevel). The superficial cervical plexus block therefore represents an attractive anaesthetic technique to facilitate interscalene catheter placement with the added advantage of ensuring blockade of the cutaneous nerves innervating the skin.
of the shoulder. It does, however, involve an additional procedure, which at least theoretically, carries a small risk of trauma to the nerves of the cervical plexus.

2.12. Conclusion

In conclusion, the last five years have seen significant advances in the management of pain after shoulder surgery. Recent, large, high quality placebo controlled trials of subacromial/intra-articular infiltration of local anaesthetic have shown that the technique provides little if any clinical benefit. Because the technique may be a factor in the aetiology of catastrophic chondrolysis, it can no longer be recommended. While single injection nerve blocks have an important place in the management of pain after shoulder surgery, they are nevertheless limited by a short effective duration of action, which is often shorter than the duration of moderate-to-severe postoperative pain. CISB represents the most effective analgesia after this surgery.

Based on the findings of this review, a number of avenues for further research were identified. First is the determination of the optimal interscalene catheter local anaesthetic primary bolus dose, in terms of maximising block success, maximising block duration and minimising motor block and other adverse effects. Second is the optimal local anaesthetic regimen for postoperative infusion; specifically, the optimal combination of the background infusion and boluses. Third is the optimal needle approach for interscalene catheter placement (anterolateral vs. posterior); the optimal threading distance beyond the introducing needle tip, and the optimal catheter orifice configuration.
Part 2: Methodology

Chapter 3 Ethics, patient selection, anaesthesia and patient assessment
Chapter 3. Ethics, patient selection, anaesthesia and patient assessment

3.1. Ethics and patient selection

All interventional studies were approved by The Northern X or Y Regional Ethics Committees and also conformed to the Declaration of Helsinki, October 2008. All study protocols including the primary and secondary outcomes (and the time and method of each outcomes assessment), inclusion/exclusion criteria, intended sample size and methods of randomisation and blinding were pre-specified *a-priori* at the Australian and New Zealand Clinical Trials Registry as follows:

Chapter 4: ACTRN12609000347268
Chapter 5: ACTRN12611000155998
Chapter 6: ACTRN12609000740291
Chapter 7: ACTRN12609000768291
Chapter 8: ACTRN12610000201077
Chapter 9: ACTRN12612000114842

Written informed consent was obtained from all patients. All American Society of Anaesthesiologists (ASA) Physical Status 1-3 patients, aged 16-75 presenting for elective shoulder surgery, primarily in the principal investigator’s practice were eligible for inclusion. In three studies, recruitment was assisted by three anaesthetic colleagues: the study described in Chapter 4 by Dr Andrew Wong, study in Chapter 5 by Dr Amitha Abeysekera, and the study described in Chapter 6 by Drs Andrew Wong, Amitha Abeysekera and Darcy Price. Patients excluded included those refusing study participation or interscalene block, those with severe respiratory
disease, those with known neuropathy involving the arm undergoing surgery and those who had known allergy to amide local anaesthetic drugs. A research assistant made the initial invitation to participate in the study one week prior to surgery. At this consultation, patients were given a written information brochure detailing the continuous interscalene analgesic technique. All studies were performed at either the Brightside or North Harbour Southern Cross Hospitals.
3.2. Study design

The study design was either of the up-down dose finding type, or prospective randomised and varied from being unblinded to double-blind. The study methods and results were reported according to the CONSORT guidelines \textsuperscript{151} for the reporting of prospective randomised trials.

3.3. Anaesthesia

A standardised approach to anaesthesia was used for all patients in the various studies described. One hour before surgery, all patients were premedicated with oral paracetamol 1 g. Conscious intravenous sedation up to midazolam 2 mg and alfentanil 0.5 mg was administered 5 min prior to catheter placement. The specific dose of these drugs administered was dictated by the individual study protocol. A superficial cervical plexus block was placed prior to catheter placement to both facilitate catheter placement and ensure blockade of the supraclavicular nerves. The superficial cervical plexus block was performed in the initial studies by the infiltration of 5-10 mL 1\% lignocaine with adrenaline (1/200,000) along the posterior border of the sternocleidomastoid muscle midway between the level of the cricoid cartilage and mastoid process. The technique was modified during the latter studies in response to several patients reporting symptoms suggestive of superficial cervical plexus neuropathy (see chapter 13). That modification consisted of changing from a long to a short bevel needle, and a change in the injection point to 2 cm posterior to the posterior border of the sternomastoid muscle. Details of the catheter manipulations, and local anaesthetic volume and concentration are provided in the
description of individual studies. A further description of the catheter placement technique is provided in Appendix 3.

3.3.1. Intraoperative management

During surgery, all patients received at least 1000 mL intravenous crystalloid. Intraoperative monitoring conformed to the minimum standards set by the Australian and New Zealand College of Anaesthetists (ANZCA PS18, 2008) and included electrocardiography, continuous pulse oximetry, and non-invasive arterial pressure measurement. All shoulder surgery was conducted under spontaneous ventilation using a laryngeal mask airway and volatile anaesthesia without prior sensory or motor testing of the block. Most surgery was conducted using beach chair positioning (see chapter 18). Boluses of alfentanil 0.25 mg were administered during surgery for a respiratory rate > 25, but otherwise no further opioids were given unless block failure occurred in which case patients received intravenous morphine 2 mg PRN.

3.3.2. Postoperative management

The catheter was connected to an elastomeric infusion device (PainBuster, Surgical Synergies, Auckland, NZ) containing ropivacaine 0.2%. This device delivers a continuous infusion of 2 mL.hr⁻¹ and has a patient controlled bolus capability of an additional 5 mL every hour delivered at 150 mL.hr⁻¹. During the sixth and final study, approximately 70 patients received an electronic device (ambIT pump, Allied Medical, Perth, Australia). Postoperative paracetamol (1 g every 6 hours) and diclofenac SR (75 mg every 12 hours) were continued for as long as ropivacaine
boluses were required. Tramadol 100 mg SR every 12 hours was added for those patients who despite regular paracetamol, diclofenac and ropivacaine boluses, had a numerical rating pain score (NRPS) > 2 (0-10).

Successful catheter placement was defined as a worst NRPS in the post anaesthesia care unit (PACU) of two or less. Patients reporting a NRPS greater than two in the PACU were given a bolus of local anaesthetic and/or morphine 2 mg boluses every 2-3 min. If this intervention was ineffective, the catheter was replaced.

3.4. Patient assessment

Patient Assessment was divided into four parts (person recording data in parentheses):

1. At the time of catheter insertion (anaesthesia assistant or study investigator). Details regarding catheter placement e.g. catheter placement time, pain during catheter insertion were recorded.

2. During surgery (study investigator). The number of boluses of alfentanil 0.25 mg administered for a respiratory rate greater than 25 were recorded.

3. In the PACU (primary PACU nurse). The patient’s worst NRPS, details of catheter interventions and grip strength etc were recorded.

4. On postoperative day one and two (research assistant). Patients were directly questioned by a research assistant on postoperative days one and two for time to first shoulder pain, NRPS, arm numbness/weakness and satisfaction (0-10,
0=no pain, no numbness/weakness, very unsatisfied, 10=worst imaginable pain, worst numbness/weakness, very satisfied) during the first 24 postoperative hours.

### 3.5. Randomisation and blinding of treatments

Randomisation was performed by a research assistant otherwise uninvolved with the study procedures and implemented with a computer generated random number. For the studies described in Chapter 8 and 9, randomisation was in blocks of 20 to ensure even group numbers. Randomisation was not stratified by procedure. Allocation concealment was by pre-prepared sealed opaque envelopes, opened immediately after the superficial cervical block, but just prior to catheter placement.

For randomised studies, blinding of outcome assessments was as best as practicable. The aim of data collection was to blind both subjects and observers to the treatment groups throughout the study. During the informed consent process, preoperative information was limited to a discussion of the benefits and risks of each treatment arm. Data collection during catheter insertion and surgery was not blinded. The research assistant was blinded to treatment allocation during the day one and two phone calls in all studies except the study described in Chapter 6.

### 3.6. Statistical analysis

An independent statistician performed all calculations for all studies. In general, 95% confidence intervals (CIs) are reported except for the primary outcome in the studies described in Chapter 8 and 9 (% of patients reporting pain in the PACU), in which
90% CIs are reported, thus providing equivalence estimates with 95% confidence. CIs were calculated on raw values except skewed NRPS data, which were logarithmically transformed (to convert to an approximate Gaussian distribution) before CIs were calculated. Other data were summarised using appropriate descriptive statistics (mean and SD or mean and range for normally distributed or symmetric variables; median and interquartile range (IQR) for skewed variables; number and proportion for categorical variables). All statistical analyses were performed using Stata 10.0 statistical software (StataCorp LP, College Station, TX), SPSS Statistics 18.0.0 (SPSS Inc, Chicago, IL, USA) or R 2.12.1 (R Foundation, Vienna, Austria). Sample size estimates were calculated using Statmate 2.0 (GraphPad Software, San Diego, CA).
Part 3: Clinical Pharmacology

Chapter 4  Importance of primary bolus volume and concentration in preventing recovery room pain and minimising motor block

Chapter 5  Randomised study of the effect of local anaesthetic volume and concentration on the duration of peripheral nerve blockade

Chapter 6  Patient initiated mandatory boluses: An effective strategy for optimising analgesia versus side effects
Chapter 4. Importance of primary bolus volume and concentration in preventing recovery room pain and minimising motor block

4.1. Preface

As discussed in the introductory literature review Chapter, the primary bolus dose of local anaesthetic is typically injected through the catheter rather than through the needle. Local anaesthetic injection through the needle prior to catheter advancement is problematic in that catheter function is not declared until the primary block has resolved, which can be 12 hours or more following catheter placement. If local anaesthetic is injected through the catheter, catheter function will be declared on emergence, and thus suboptimally placed catheters can be repositioned before recovery room discharge. Although studies were published (during the writing of this thesis) investigating the required local anaesthetic volume for single injection ultrasound guided interscalene block, no previous studies had been conducted to determine the optimal volume and concentration for the primary local anaesthetic bolus administered via the catheter.

The following section contains an unaltered reproduction of the article “Importance of Volume and Concentration in Preventing Recovery Room Pain and Minimising Motor Block after Shoulder Surgery” published in the journal *Anesthesiology*. The 2010 impact factor of the journal at 5.39 was the highest in the Anaesthesia field.
Importance of Volume and Concentration for Ropivacaine Interscalene Block in Preventing Recovery Room Pain and Minimizing Motor Block after Shoulder Surgery


ABSTRACT

Background: This three-staged study estimated the volume and concentration of interscalene ropivacaine that would prevent recovery room pain after shoulder surgery under general anesthesia.

Methods: Stages 1/2: Interscalene catheter administration of ropivacaine was by a 10% incremental up–down sequential manner depending on the presence of recovery room pain in the previous patient. Stage 1: Ropivacaine (0.5% volume) was varied from 30 mL. Stage 2: Ropivacaine (20 mL, the ED(volume)20 estimate from stage 1) concentration was varied from 0.45%. Stage 3: Subjects were randomly assigned to receive 30 mL of ropivacaine, 0.5% (“conventional dose”), or 20 mL of ropivacaine, 0.375% (the estimated ED(volume + concentration)20 from stages 1/2). A postoperative dermatome infusions of 0.2% ropivacaine (2 mL/h) was administered. Grip strength was measured in the recovery room and time to first pain at 24 h.

Results: Stage 1 (n = 34): Ropivacaine 0.5% ED(volume)100/ED(volume)20 (95% CI) estimates were 2.78–20.5 mL (2.4–9.5) 17.3–25.8. Stage 2 (n = 29): Ropivacaine 20 mL ED(concentration)20/ED(concentration)100 (95% CI) estimates were 0.15/0.34% (0.13–0.30.90.29–0.43). The ED(dose)20 was similar for stages 1/2 (13.5 vs. 30 mg), but the ED(dose)20 was higher for stage 1 (102.5 vs. 68 mg). Stage 3 (n = 40): Satisfaction (0–10) was modestly higher for the lower dose (median [interquartile range] = 10 [10–10] vs. 9 [8–10]). P < 0.007. Pooled data regression analysis showed that increasing ropivacaine concentration increased grip weakness but not block duration.

Conclusions: Ropivacaine interscalene block requires a threshold volume and concentration, with concentration primarily determining motor block. When combined with continuous blockade, suprathreshold ropivacaine doses do not significantly prolong primary block duration but may compromise patient satisfaction.
little is known regarding the optimal primary bolus dose of interscalene local anesthetic required to prevent recovery room pain, minimize motor block, and prolong block duration after shoulder surgery.\textsuperscript{3-11}

With the commonly used combined interscalene block/general anesthesia approach to anesthesia/analgesia for shoulder surgery, the relative role of nerve blockade for postoperative analgesia assumes greater importance over the requirement for surgical anesthesia and so does the duration of effect of the block. However, adding a continuous interscalene infusion to a single injection block renders the duration of action of the preoperative local anesthetic bolus less important and, therefore, allows the administration of a lower primary local anesthetic bolus dose, which might theoretically reduce block-related side effects: mild dyspnea, hoarseness, pruritis, and motor block.\textsuperscript{12} Many patients experience dissatisfaction with a densely blocked hand. Furthermore, time required for surgery can be problematic when early active (as opposed to passive) physiotherapy is planned, such as following procedures for "frozen shoulder" and some shoulder replacement surgeries.\textsuperscript{13} However, reducing the preoperative local anesthetic dose could potentially shorten the duration of potent post shoulder surgery analgesia and, therefore, result in an earlier time to first demand for analgesic rescue. This is relevant not only for single injection techniques but also for ambulatory patient-controlled interscalene analgesia where a well-accepted limitation is early ambulatory pump exhaustion.\textsuperscript{14}

The primary aim of this study was to estimate, at a predetermined ropivacaine concentration and then volume, the ED(\text{vol})\textsubscript{50}/ED(\text{vol})\textsubscript{50}, and ED(\text{conc})\textsubscript{50}/ED(\text{conc})\textsubscript{50}, that is, the volume and concentration respectively, of interscalene ropivacaine that in 50 or 95% of patients would prevent recovery room pain in those who had undergone shoulder surgery under general anesthesia. Secondary aims were to evaluate the relative influence of local anesthetic volume and concentration on recovery room hand strength and time to the first onset of operative site pain.

Materials and Methods

Following institutional review board (Northern Y Regional Ethics Committee, Hamilton, New Zealand) approval and trial registration (ANZCTR—12609000347268), American Society of Anesthesiologists physical status 1 to 2 patients scheduled for elective shoulder surgery in two of the authors’ practices (M.F. and A.W.) were recruited. Exclusion criteria included patient refusal of interscalene block, severe respiratory disease, known allergy to amide local anesthetic drugs, and preoperative opioid therapy administered for more than 1 month before surgery. Written informed consent was obtained from all patients.

Oral acetaminophen (1 g) with or without diclofenac slow-release (75 mg) and omeprazole (20 mg) were administered 1 h before surgery. Intravenous sedation up to 2 mg of midazolam and 0.5 mg of alfentanil was administered 5 min before catheter placement. A superficial cervical plexus block was administered to all patients to facilitate catheter placement and ensure blockade of the supraclavicular nerves.

Perineural Catheter\textsuperscript{44}

A perineural catheter was placed by one of two investigators (M.F. and A.W.), both of whom were experienced in ultrasound and nerve stimulation-assisted interscalene catheter insertion. The scalene muscles and interscalene brachial plexus were imaged in the short axis at approximately the level of the 6th or 7th cervical vertebra with a 38-mm 13-6 MHz linear ultrasound probe (SonoSite HFL1 MicroMaxx, Bothell, WA). A 3.8-cm 18G insulated Tuohy needle (Cortiplex Tuohy, B Braun, Bethlehem, PA) was inserted at the posterior border of the sternocleidomastoid muscle approximately 3 cm cephalad of the level of the 6th or 7th cervical vertebra. The needle was advanced using out-of-plane needle-probe orientation, and was guided superficially in an anteroposterior direction, into the middle scalene muscle until tissue displacement was observed just lateral to the two most superficial elements of the brachial plexus. At the 6th or 7th cervical vertebral level, these correspond to the 5th or 6th cervical roots/superior-middle trunk. The tip of the needle was then angled medially toward the two most superficial brachial plexus roots/trunks until a resultant median movement was observed. The position of the needle tip was ultimately determined by the injection of 10 mL dextrose, 5%, and observation of injectate spread immediately lateral to the target roots/trunks, or alternatively by elicitation of a sustained defet or biceps motor response at less than 0.5 nA (0.1 mV, 2 Hz) (Pajunk Vario, Tucker, GA). The choice of endpoint was left to operator experience or preference based on the results of a recent study.\textsuperscript{15} In both groups, a non-stimulating multifixed catheter was advanced blindly and then withdrawn such that 2 cm of catheter remained past the original needle tip position.

The study was conducted in three stages, each stage having a different protocol for allocating the dose of ropivacaine to be administrated preoperatively via the catheter as follows:

**Stage 1 and 2.** By using up-down sequential dose allocation (in increments of 10% of the starting volume/concentration) depending on the presence or absence of pain in the recovery room in the previous patient, that is, if the previous patient had a successful block, the dose of ropivacaine for the subsequent patient was reduced by 10%. If the block was unsuccessful, the dose was increased by 10%. Block success was defined as the worst numerical rating pain score (NRPS) (0–10) in the shoulder, upper arm, or elbow on emergence of 2 or less without the requirement for any additional rescue local anesthetic bolus.

**Stage 1.** The ropivacaine concentration was set at 0.5%, and the volume was sequentially allocated in increments of 3 ml with a starting volume of 30 ml.

**Stage 2.** The ropivacaine volume was set at 20 ml, and the concentration was sequentially allocated in increments of 0.05%, with a starting concentration of 0.45%. The volume of 20 ml was based on the a priori plan of using the ED(\text{vol})\textsubscript{50}.
(the volume estimate of ropivacaine 0.5% that would prevent recovery room pain in 95% of patients) determined in stage 1 of the study.

**Stage 3.** Patients were randomly assigned to receive a "conventional" dose of 30 ml of ropivacaine (0.5%)3,5-7,16 or a new dose (as determined during stages 1 and 2) that was estimated to prevent recovery room pain in 95% of patients. Randomization was performed using a computer random number generator and implemented using a sealed opaque envelope system, with group allocation being revealed immediately after catheter placement. The purpose of stage 3 was to allow a randomized comparison between two clinically relevant doses.

**Intraoperative Management**

For the reasons stated previously, all patients were given a standardized light general anesthetic (end-tidal minimum alveolar concentration 0.8-1.0) using a laryngeal mask airway, desflurane anesthesia, and spontaneous respiration. Sensory and motor testing before surgery was not performed. No long-acting opioid was administered; however, 0.25 mg of alfentanil was administered as required for a respiratory rate more than 25.

**PACU Protocol**

In the postanesthesia care unit (PACU), patients reporting an NRPS of more than 2 were first given a bolus of 10 ml of lidocaine (1%). If the NRPS subsequently remained more than 2, the catheter was withdrawn 1 cm and an additional 10 ml lidocaine, 1%, was administered. If the NRPS still remained more than 2, the catheter was replaced (table 1). In stages 1 and 2, the patients who received a replacement catheter were excluded from subsequent analysis; in stage 3, the patient was retained on an "intention-to-treat" basis with the randomly allocated ropivacaine dose repeated via the replacement catheter. In stages 1 and 2, patients who received a replacement catheter did not influence the management of subsequent patients in the up-down sequential dose allocation stages of the study, that is, the next patient received the same dose as the patient having just received the replacement catheter. Patients who achieved an NRPS of 2 or less after a local anesthetic bolus with or without a catheter withdrawal intervention were regarded as having satisfactory catheter placement but an unsuccessful block, that is, during stages 1 and 2, subsequent patients had their ropivacaine dose increased by 10%.

**Table 1. Protocol for Sequential Ropivacaine Dose Allocation (Stages 1 and 2)**

<table>
<thead>
<tr>
<th>NRPS in the PACU</th>
<th>Dose for Next Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRPS ≤ 2</td>
<td>Decrease by 10%</td>
</tr>
<tr>
<td>NRPS ≤ 2</td>
<td>Increase by 10%</td>
</tr>
<tr>
<td>NRPS ≤ 2 with lidocaine bolus</td>
<td>Same</td>
</tr>
<tr>
<td>catheter withdrawal</td>
<td></td>
</tr>
<tr>
<td>NRPS &gt; 2</td>
<td>Same</td>
</tr>
<tr>
<td>despite lidocaine bolus and catheter withdrawal</td>
<td></td>
</tr>
</tbody>
</table>

NRPS = numerical rating pain score; PACU = postanesthesia care unit.

**Postoperative Management**

Postoperative management of the catheter was as described previously.12 Specifically, the patient was monitored via an elastometric pump (PainBuster, Surgical Synergies, Auckland, New Zealand) delivering 2 ml/h with patient-controlled boluses of an additional 5 ml every hour. Patients were instructed to depress the ropivacaine bolus button if the NRPS increased to more than 2. Acetaminophen (1 g every 6 h) and diclofenac (75 mg every 12 h) were continued postoperatively if any postoperative pain occurred. If the NRPS was more than 3 despite regular acetaminophen, diclofenac, and ropivacaine boluses, 100 mg of tramadol slow release was added every 12 h. Discharge home occurred either on the day of surgery or on the morning of postoperative day 1.

**Data Collection**

The operating investigator recorded grip strength in the operative limb using a dynamometer (Jamar, Sammons Preston, Nottinghamsire, United Kingdom), immediately before the administration of intravenous sedation. The needle endpoint used for catheter placement (ultrasound or neurostimulation) and the number of alfentanil (0.25 mg boluses) administered during surgery were also recorded. The patient’s primary PACU nurse recorded the worst NRPS in the PACU and details of catheter interventions. The PACU nurse measured operative limb grip strength just before PACU discharge using the same dynamometer. A research assistant phoned all subjects on the afternoon of postoperative day 1 and questioned for time to first shoulder pain. She also questioned for NRPS, arm numbness or weakness, and satisfaction (0-10; 0 = no pain, numbness/weakness, very unsatisfied; 10 = worst imaginable pain, numbness/weakness, very satisfied) during the first 24 postoperative hours.

**Statistical Analysis**

**Stages 1 and 2.** For each of the stages 1 and 2, the effective 50th and 95th percentiles for volume and concentration were estimated using the  , estimator following application of the pooled conditional violators’ algorithm (also known as isotonic regression).17 Ninety-five percentage CIs were obtained by bootstrapping using the bias-corrected method,18 with 2,000 bootstrap replicates of the original data set generated for each percentile. As a sensitivity analysis, percentiles were also estimated following probit regression, with the delta method used to estimate the appropriate nonlinear combinations of regression coefficients.19 A sample size of 30 was chosen for each up-down sequential stage, with a view to recruiting further patients into a stage if the 95% CI around the percentile estimate was judged unacceptable wide (approximately 7 ml for volume and 0.15% for concentration). In this event, we planned to recruit a further five subjects before recalculating the isotonic estimators. This procedure does not involve multiple testing, as it involves establishing precision rather than performing a statistical comparison.
As the SD for the effective 50th percentiles were unknown, the optimum incremental size (generally accepted as 0.5–2 times the expected SD) could not be calculated; therefore, the incremental size was arbitrarily set at 10% of the starting volume and concentration, an incremental size consistent with similar previous studies.21,22

**Stage 3.** The sample size was based on the time to the first onset of operative site pain. The “new” dose represented a 50% reduction in drug dose, and the primary interest was whether this 50% reduction in dose would negatively impact on the time to first pain. Given that all patients had the benefit of patient-controlled local anesthetic boluses, it was considered that anything less than a 4-h reduction in time to first pain would be clinically unimportant. A previous study reported that time to first pain after shoulder surgery under interscalene block had a mean (SD) of 10 (5) h. Therefore, using this distributional assumption, 40 patients would be required to detect a 4-h reduction in time to first pain (one-sided paired t test, type I error = 0.05, power 80%). However, the analysis of the stage 3 data revealed that approximately 50% of patients had not experienced pain at the time of the 24-h phone consultation. A revised calculation indicated that 40 patients would provide 89% power to detect a 35% reduction (50–15%) in the proportion of patients still pain free at 24 h using a type 1 error rate of 5%. A difference of less than 35% was still considered clinically acceptable in the context of patient-controlled interscalene analgesia.

The proportion of patients in each group pain-free at 24 h was compared using Pearson’s chi-square test. Kaplan–Meier (product-limit) survival curves were also constructed and compared with the log-rank test. The change in grip strength was compared between groups using linear regression (adjusted for baseline grip strength) with robust standard errors. Ordinal outcomes (numerically rated pain, numbness, weakness, and satisfaction) were compared using the Mann–Whitney U test. Pless than 0.05 was considered statistically significant. Two-tailed tests were used for all experimental outcomes.

The associations among ropivacaine volume, concentration, and change in grip strength were investigated using linear regression adjusting for baseline grip strength, whereas the associations of volume and concentration with pain at 24 h were investigated using logistic regression. These analyses used data from all stages of the study. Subjects who had received a rescue local anesthetic bolus in the PACU were included in this analysis.

Other data were summarized using appropriate descriptive statistics (mean and SD for normally distributed or symmetric variables; median and interquartile ranges for skewed variables; number and proportion for categorical variables). All statistical analyses were performed using Stata version 10.0 statistical software (StataCorp LP, College Station, TX).

**Post Hoc Protocol Deviation**

During stage 1, the minimum incremental volume (3 ml) was reached, and there were several successive “successful” blocks at this volume. Consequently (after recruitment of the first 30 patients), the isotonic regression estimate of success at this volume was 58%. To approach ED(min) more closely, it was necessary to reduce the minimum volume, which we arbitrarily set at 1.5 ml, in the event of 3 ml being associated with successful block.

**Results**

One hundred seven patients were recruited. Four patients (two patients each from stages 1 and 2) were excluded after enrollment, one as a result of a protocol deviation during catheter placement, and three as a result of unsuccessful catheter placements. Therefore, 103 subjects completed the study according to protocol and were, thus, retained for analysis. Patient characteristics of all patients and those patients in each group of stage 3 are presented in table 2.

**Stages 1 and 2**

**Stage 1 (n = 34).** The ED(min) 34/ED(min) 35 (95% CI) of ropivacaine (0.5%) estimated by isotonic regression was 2.7/20.5 ml (2.4–9.5/17.3–25.8) and by probit regression 1.6/34.5 ml (–12.1 to 16.9/1.5 to 67.6) (fig. 1).

**Stage 2 (n = 29).** The ED(min) 34/ED(min) 35 (95% CI) of 20 ml ropivacaine estimated by isotonic regression was 0.15/0.34% (0.13–0.30/0.29–0.43) and by probit regression 0.17/0.37% (0.11–0.24/0.21–0.53) (fig. 2).

The ED(min) 34 (95% CI) was similar for stages 1 and 2 (13.5 [12–47.5] ml [26–60] mg), but the ED(min) 35 (95% CI) was higher for stage 1 (102.5 [86.5–129] vs. 68 [58–86] mg).

**Table 2. Patient, Anesthesia, and Surgical Characteristics (Stages 1–3)**

<table>
<thead>
<tr>
<th>Stages</th>
<th>Surgical 3</th>
<th>Male sex</th>
<th>Age, yr</th>
<th>Weight, kg</th>
<th>US (v. NS)</th>
<th>Surgery (n)</th>
<th>Acromioplasty/ excision lateral clavicle</th>
<th>Stabilization</th>
<th>Rotator cuff repair</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 and 2</td>
<td>20 ml 0.375%</td>
<td>45 (71)</td>
<td>40 (16)</td>
<td>76 (14)</td>
<td>65 (88)</td>
<td>19 (50)</td>
<td>26 (44)</td>
<td>15 (23)</td>
<td>1 (11)</td>
<td></td>
</tr>
<tr>
<td>(n = 63)</td>
<td>(n = 21)</td>
<td>(n = 18)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td>(n = 15)</td>
<td></td>
</tr>
<tr>
<td>30 ml 0.5%</td>
<td>16 (76)</td>
<td>44 (16)</td>
<td>85 (14)</td>
<td>21 (100)</td>
<td>3 (14)</td>
<td>8 (38)</td>
<td>8 (38)</td>
<td>2 (10)</td>
<td>3 (16)</td>
<td></td>
</tr>
<tr>
<td>(n = 21)</td>
<td>(n = 10)</td>
<td>(n = 13)</td>
<td>(n = 10)</td>
<td>(n = 13)</td>
<td>(n = 13)</td>
<td>(n = 13)</td>
<td>(n = 13)</td>
<td>(n = 13)</td>
<td>(n = 13)</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as n (%) or mean (SD). NS = neurostimulation; US = ultrasound.
Stage 2 (n = 40)

There was no evidence for an association between dose and pain at 24 h ($P = 0.34$; 8/19 (42%) of patients at the conventional dose were pain-free at 24 h, compared with 12/21 (57%) of patients at the lower dose (table 3; fig. 3).

There was no evidence that grip strength differed between the two groups ($P = 0.81$). There was also no evidence to indicate that pain on movement, numbness, and weakness during the first 24 postoperative hours differed between groups ($P > 0.73$). Satisfaction was modestly higher for the new and lower dose (median satisfaction 10 compared with 9 for the conventional dose, $P = 0.007$). This result should be interpreted with caution, given the small difference and the lack of corresponding differences in other patient-rated outcomes.

Linear regression of all study data found moderate evidence for an association between ropivacaine concentration and grip strength in the PACU after adjusting for baseline grip strength ($P = 0.02$), with PACU grip strength decreasing by 0.7 units for every 0.05% increase in concentration (95% CI 0.1 decrease to 1.3 decrease; fig. 4). However, the aggregated data do not indicate that PACU grip strength differs between the two doses used in stage 3 ($P = 0.90$). No such association was found for ropivacaine volume ($P = 0.91$, 0.01 decrease per 1-ml increase, 95% CI 0.2 decrease to 0.2 increase; fig. 5). There was no evidence that ropivacaine volume ($P = 0.49$) or concentration ($P = 0.93$) was associated with remaining pain-free at 24 h.

Discussion

To our knowledge, this is the first study in humans to investigate, with up-down methodology, the relative importance of both local anesthetic volume and concentration for peripheral nerve blockade, in this instance, as assessed by the prevention of pain after surgery. The current results es-

![Fig. 1. Up–down sequential volume allocation of 0.5% ropivacaine.](image1)

![Fig. 2. Up–down sequential concentration allocation of 20 ml of ropivacaine.](image2)

![Fig. 3. Kaplan–Meier curves for time to first onset of surgical site pain for 0.375% ropivacaine, 20 ml (“new dose”), versus 30 ml of 0.5% ropivacaine (“conventional dose”). Difference between curves was not significant (chi-square test = 0.24; $P = 0.62$).](image3)

Table 3. Outcomes for the “New” vs. “Conventional” Doses (Stage 2)

<table>
<thead>
<tr>
<th></th>
<th>20 ml</th>
<th>30 ml</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.375%</td>
<td>0.5%</td>
<td>Value</td>
</tr>
<tr>
<td>Intraoperative alfentani bolus ≥ 1</td>
<td>4 (19)</td>
<td>3 (16)</td>
<td></td>
</tr>
<tr>
<td>PACU catheter bolus only</td>
<td>1 (5)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>PACU catheter withdrawal + bolus PACU catheter replacement</td>
<td>0 (0)</td>
<td>1 (5)</td>
<td></td>
</tr>
<tr>
<td>PACU grip strength, kgf</td>
<td>30.2 (12.1)</td>
<td>26.6 (8.2)</td>
<td>0.81</td>
</tr>
<tr>
<td>Ward/home</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain free at 24 h</td>
<td>12 (57)</td>
<td>8 (42)</td>
<td>0.34</td>
</tr>
<tr>
<td>Worst NRPS with movement</td>
<td>1 (0–3)</td>
<td>2 (0–3)</td>
<td>0.73</td>
</tr>
<tr>
<td>Numbness NRS</td>
<td>8 (6–10)</td>
<td>10 (7–10)</td>
<td>0.74</td>
</tr>
<tr>
<td>Weakness NRS</td>
<td>9 (7–10)</td>
<td>9 (7–10)</td>
<td>0.78</td>
</tr>
<tr>
<td>Satisfaction NRS</td>
<td>10 (10–10)</td>
<td>9 (8–10)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Data expressed as n (%), mean (SD), or median (interquartile range). kgf = kilogram-force; 1 kgf = 10 N; NRPS = numerical rating pain score (0–10; 0 = no pain, 10 = worst imaginable pain); NRS = numerical rating score (0–10; 0 = no numbness/weakness or very satisfied, 10 = very numb/weak or very satisfied); PACU = postanesthesia care unit.

0.2 increase; fig. 5). There was no evidence that ropivacaine volume ($P = 0.49$) or concentration ($P = 0.93$) was associated with remaining pain-free at 24 h.
Fig. 4. Scattergram of recovery room grip strength by ropivacaine concentration for all patients. Predicted values are shown for a patient with mean preoperative grip strength (41 kgf). After adjusting for baseline grip strength, there was evidence for an association ($P = 0.02$). *kgf = kilogram-force (1 kgf = 10 N).

Fig. 5. Scattergram of recovery room grip strength by ropivacaine volume for all patients. Predicted values are shown for a patient with mean preoperative grip strength (41 kgf). After adjusting for baseline grip strength, there was no evidence for association ($P = 0.91$). One patient at 12 ml volume/grip strength = 65 not plotted. *kgf = kilogram-force (1 kgf = 10 N).

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stages 1 and 2. Moreover, we surmise that just as individual patients may have different responses to the same dose of the same drug delivered in exactly the same location (in relation to the target nerves), the accuracy with which the local anesthetic drug is deposited, in reality, differs between patients. In other words, in 50% of patients in stage 1, the sonographic images and/or needle-to-nerve proximity was probably such that local anesthetic deposition was achieved with an accuracy such that only 3 ml of 0.5% ropivacaine was required for satisfactory blockade: the 50th dose percentiles were consequently relatively similar between stages 1 and 2.

In the other 50% of patients during stage 1, the sonographic images and/or needle-to-nerve proximity was probably less than ideal, such that local anesthetic deposition was less accurate, and, therefore, required a larger volume of ropivacaine. This was also reflected during stage 1 in the very large disparity between the 50th and 95th percentiles for volume. In stage 2, with the administration of a larger volume of ropivacaine (20 ml), the placement accuracy was less critical, as reflected by the less marked difference between the 50th and 95th percentiles for concentration.

The second clinically important finding from this study was the determination of the minimum primary bolus dose of interscalene ropivacaine required to prevent recovery room pain after shoulder surgery. The estimated ED(50)/ ED(95) of ropivacaine, 0.5%, was 2.72/20.5 ml, and the ED(95%)/ED(50%) of ropivacaine 20 ml was 0.15/ 0.34%. In the context of a low-dose postoperative continuous ropivacaine infusion, when compared with a commonly administered interscalene ropivacaine dose (20 ml 0.5%), the administration of the derived ED50 for volume and concentration (20 ml 0.375%) did not compromise postoperative block duration, but it was associated with a modest increase in patient satisfaction. Strictly, on the basis of our data, we cannot conclude for certain the reason for the observed modest increase in patient satisfaction with the new and lower dose of ropivacaine. Previous studies have suggested that an increase in postoperative motor block (as defined by the frequency of episodes of an insensitive or densely blocked upper extremity) is associated with a reduction in patient satisfaction. The current findings are consistent with these previous data, in that an association was demonstrated, from the aggregated data, between ropivacaine concentration (but not volume) and motor block. However, the stage 3 protocol did not allow us to differentiate between the relative role of ropivacaine concentration and the volume, and therefore, any real association between satisfaction and motor block (and by extrapolation, ropivacaine concentration) remains speculative. This potential association should, therefore, be subject to further study.

We were unable to demonstrate an association between ropivacaine concentration and block duration; however, this was almost certainly influenced by the utilization of a continuous ropivacaine infusion (albeit at a lower dose) after the administration of the primary ropivacaine bolus. This
lack of association may have also been influenced by the absence of outcome data for blocks lasting more than 24 h. Our study design incorporated an up-down methodology to accurately determine the 90th percentiles, and then by derivation, the 95th percentiles. This may be seen as a study weakness. It could be argued that a "k-in-a-row" or "biased coin" design focusing on the 95th percentile would be more appropriate. However, utilization of an indwelling catheter readily enables the administration of supplemental local anesthetic only in event of inadequate blockade or recovery room pain. Therefore, primary determination of the 95th percentile (as opposed to the 90th percentile) is not as important when using this analgesic technique. Nevertheless, the use of isostonic regression combined with a relatively large number of subjects enabled the estimation of the 95th percentiles with acceptable precision.

A potential limitation was our method that was used to assess patient satisfaction: a single-dimensional numerical rating scale at 24 postoperative hours. However, patient satisfaction is a complex multidimensional concept and best quantified using an instrument that has undergone appropriate psychometric validation.23 Use of such an instrument would have increased the validity of our results. A well-recognized limitation of simple one-dimensional scales is that most patients reporting pain tend to report high scores, and further, their ability to detect subtle changes is limited.24,25 Nevertheless, in the current study, a difference in satisfaction was demonstrated using a scale similar to an instrument previously shown to demonstrate convergent validity with a psychometrically constructed expanded 40-item questionnaire.26 Another limitation was the protocol for the management of patients reporting pain in the PACU, which included a catheter withdrawal intervention (of 63 patients in stages 1 and 2). This may not reflect typical practice in other settings. Furthermore, including these "suboptimal" catheters in the up-down sequential dose allocation might seem inappropriate; however, a comprehensive review of this study methodology suggested that these patients should be included in up-down sequencing as removing them would misleadingly underestimate the respective percentiles.17

One of the goals of reducing the preoperative ropivacaine dose was to reduce motor block. Our previous experience had revealed that some patients experience dissatisfaction with a paralyzed hand, despite reassurance that this usually resolves with resolution of the primary block. Motor blockade can also be problematic when early active physiotherapy is planned or in some arthroplasty procedures (e.g., "reverse" shoulder joint replacement), where there is a risk of joint dislocation from relaxation of the rotator cuff muscles.27 However, it should be recognized that dense motor block of the entire upper extremity can be advantageous during emergence from general anesthesia, to protect some surgical repairs, for example, rotator cuff repair. In these patients, it may be preferable to use a short-acting local anesthetic (e.g., lidocaine, mepivacaine) at a concentration likely to result in motor block, with or without a long-acting agent (e.g., 10 ml ropivacaine, 0.75%, diluted with 10 ml lidocaine, 1–2%).

Although an association between ropivacaine concentration and motor block was demonstrated, patients were not assessed for other interscalene block–related side effects such as dyspnea, hoarseness, and paresis. Previous investigators have already demonstrated a clear association between local anesthetic volume and phrenic nerve blockade as assessed by objective measures of diaphragmatic function.19,20 It would be tempting to speculate that hoarseness and Horner’s syndrome are also volume- and dose-dependent given that these side effects require local anesthetic to have to spread to the adjacent recurrent laryngeal nerve and sympathetic chain. If the goal is the prevention of recovery room pain and extended postoperative analgesia, the results of this study show that in the context of a low-dose postoperative ropivacaine infusion, there is little advantage in administering a primary bolus dose of more than approximately 20 ml of 0.34% ropivacaine.

Finally, caution against the extrapolation of our results to other nerve block locations. Intuitively, the demonstrated critical importance of both local anesthetic volume and concentration could be expected to apply to other peripheral nerve block locations; however, quantitatively, the current results can only really be applied to the interscalene area. In summary, on the basis of the estimates for the ED(wo).<sub>50</sub> and ED(conc).<sub>50</sub>, in the context of patient-controlled interscalene analgesia, we recommend 20 ml of 0.375% ropivacaine as a convenient dose (0.75% 10 ml + 10 ml diluent) that will prevent recovery room pain in approximately 95% of patients. Using a higher primary ropivacaine bolus dose will not increase peripheral block duration but may compromise patient satisfaction. Finally, on the basis of the observed disparity between the ED(dose).<sub>50</sub> estimates when varying either drug volume or concentration, which is in keeping with previous laboratory studies in animals,28 this study provides a compelling argument for future peripheral nerve block dose-finding studies incorporating methodology to estimate the required threshold for both drug volume and concentration.

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4.2. Discussion

4.2.1. Contribution and significance

The study conducted in this chapter investigated the effect of local anaesthetic volume and concentration on recovery room pain, motor block and block duration. The estimated $ED_{vol50}/ED_{vol95}$ of ropivacaine 0.5% was 2.7/20.5 mL and the $ED_{conc50}/ED_{conc95}$ of ropivacaine 20 mL was 0.15/0.34%. Comparison of the derived optimal dose (20 mL ropivacaine 0.375%) with a higher conventional dose (30 mL 0.5%) demonstrated improved satisfaction with the “optimal” dose. Ropivacaine concentration was inversely associated with recovery room grip strength but not block duration.

This was the first investigation in humans, using up-down methodology, to identify the relative importance of both local anaesthetic volume and concentration for peripheral nerve blockade. Previous studies have simply compared 2 different combinations of volume and concentration at a fixed total dose. This study was also the first to investigate the optimal primary bolus dose of local anaesthetic to administer via an interscalene catheter as opposed to the block needle. As previously mentioned, administration of the primary bolus dose of local anaesthetic via the catheter is advantageous in that it provides confirmation of catheter plexus proximity. Administration of the primary bolus dose via the needle leaves the operator less sure about satisfactory catheter-plexus proximity until the primary local anaesthetic bolus has resolved – typically 12 hours following the first dose.
Regarding the estimates for ropivacaine volume and concentration, animal studies have shown that nerve blockade is dependent on a minimum drug concentration sufficient to inhibit \( \text{Na}^+ \) channels to the point of impulse failure, and a minimum length of nerve exposed to the drug to render a segment of the nerve ‘non-excitable’, thus preventing the impulse from ‘jumping over’ the blocked segment. Exposure of a minimum length of nerve to local anaesthetic is primarily dependent on drug volume. \(^{156,157}\) Of local anaesthetic concentration and volume, concentration is the main determinant of the intensity and duration of functional nerve blockade, as volumes administered in vivo are typically higher than those required to block the critical length of nerve in vitro (with nerve exposure by dissection and subsequent direct application of local anaesthetic). Furthermore, for plexus blocks, administered volumes are typically even higher (than tightly controlled animal studies of individual nerves) as local anaesthetic volume is additionally required to enable the spread of local anaesthetic drug to the nerves innervating the target area (e.g. 5th-6th cervical nerve roots for shoulder surgery). The estimated \( \text{ED(volume)}_{95} \) for ropivacaine 0.5% was 20.5 \( \text{mL} \), a volume almost identical to that estimated by Casati et al\(^{158}\) as being required to block femoral nerve distribution pin-prick sensation. This contrasts with the findings from a recent study of 11 patients undergoing axillary brachial plexus block, \(^{159}\) and a study of 17 volunteers in which the \( \text{ED(volume)}_{95} \) of mepivacaine 1% required to block the ulnar nerve was approximately 0.11 \( \text{mL} \cdot \text{mm}^{-2} \) nerve cross sectional area. \(^{160}\) The estimated ropivacaine \( \text{ED(volume)}_{95} \) from the present study is substantially higher than that estimated from the previous studies and could be explained by patient factors (large heterogeneous patient group vs. small number of volunteers, the plexus occupying a larger surface area vs. single nerve), the block technique (single point injection vs. multi-point injection) or differences in the
outcome measurements (analgesia vs. loss of pin-prick sensation, different statistical estimators).

4.2.2. Limitations

It should be noted that the study in this chapter was undertaken in the context of shoulder surgery performed under combined interscalene block/general anaesthesia. Shoulder surgery under interscalene block is usually combined with general anaesthesia in order to improve patient acceptance, particularly when performed in the lateral or steep sitting (‘beach chair’) positions. 114, 141, 153 Supplementing interscalene block with general anaesthesia also accelerates time to surgical readiness, which can be important in practice settings where the anaesthesiologist has to both place blocks and also administer monitored anaesthesia care. However, it should be noted that the estimates for ropivacaine volume and concentration apply only to interscalene block combined with general anaesthesia, and not awake shoulder surgery performed under interscalene block alone. Local anaesthetic concentration was fixed first to derive the optimal local anaesthetic volume and then volume to derive the optimal concentration. It is conceivable that first fixing volume may have produced different estimates for the optimal volume and concentration. The former approach was chosen because ropivacaine 0.5% is a widely accepted concentration for peripheral blocks. Another limitation was the heterogeneous nature of the surgical procedures – a factor that may have influenced block success during the up-down methodology. In fact, a significant proportion of patients receiving the 3 mL volume underwent simple arthroscopic acromioplasty, which may not be associated with the same requirement for regional blockade than more extensive procedures such as total shoulder joint replacement. The closeness of the total local
anaesthetic dose used between “optimal” and “traditional” in stage 3 may explain the lack of treatment effect demonstrated. A higher traditional dose $^{34}$ may have resulted in a between group difference. Finally, operator experience may have influenced the findings, thus the results may not apply to less experienced practitioners.

Although the focus of the present study was on local anaesthetic injection via the catheter, there are two situations where primary local anaesthetic bolus administration via the catheter may not be indicated. The first is to maximise surgical anaesthesia success; the second to maximise analgesic success during the first 12 hours. For these goals, it may be preferable to inject local anaesthetic through the needle, so that the needle can be repositioned depending on the observed local anaesthetic spread. Certainly for sciatic block, studies have shown that to maximise primary block success, a two point subfascial local anaesthetic injection is preferable to a single injection. $^{161}$ This approach would require local anaesthetic injection through the needle following needle repositioning after the first half of the injection.

4.2.3. Literature following

Subsequent to this study being published, similar up-down dose finding studies for interscalene block appeared. Unfortunately, these studies used the surrogate outcome of observer assessed sensory and motor block, rather than a concrete outcome such as successful surgical anaesthesia or absence of pain on emergence. Gautier et al’s single injection block study was stopped after 10 successful blocks using 5 mL ropivacaine 0.75%, but rightly concluded that the lower limit of the confidence interval does include the possibility of a 25% failure rate at that dose. $^{162}$ Falcao et al using similar methodology calculated the ED$(vol)_{90}$ as 0.95 mL, but again the use of
a surrogate outcome for block success makes the study difficult to compare to the study in the current chapter. Vandepitte performed an up-down dose finding study using ropivacaine 0.75% and also used a surrogate outcome for block success. Their calculated ED(\text{vol})_95 for ropivacaine 0.75% was 7 mL, which is comparable with the present study. Furthermore, Vandepitte et al constructed dose-response curves which suggested that 7 mL was the threshold volume, below which block success reduced steeply. Dose-response curves were not conducted for the present study, but may have provided additional insights.

### 4.2.4. Future directions

Even though this study used block duration as a study outcome, stage three of the study only had 89% power to detect a 35% difference in the proportion of patients reporting pain at 24 hours. Therefore, further study with higher statistical power would be beneficial in assessing whether in fact, local anaesthetic volume and concentration has an influence on block duration. Block duration is not only relevant for single injection blocks, in that the risk of local anaesthetic toxicity is theoretically reduced, but it is also relevant for ambulatory continuous interscalene analgesia as ambulatory pump reservoir exhaustion can be an important clinical issue. Indices of phrenic nerve dysfunction were not assessed during the present study and future dose finding studies should ideally assess this outcome.
Chapter 5. Randomised study of the effect of local anaesthetic volume and concentration on the duration of peripheral nerve blockade

5.1. Preface

The study conducted in Chapter 4 used block duration as a study outcome, but was inadequately powered to draw conclusions about the influence of local anaesthetic dose. Block duration has relevance not only for single injection blocks, but also continuous techniques. This relates to ambulatory pump depletion which have a finite reservoir volume – a longer duration for the primary local anaesthetic bolus will reduce the requirement for rescue boluses during the first 12-24 hours, which will enable a longer pump duration for a given reservoir volume. 87,138,165 As stated, the study in Chapter 4 had low power to detect a clinically relevant block duration change (89% power for a 35% difference between groups in the proportion of patients pain free at 24 hours). The study conducted in Chapter 4 also suggested an inverse association between motor block and patient satisfaction. Block duration (and therefore motor block) and patient satisfaction may therefore be associated. The study conducted in this chapter was therefore conducted primarily to detect whether local anaesthetic volume and concentration affects block duration.

The following section contains an unaltered reproduction of the online advanced access version of the article “Randomised Study of the Effect of Local Anaesthetic Volume and Concentration on the Duration of Peripheral Nerve Blockade” published in the journal Regional Anesthesia and Pain Medicine. Regional Anesthesia and Pain Medicine is the official journal of the American Society of Regional Anesthesia
(ASRA). The journal covers research in the fields of regional anaesthesia and pain medicine, and in 2011, had an impact factor of 4.079.
Randomized Study of the Effect of Local Anesthetic Volume and Concentration on the Duration of Peripheral Nerve Blockade

Michael J. Fredrickson, MD, FANZCA,*† Amitha Aberysekera, FANZCA,† and Richard White, MA‡

Background and Objectives: Ultrasound guidance reduces the required local anesthetic volume for successful peripheral nerve block, but it is unclear whether this influences block duration. We investigated the ropivacaine volume and concentration effect on interscalene block duration.

Methods: One hundred eighty-five patients were randomized to 5 ropivacaine volume/concentration combinations (0.75%, 1, 16, and 20 mL; 0.375%, 20 and 40 mL) administered preoperatively via an interscalene catheter before shoulder surgery under general anesthesia. An elastometric ropivacaine infusion commenced at the onset of pain. Patients were questioned at 24 hours primarily for the primary outcome: time to first pain. Group 5 mL was excluded post hoc because of an unacceptably high block failure rate. Multivariate Cox regression was used to assess the effect of volume and concentration (each corrected for the other) on the primary outcome.

Results: Probability of pain as a function of time was associated with not only dose, but also volume corrected for concentration and concentration corrected for volume: hazard ratio (95% confidence interval) for dose = 0.992 (0.987–0.997) (P = 0.002), volume = 0.959 (0.937–0.982) (P = 0.001), concentration = 0.852 (0.743–0.976) (P = 0.021). Increasing the volume of ropivacaine 0.375% from 10 to 40 mL was estimated to increase median (quartiles) block duration from 10.0 (9.5–11.5) to 15.0 (10.75–21) hours. Similarly, increasing the concentration of 20 mL ropivacaine from 0.375% to 0.75% was estimated to increase median (quartiles) block duration from 10.75 (9.75–14.0) to 13.75 (10.5–21.0) hours.

Conclusions: Block duration is influenced by both local anesthetic volume and concentration, a finding of increasing relevance with the current trend to lower volumes for ultrasound-guided regional anesthesia. (Reg Anesth Pain Med 2012;00: 00-00)

Although peripheral nerve blocks have been used for more than a century, no previous studies have evaluated the effect of local anesthetic volume and concentration primarily on block duration. Of previous modern studies that incorporated block duration as a study outcome, 1,4,9 2 methodological issues limited their interpretation. Block duration was either a secondary outcome, 1,2,4,7,9 or volumes/concentrations were administered using different neurolocalization techniques. 8,9

The importance of this knowledge deficit has gained new relevance because of the recent increase in popularity of ultrasound-guided regional anesthesia. Ultrasound guidance reduces the required local anesthetic volume for successful block, a factor resulting in a recent trend for administering lower local anesthetic volumes for regional anesthesia. 1,5,8,10,12 Block duration has clinical importance, as it is a well recognized key to the effectiveness of regional anesthesia for postoperative analgesia.

Compared with other blocks, in particular, those involving the lower extremity, interscalene block for shoulder surgery represents an ideal block-procedure combination to test the effect of local anesthetic volume/concentration on block duration: a block provided from a single injection can provide complete analgesia to the operative area.

We performed a prospective randomized trial to investigate the impact of local anesthetic volume (and concentration), primarily on the duration of interscalene block as assessed by the time to first pain after shoulder surgery. We hypothesized that block duration would be dependent on each variable. We also evaluated the effect of these variables on postoperative analgesia effectiveness and block-related adverse effects.

METHODS

The local institutional review board (Northern Y Regional Ethics Committee, Hamilton, New Zealand) approved the trial. Primary and secondary endpoints, including the specific timing of their measurement together with the intended sample size, were prespecified before trial commencement (ie, "a priori") 14 at the Australian and New Zealand Clinical Trials Registry (ACTRN12611001555998, February 2011). A statement regarding the background and rationale for the trial was also made at this time. The primary statistical method, which was regression analysis, was stated on record in the ethics committee application. We enrolled consenting consecutive adult patients, American Society of Anesthesiologists physical status 1 to 3, of all body mass indices, aged 16 to 80 years, scheduled for elective shoulder surgery in the investigators’ practice at the Southern Cross Brightside (M.J.E) and North Harbour (A.A.) Hospitals from February through December 2011. We excluded subjects who refused brachial plexus block, had known neuropathy involving the arm undergoing surgery, had known amide local anesthetic allergy, or received preoperative opioid therapy administered for more than 1 month before surgery. Written and oral informed consent was obtained from all patients, and the trial was in keeping with the Helsinki Declaration. A research assistant made the initial invitation for participation, but definitive recruitment was by the operating investigator. The design was a dual-center, prospective, randomized, observer-blinded trial.

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The authors declare no conflict of interest.

This study has not been presented in any meeting.


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Study Interventions and End Points

The randomly assigned groups were ropivacaine 0.75%, 5, 10, and 20 mL and 0.375% 20 and 40 mL. The primary end point was time to first shoulder pain. The main secondary end points were numerically rated pain, tramadol consumption, numerically rated hand numbness/weakness, and adverse effects during the first 24 hours.

Randomization and Blinding

One hundred eighty-five patients were randomly assigned to the 5 combinations of ropivacaine volume and concentration. Randomization was not procedure or operator stratified. Using a computer-generated random number in blocks of 20 (www.random.org), random assignment to the 5 groups was implemented by a research assistant remote from the study procedures. Because of a higher-than-expected exclusion rate because of recovery room pain in groups 5 and 10 mL, from patient ID 130 onward, randomization was modified to increase the number of patients assigned to these groups. Randomization was to 7 groups as follows: 1 + 2 = 5 mL 0.75%, 3 + 4 = 10 mL 0.75%, 5 + 20 mL 0.375%, 6 = 20 mL 0.75%, and 7 = 40 mL 0.375%. Group concealment was by 185 prepared, sealed opaque envelopes, opened immediately after catheter placement.

Anesthesia and Analgesia

A standardized technique was used.15 Multimodal oral analgesia consisted of oral acetaminophen 1 g (started 1 h before surgery) and intraoperative intravenously administered paracetamol 0.5 mg/kg to a maximum of 40 mg. A hospital policy change in August 2011 mandated a change in acetaminophen administration from preoperative oral to intravenous intravenously administered.

Intravenous sedation up to midazolam 2 mg and alfentanil 0.5 mg was administered immediately outside the operating room. Both investigators, who were experienced with this procedure, performed all blocks.

Perineural Catheter Placement

To facilitate catheter placement and ensure supracricoid nerve(s) blockade, a "modified"16 superficial cervical plexus block was first placed, using a 22-gauge, 2-in (5-cm) B-Plex needle (Plexusfix, BiBraun, Bethlehem, Pennsylvania) bent by hand at its midpoint to 30 degrees to facilitate subcutaneous injection.17 Subsequently, an ultrasound-guided (SonoSite HFL-3M-Turbo; SonoSite, Bothell, Washington) anterolateral approach intercalene catheter was placed, using a previously described technique (see www.ultrasoundblock.com).13 A 10-mL, 5% dextrose-filled syringe connected to a nerve stimulator (Pajunk Varito, Tucker, Georgia) set at 0.8 mA (0.1 ms, 2 Hz) was inserted approximately 1 cm posterior to the sternomastoid muscle dorsal border approximately 3 cm cephalad of the sixth/seventh cervical vertebral level. Appropriate root/trunk visualization (fifth and sixth cervical roots/superior or middle trunks) was confirmed by brief elicitation of a deltoid, biceps, or triceps motor response, with final needle tip position confirmed by the injection of 10 mL 5% dextrose and observation of injectate spread directly lateral to the target roots/trunks. If motor responses persisted or reappeared after dextrose injection, sonography was abandoned (to free up a hand), and the current reduced from 0.8 mA until responses ceased. This needle end point was still labeled as an ultrasound end point because the end point was primarily based on dextrose visualization rather than deliberate elicitation of a sustained motor response. If a satisfactory brachial plexus ultrasound image could not be obtained, appropriate needle tip position was confirmed by elicitation of a sustained deltoid, biceps, or triceps motor response at less than 0.5 mA. This needle end point was designated a neurostimulation end point because it was based primarily on neurostimulation rather than ultrasound.

A nonstimulating catheter was blindly advanced several centimeters beyond needle tip, and then after needle withdrawal, the catheter was withdrawn 3 cm of catheter remained past the original needle tip position.

Intraoperative Management

General anesthesia was also standardized using a laryngeal mask airway and spontaneous desflurane respirations (end-tidal minimum alveolar concentration, 0.8–1.0). After general anesthesia induction but before surgery, the studied ropivacaine bolus was injected using a 20-mL syringe at a rate of approximately 10 mL/min (5 mL = 30 s, 40 mL = 4 min; flow rate expected, ~400 mL/h). No long-acting opioid was administered; however, alfentanil 0.25 mg was administered pro re nata for a respiratory rate greater than 25 breaths/min.

Postanesthesia Care Unit Protocol

In the postanesthesia care unit (PACU), patients reporting a numerical rating pain score (NRPS, 0–10) of greater than 2 were excluded from further data collection. These patients received a 20-mL bolus of local anesthetic and morphine 2 mg every 2 to 3 minutes to achieve an NRPS of 2 or less. If the NRPS remained greater than two 60 minutes after the local anesthetic bolus, the catheter was replaced.

Postoperative Management

An elastomeric pump preset to deliver ropivacaine 0.2% at 2 mL/h with patient-controlled 5-mL boluses of up to 1 bolus every hour (PainBuster; Surgical Synergies, Auckland, New Zealand) was connected to the catheter but was clamped off with a screw clamp on the tubing distal to the bolus device. At the onset of operative site pain, patients or nurses removed the clamp and delivered the first ropivacaine bolus. From the onset of shoulder pain until 48 hours postoperatively, patients depressed the ropivacaine bolus button “on the clock” every 6 hours irrespective of the NRPS.15 Additional 5-mL boluses were administered in between mandatory 6 hourly boluses if the NRPS increased to more than 2. Multimodal analgesia was continued after surgery; acetaminophen (1 g every 6 h) and dicyclofenac slow release (75 mg every 12 h) if any postoperative pain occurred; tramadol slow release (100 mg every 12 h) if the NRPS increased to greater than 2 despite regular acetaminophen, dicyclofenac, and 2 consecutive ropivacaine boluses. Home discharge occurred on the day of surgery, day 1 (all open procedures), or, for total shoulder joint replacement, on day 2.

Data Collection

The operating investigator recorded the catheter placement needle end point (ultrasound or neurostimulation) and the specific motor response with current threshold. The principal investigator also recorded the number of alfentanil 0.25-mg boluses administered during surgery. The patient’s primary PACU nurse recorded the emergence NRPS in the shoulder, arm, or elbow and details of PACU interventions (local anesthetic bolus, morphine rescue). After surgery, patients were instructed to note when they first experienced pain. A research assistant phoned all subjects at 24 postoperative hours and questioned for time to first pain, supplemental tramadol consumption, ropivacaine bolus demands, numerically rated pain (worst and “average”),

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TABLE 1. Patient and Surgical Characteristics (n = 185)

<table>
<thead>
<tr>
<th></th>
<th>5 mL 0.75% (n = 40)</th>
<th>10 mL 0.75% (n = 41)</th>
<th>20 mL 0.375% (n = 35)</th>
<th>20 mL 0.75% (n = 33)</th>
<th>40 mL 0.375% (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>24 (60)</td>
<td>30 (73)</td>
<td>22 (63)</td>
<td>24 (73)</td>
<td>29 (81)</td>
</tr>
<tr>
<td>Age, y</td>
<td>49 (12)</td>
<td>48 (15)</td>
<td>49 (16)</td>
<td>49 (14)</td>
<td>46 (18)</td>
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<td>Weight, kg</td>
<td>83 (53–121)</td>
<td>85 (47–115)</td>
<td>83 (52–134)</td>
<td>86 (64–125)</td>
<td>87 (61–125)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28 (19–45)</td>
<td>29 (19–41)</td>
<td>27 (18–47)</td>
<td>29 (21–38)</td>
<td>29 (20–39)</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open rotator cuff repair</td>
<td>6 (15)</td>
<td>12 (30)</td>
<td>9 (26)</td>
<td>11 (33)</td>
<td>9 (26)</td>
</tr>
<tr>
<td>Arthroscopic rotator cuff repair</td>
<td>12 (30)</td>
<td>9 (22)</td>
<td>8 (24)</td>
<td>8 (24)</td>
<td>7 (21)</td>
</tr>
<tr>
<td>Arthroscopic stabilization</td>
<td>5 (12)</td>
<td>8 (20)</td>
<td>9 (26)</td>
<td>8 (24)</td>
<td>11 (31)</td>
</tr>
<tr>
<td>Arthroscopic lateral clavicle resection</td>
<td>4 (10)</td>
<td>3 (8)</td>
<td>2 (6)</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Arthroscopic acromioplasty</td>
<td>8 (20)</td>
<td>6 (15)</td>
<td>9 (26)</td>
<td>3 (9)</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Arthroscopic capsular release</td>
<td>2 (5)</td>
<td>1 (2)</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Total shoulder joint replacement</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>4 (12)</td>
<td>2 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (5)</td>
<td>1 (2)</td>
<td>2 (6)</td>
<td>2 (6)</td>
<td>2 (6)</td>
</tr>
</tbody>
</table>

Values are mean (SD), mean (range), or n.

hand numbness/weakness, and satisfaction during the previous 24 hours (0–10, 0 = no pain, numbness/weakness, very unsatisfied; 10 = worst imaginable pain, numbness/weakness, very satisfied). Patients were also questioned for breathlessness or difficulty taking a deep breath present at any time during the previous 24 hours.

Statistical Analysis

An independent statistician (R.W.) performed all calculations. After trial conclusion, we excluded all group 5 mL patients from post-PACU discharge data analysis because of an unacceptably high block failure rate and therefore a high probability that the remaining pain-free patients in this group would not represent the population (eg, more accurately placed catheters and/or patients with "higher pain thresholds").

Because the primary outcome was subject to 2 variables (volume and concentration), it was not appropriate to analyze this outcome by simply comparing the raw data from each group (eg, using the Mann-Whitney U test), as the relative influence of each variable would remain unknown. Instead, a multivariate regression method was used; it tests for the effect of the variable of interest (eg, volume) "controlled" for another variable (called a covariate; eg, concentration) on the outcome of interest (time to first pain). A significant proportion of patients had not reported pain by the 24-hour follow-up time point. Therefore, survival analysis was used; we used a Cox proportional hazards model, which is a multivariate regression method specific for survival data. The effect of the variable of interest is expressed as a hazard ratio, which is the probability of pain at a particular time for a 1-unit increase in the variable of interest relative to a specified value (called the baseline level). This hazard ratio assumes the subject has no pain up until that time. The Cox proportional hazards model also assumes that the effect of the variable of interest, relative to the baseline, is constant over time. Variables incorporated into the Cox proportional hazards model included dose, volume, and concentration. Because hazard ratios

TABLE 2. Catheter Placement and Intraoperative and PACU Interventions (n = 185)

<table>
<thead>
<tr>
<th></th>
<th>5 mL 0.75% (n = 40)</th>
<th>10 mL 0.75% (n = 41)</th>
<th>20 mL 0.375% (n = 35)</th>
<th>20 mL 0.75% (n = 33)</th>
<th>40 mL 0.375% (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound needle end point</td>
<td>38 (97)</td>
<td>40 (98)</td>
<td>32 (91)</td>
<td>32 (97)</td>
<td>34 (94)</td>
</tr>
<tr>
<td>Stimulated motor response:</td>
<td>11/9/4/16</td>
<td>11/10/2/16</td>
<td>3/8/6/18</td>
<td>8/6/3/16</td>
<td>11/5/2/18</td>
</tr>
<tr>
<td>Minimum stimulation threshold, mA</td>
<td>0.65 (0.5–0.80)</td>
<td>0.70 (0.5–0.80)</td>
<td>0.60 (0.3–0.7)</td>
<td>0.70 (0.5–0.80)</td>
<td>0.70 (0.39–0.80)</td>
</tr>
<tr>
<td>Intraoperative alfentanil bolus ≥1</td>
<td>3 (8)</td>
<td>4 (10)</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Surgery duration</td>
<td>75 (60–90)</td>
<td>80 (60–90)</td>
<td>80 (60–105)</td>
<td>80 (75–90)</td>
<td>75 (60–91)</td>
</tr>
</tbody>
</table>

Values are n (%), n, or median (interquartile range).

*P values refer to a 5-group comparison.
†With group 5 mL excluded, P = 0.50.
have limited clinical applicability of their own, they were used to estimate changes in the overall survival curve from baseline (which was specified as 20 mL 0.375% for volume changes of −10, −5, +5, +10, and +20 mL) and concentration changes of −0.4%, −0.1%, +0.1%, and +0.4%. From these estimated survival curves, 25th, 50th, and 75th percentiles for survival time were calculated. All reported hazard ratios (and associated P values) are without inclusion of the 0.75% 5 mL group.

Categorical outcomes were compared using the Fisher test (needle end point, stimulated muscle response, frequency of pain on emergence, adverse effects). Non-normally distributed continuous variables (minimum stimulation threshold, surgery duration) and ordinal outcomes (tramadol consumption, ropivacaine boluses, all numerical rating scores) were compared using the Kruskal-Wallis test. P < 0.05 was designated statistically significant. Two-sided tests were used for all study outcomes.

Other data were summarized using appropriate descriptive statistics (mean [SD] or mean [range] for normally distributed or symmetric variables; median [interquartile ranges] for skewed variables; number [proportion] for categorical variables). All statistical analyses were conducted using R 2.12.1 (R Foundation, Vienna, Austria).

Sample size estimates were based on Hsieh and Lavori’s19 method for calculating event numbers required for a Cox proportional hazards model with a nonbinary covariate. Dose was used as the explanatory variable of interest, with a variance of 2000 obtained by planned treatment allocation. To achieve an α of 5% and a power of 80%, for an expected hazard ratio of 0.995 per milligram dose, it was calculated that approximately 150 pain events were needed. To allow for dropouts, we planned to recruit 180 patients.

RESULTS

One hundred eighty-five patients presenting for elective shoulder surgery were enrolled: 40, 41, 35, 33, and 36 patients were randomized to the 5 mL 0.75%, 10 mL 0.75%, 20 mL 0.375%, 20 mL 0.75%, and 40 mL 0.375% groups, respectively. Patient and surgical characteristics were comparable across groups (Table 1). Needle end points, stimulated muscle groups, and the associated minimum stimulation thresholds were similar among groups; however, 12 patients (30%) in the 5 mL group had pain on emergence (P = 0.006) (Table 2). A total of 61 patients were excluded. Forty patients from group 5 mL were excluded, and another 21 patients were excluded in the other 4 groups: 11, because of pain on emergence (difference between groups not significant); 3, because of catheter failures requiring reinsertion; 2 patients activated the pump before experiencing pain; and 5 patients could not be contacted on day 1 (Table 2).

The proportion of patients experiencing pain as a function of time was associated with dose, volume corrected for concentration, and concentration corrected for volume: dose hazard ratio,

![Image 1](https://via.placeholder.com/150)

![Image 2](https://via.placeholder.com/150)

![Image 3](https://via.placeholder.com/150)

![Image 4](https://via.placeholder.com/150)
TABLE 3. Postoperative Outcomes (n = 152)

<table>
<thead>
<tr>
<th></th>
<th>5 mL 0.75% (n = 28)</th>
<th>10 mL 0.75% (n = 33)</th>
<th>20 mL 0.375% (n = 32)</th>
<th>20 mL 0.75% (n = 30)</th>
<th>40 mL 0.375% (n = 29)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol consumption</td>
<td>0 (0–1)</td>
<td>0 (0–1)</td>
<td>0 (0–1)</td>
<td>0 (0–1)</td>
<td>0 (0–1)</td>
<td>0.50</td>
</tr>
<tr>
<td>Ropivacaine boluses</td>
<td>3 (2–4)</td>
<td>3 (1–5)</td>
<td>3 (2–4)</td>
<td>3 (2–5)</td>
<td>2 (1–4)</td>
<td>0.62</td>
</tr>
<tr>
<td>Worst shoulder pain NRS</td>
<td>3 (2–6)</td>
<td>5 (3–6)</td>
<td>4 (3–6)</td>
<td>4 (3–6)</td>
<td>3 (3–5)</td>
<td>0.42</td>
</tr>
<tr>
<td>“Average” shoulder pain NRS</td>
<td>1 (0–3)</td>
<td>2 (0–3)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>0.98</td>
</tr>
<tr>
<td>Hand numbness NRS</td>
<td>9 (6–10)</td>
<td>8 (5–10)</td>
<td>7 (5–6)</td>
<td>8 (6–10)</td>
<td>8 (7–9)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hand weakness NRS</td>
<td>8 (5–10)</td>
<td>7 (3–9)</td>
<td>7 (5–9)</td>
<td>7 (5–10)</td>
<td>8 (5–10)</td>
<td>0.85</td>
</tr>
<tr>
<td>Adverse effects**</td>
<td>9 (32)</td>
<td>12 (36)</td>
<td>9 (28)</td>
<td>17 (56)</td>
<td>12 (41)</td>
<td>0.14</td>
</tr>
<tr>
<td>Satisfaction NRS</td>
<td>9 (8–10)</td>
<td>10 (8–10)</td>
<td>10 (8–10)</td>
<td>9 (7–10)</td>
<td>10 (9–10)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Values are n (%) or median (interquartile range).

*P values refer to comparisons of the 4 groups excluding 5 mL 0.75%. Respective P values were similar with inclusion of the 5 mL group.

NRS indicates numerical rating score (0–10; 0 = no pain, hand numbness/weakness, very unsatisfied; 10 = worst imaginable pain, hand numbness/weakness, very satisfied).

**Adverse effects included “breathlessness” or “difficulty taking a deep breath.”

0.992 (95% confidence interval [CI], 0.987–0.997; P = 0.002) (Fig. 1); volume hazard ratio 0.959 (95% CI, 0.937–0.982; P = 0.001); concentration hazard ratio, 0.852 (95% CI, 0.743–0.976; P = 0.021) (Fig. 2). (A volume hazard ratio of 0.959 means that, at a specific time, a patient given a 1-L, higher volume than another patient has a 4% lower risk [or “hazard”] of experiencing pain, assuming neither experienced pain.) Associations for all 3 variables were maintained with inclusion of the 5 mL group. Figures 3 and 4 depict estimates of the proportion of patients pain-free as a function of time for given changes in volume (Fig. 3) or concentration (Fig. 4) relative to a 20 mL 0.375% baseline. Corresponding estimates for the effect of volume and concentration on median time to first pain were 10.6 (interquartile range, 9.5–11.5), 10.75 (interquartile range, 9.75–14.0), and 15.0 (interquartile range, 10.75–21) hours for 10, 20, and 40 mL, respectively, and 10.75 (interquartile range, 9.75–14.0), 11.5 (interquartile range, 10.0–16.75), and 13.75 (interquartile range, 10.5–21.0) hours for 0.375%, 0.5%, and 0.75%, respectively.

Secondary outcomes associated with block effectiveness (tramadol consumption, ropivacaine boluses, numerically rated pain and adverse effects (dyspnea) were similar across groups; however, the study did not have sufficient power to confidently conclude these secondary outcomes were equivalent (Table 3). One patient required catheter reinsertion (before local anesthetic placement) because of likely intravascular placement. No patient demonstrated symptoms or signs of systemic local anesthetic toxicity. No patient reported significant dyspnea, requiring more than simple reassurance, before or after hospital discharge.

DISCUSSION

This study demonstrated a clear association between local anesthetic volume, concentration (and dose), and the duration of interscalene block. No differences were noted among groups during the first 24 hours for the effectiveness of analgesia (non adverse effects); however, the study was not designed or adequately powered to detect-between-group differences for these secondary outcomes.

Although peripheral nerve blocks have been used for more than a century, a clinical trial specifically evaluating the effect of local anesthetic volume and concentration on nerve block duration has not been conducted. The clinical relevance of the issue has recently attracted attention because of the increased popularity of ultrasound-guided regional anesthesia using low local anesthetic volumes; volumes as low as 0.11 mL/mm nerve cross-sectional area have been advocated.50 Despite multiple studies showing that these “ultra-low” volumes can result in successful block,32–35 no clinical studies have specifically evaluated the effect of volume (or concentration) on block duration.

A previous tightly controlled laboratory study in rat sciatic nerves demonstrated an association between lidocaine concentration and block duration.31 However, the study method did not permit an assessment of the effect of volume corrected for concentration. Previous clinical studies evaluating the effect of volume (or concentration) on block duration have been limited in their interpretation for 3 possible reasons. In 2 studies, the studied variables were confounded by the use of different neurolocalization techniques.13 In 1 of these studies, blocks also involved the blockade of multiple nerves: local anesthetic volume administered at each individual nerve, for each group, was not constant for each subject.4 In other studies, block duration was a secondary outcome.12,13,14,37 Drawing conclusions from secondary outcomes, particularly negative outcomes, can be problematic because the studies may not be powered to detect secondary outcome effects.1,2,4,5,14,16 On the other hand, without correction for multiple comparisons, the probability of a type 1 error increases with the number of secondary outcomes studied.14 Nevertheless, 2 tightly controlled, sequential, up-down dose-finding studies for sciatic and median/ulnar nerve blocks are notable in that they suggest a correlation between local anesthetic volume and the secondary outcome, block duration.5,7

Despite the present study’s demonstration of a clear association between local anesthetic volume, concentration (and dose), and the primary outcome block duration, the clinical relevance of the shift demonstrated might be questioned: the estimated effect of a volume increase from 10 to 40 mL was a median to 15 hours and a concentration increase from 0.375% to 0.75%, 10.75 to 13.75 hours. However, for interscalene block, volumes as low as 3 mL and as high as 60 mL have been used.3,12,24 Based on the association currently demonstrated, this volume range might represent an even greater difference in block duration. That said, this speculation assumes the association remains at these volume extremes, which cannot be assumed from the present data.
Regardless of the treatment effect demonstrated, practitioners might argue that a theoretical reduction in the local anesthetic systemic toxicity risk from lower volumes and concentrations outweighs the downside of shorter block duration, even though published clinical evidence does not support this principle.25,26 Similarly, the relatively modest effect of both volume and concentration could be interpreted to mean that the only way to significantly prolong block duration is through perineural catheter placement.

We decided after study completion to exclude the 5 mL group because of an unacceptably high block failure rate (30%); there existed the possibility that the remaining patients were not representative of the population. First, the excluded patients may have represented patients with “low pain thresholds” and would be expected to report pain earlier after block resolution compared with the population. Second, the excluded patients may have represented less accurately placed catheters—the less accurately placed catheters in the other groups were likely retained because of the higher administered volumes that likely masked these catheters. Both factors may have rendered the remaining pain-free patients in the 5 mL group unrepresentative of the studied population. Nevertheless, with inclusion of the 5 mL group, the demonstrated associations between volume, concentration, and block duration were maintained.

The technique used for local anesthetic deposition warrants comment. We injected local anesthetic at a single point immediately lateral to the appropriate roots/trunks. However, practitioners often inject local anesthetic at several locations based on the elicitation of more than 1 motor response, or sonographic assessment of inadequate local anesthetic spread. A single-point injection was used because it was thought to minimize data variability across groups (randomized controlled trial). We cannot automatically conclude that the study findings can be generalized to such a multipoint injection technique.

The raw post-PNCU discharge outcome data for indices of catheter effectiveness and adverse effects (Table 3) should be interpreted with caution. First, each group was associated with changes to 2 independent variables (volume and concentration); thus, an effect from 1 variable may have been countered by an effect from the other variable. Second, the study was not powered to detect differences for secondary outcomes: “absence of evidence is not evidence of absence.” Third, from the onset of pain, patients received a continuous ropivacaine infusion supplemented with patient-controlled boluses. It is therefore not surprising that pain scores were similarly low for all groups and lacked a between-group difference.

We performed the present study in the interscalene area because it represents an ideal block surgery combination to study the tested hypothesis: the operative area can be blocked by a single local anesthetic injection. The results may similarly apply to other peripheral nerve blocks; however, ideally, confirmatory studies should be conducted.

In summary, this study found a clear association between local anesthetic volume, concentration (and dose), and the duration of interscalene block, findings that have particular relevance for the current trend in ultrasound-guided regional anesthesia of administering low local anesthetic volumes.

REFERENCES

1. Klein SM, Greengrass RA, Strole SM, et al. A comparison of 0.5% bupivacaine, 0.5% ropivacaine, and 0.75% ropivacaine for interscalene brachial plexus block. Anesth Analg. 1998;87:1316-1319.


5.2. Discussion

5.2.1. Contribution and significance

In this study, local anaesthetic volume and concentration (and dose) were associated with the duration of interscalene block. No association between these variables and analgesia (as measured by pain scores) or side effects were demonstrated. It should be noted, however, that the study was not adequately powered for these secondary outcomes.

5.2.2. Limitations

As discussed in the published article, a limitation to this study includes the use of subjective reporting for postoperative pain. Pain onset is an imprecise method to measure block duration, and previous investigators have noted marked interpatient variability in this outcome. As a result, the effect of each variable may have been underestimated because of this methodology. This may in part explain why little research as been conducted on this issue thus far.

The clinical relevance of the treatment effect could also be questioned. An increase in block duration of 3-5 hours, with changes in volume and concentration is modest in the context of the expected duration of postoperative pain. However, significantly higher and lower local anaesthetic volumes are commonly used for interscalene block, which might equate to a higher local anaesthetic volume determined block duration effect. More importantly, our literature review concluded that the only way to significantly prolong block duration and therefore improve postoperative analgesia is through interscalene catheter placement.
Other potential limitations include the posthoc exclusion of the 5 mL group and the method for local anaesthetic deposition, which involved a single point injection via the catheter rather than a multipoint injection through the needle.

5.2.3. Literature following

Lee et al randomised 60 patients undergoing arthroscopic rotator cuff surgery to a single injection of either 5 or 10 mL of interscalene ropivacaine 0.75%. Time to first pain and “VAS score” were not different between groups, although there was radiological evidence for reduced hemidiaphragmatic paralysis in the 5 mL group. Both groups had a very low requirement for analgesics in the recovery room, which could be explained by the protocol involving local anaesthetic injection via the needle. Local anaesthetic injection via needle, as stated, enables repositioning of the needle in the event of inadequate injectate spread. Similarly, Sinha et al compared 10 and 20 mL ropivacaine 0.5% for the same surgery. Indices of block success and pulmonary function were not different between groups. Hartrick et al randomised 36 patients receiving an interscalene catheter to 5, 10 and 20 mL ropivacaine 0.5%. The 20 mL group was associated with better analgesia than the 5 mL group but a higher incidence of dyspnoea. After the present study was accepted for publication, Schoenmakers et al reported a randomised study in which they showed that increasing the volume of mepivacaine from 10 to 40 mL (via the needle) increased axillary block duration by approximately 30%. All these studies, in addition to the study conducted in Chapter 4 support the use of approximately 5 mL local anaesthetic for a multipoint injection via the needle, and > 10 mL volume when injected via the catheter. Local anaesthetic volume influences block duration, but to a limited degree.
5.2.4. Future directions

The present study demonstrated that block duration is dependent on both local anaesthetic volume and dose. Further study is required to evaluate whether the demonstrated increase in block duration according to volume applies to block techniques involving a multi-point injection. The current study used a single point injection via the catheter, but ultrasound guided blocks often involve multi-point injections depending on satisfactory or inadequate local anaesthetic spread.
Chapter 6. Patient initiated mandatory boluses: an effective strategy for optimising analgesia versus side effects

6.1. Preface

The studies reported in Chapter 4 and 5 formed an objective basis for choosing the optimal local anaesthetic dose to establish interscalene block via the catheter. Attention then turned to maintenance of the block for continuing postoperative analgesia. The review of the literature concluded that the optimal local anaesthetic rate, volume and concentration for continuous interscalene block remains largely unknown. The study conducted during the previous thesis compared ropivacaine 0.2% and 0.4% at 2 mL.hr\(^{-1}\) with PRN 5 mL boluses following rotator cuff repair, and found that the higher concentration provided minimal analgesic benefit, but may increase motor block.\(^{173}\) That study also revealed a significant number of patients undergoing rotator cuff repair experience significant breakthrough pain on that infusion regimen. Some evidence exists to suggest that intermittent boluses are preferable to continuous only infusion for continuous peripheral nerve blocks.\(^{104}\) The study reported in this chapter was therefore conducted to evaluate the relative effectiveness of a higher background infusion and PRN boluses versus a lower background infusion with mandatory boluses; both techniques at an approximately equivalent local anaesthetic dose. The study dates overlapped with the study conducted in Chapter 4.

The following section contains an unaltered reproduction of the article “Patient Initiated Mandatory Boluses: an Effective Strategy for Optimising Analgesia versus Side Effects” published in the *British Journal of Anaesthesia*. The *British Journal of
Anaesthesia is the official journal of the College of Anaesthetists (UK). The journal covers preclinical and clinical anaesthesia and pain medicine, and in 2010, had an impact factor of 4.224.
Patient-initiated mandatory boluses for ambulatory continuous interscalene analgesia: an effective strategy for optimizing analgesia and minimizing side-effects

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**Key points**
- Continuous interscalene analgesia facilitates shoulder surgery being performed as an overnight or even day stay procedure.
- Following rotator cuff repair, a 2 ml h⁻¹ ropivacaine infusion combined with 6 hourly mandatory and PRN boluses provided similar analgesia to a 5 ml h⁻¹ infusion and PRN only boluses.
- The higher background infusion resulted in more patients experiencing side-effects.

**Background.** This prospective, randomized study tested the hypothesis that a reduced dose continuous interscalene regimen incorporating a low background infusion with mandatory boluses would provide similar shoulder surgery analgesia compared with a dose regimen incorporating a conventional higher background infusion.

**Methods.** After rotator cuff surgery, patients received via an interscalene catheter, one of two elastomeric pumps, each having a 5 ml per 60 min bolus function and a 2 ml h⁻¹ (n=38) or 5 ml h⁻¹ (n=43) ropivacaine 2 mg ml⁻¹ infusion. Boluses commenced from the onset of pain and continued for >48 h as required (pro re nata, PRN) up to every hour for a numerical rating pain score (NRPS, 0-10) >2. Group 2 ml h⁻¹ received mandatory 6 hourly boluses irrespective of the NRPS. Rescue tramadol was available. Patients were questioned on postoperative days 1 and 2 for treatment effectiveness and side-effects.

**Results.** Postoperative pain was similar between the groups (Group 2 ml h⁻¹ day 2 median (IQR) (95% confidence interval of the mean) worst movement pain=4 (1–5) (2.8–4.7) vs 4 (2–5) (3.1–4.6), P=0.99), as were night awakenings and tramadol consumption. Numerically rated numbness and weakness were similar between the groups; however, nine patients (21%) in the 5 ml h⁻¹ group vs one (3%) in the 2 ml h⁻¹ group required a temporary infusion cessation due to side-effects (predominantly hand numbness) (P=0.02).

**Conclusions.** Continuous interscalene ropivacaine 0.2% 2 ml h⁻¹ with mandatory 6 hourly (and PRN) boluses provides similar analgesia after rotator cuff repair but with reduced side-effects compared with 5 ml h⁻¹ with PRN only boluses.


**Keywords:** anaesthetic techniques, regional brachial plexus; anaesthetics local, ropivacaine

Accepted for publication: 30 September 2010

Significant advances have occurred in the perioperative management of pain after shoulder surgery.¹ This surgery traditionally required a two to three night hospital stay for opioid analgesia, but with steady progress over the last 5 yr in our understanding of the requirements for successful continuous interscalene analgesia in the ambulatory setting, this surgery can now be performed as an overnight or even day-stay procedure, with patients experiencing excellent analgesia and generally high satisfaction.² ³

Despite the well-demonstrated effectiveness of continuous interscalene analgesia, for rotator cuff repair, interscalene ropivacaine 0.2% 2 ml h⁻¹ with PRN (pro re nata) 5 ml h⁻¹ boluses was associated with a significant number of patients experiencing episodes of moderate-to-severe breakthrough pain.⁴ An intervention to reduce breakthrough pain involves increasing the basal infusion, but this can be problematic. First, a larger and therefore heavier reservoir is required, potentially compromising patient satisfaction. Without a larger reservoir, the infusion duration (and consequent potent analgesia) is limited.⁵ Secondly, higher basal infusions might increase unwanted motor block, which can further compromise patient satisfaction.⁶ ⁷

Compared with a continuous only infusion, an automated electronic bolus system has been recently shown to reduce local anaesthetic consumption⁸ and improve the analgesic effectiveness of continuous popliteal sciatic blocks.⁹ However, this automated delivery system is not presently available in the commonly used disposable ambulatory
pumps. An analogous alternative with these pumps is to have patients ‘self automate’ through bolusing at pre-specified time intervals.

Therefore, we sought to determine in this prospective, randomized study whether a reduced dose ‘mandatory + PRN bolus’ regimen incorporating a low background infusion with mandatory (and PRN) boluses would provide similar analgesia compared with a ‘PRN only’ regimen incorporating a conventional but higher dose, higher background infusion with boluses administered PRN only. The primary outcome endpoint was postoperative pain on postoperative days 1 and 2. The main secondary endpoints included side-effects of treatment, in particular, extremity numbness and weakness.

**Methods**

Local institutional review board (Northern X Regional Ethics Committee, Auckland, New Zealand) approval for the study was obtained and the trial was prospectively registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12609007402911). We enrolled adult American Society of Anesthesiologists physical status I–III patients undergoing elective shoulder surgery involving arthroscopic or open rotator cuff repair at the Southern Cross Brightside and North Harbour hospitals between May 2009 and April 2010. Subjects were identified from the investigators’ regular operating lists. Initial invitation to participate was made by a research assistant but definitive enrolment was by the operating investigator. Exclusion criteria included patient refusal of interscalene block, severe respiratory disease, known amide local anaesthetic drug allergy, non-steroidal anti-inflammatory drug intolerance, and preoperative opioid therapy administered for >1 month before surgery. Written informed consent for study procedures was obtained from all patients.

Oral acetaminophen 1 g was administered 1 h before surgery. In an area immediately adjacent to the operating theatre, i.v. sedation with up to midazolam 2 mg and alfentanil 0.5 mg was administered. All blocks were administered by one of the four investigators, all of whom were experienced in ultrasound and nerve stimulation-assisted interscalene catheter placement.

A superficial cervical plexus block was performed using standard landmarks and lidocaine 1% (5–10 ml) with epinephrine 1/200,000. The patient was transferred to the operating table, a pulse oximeter was applied, and appropriate aseptic precautions were observed.

**Interscalene catheter placement**

The patient was positioned supine with the head turned to the contralateral side and supported with one to two pillows. The scalene muscles and interscalene brachial plexus were imaged in the short axis at approximately the level of the 6th/7th cervical vertebrae with a 38 mm 13-6 MHz linear ultrasound probe (SonoSite HFL/MicroMaxx or M-Turbo, Bothell, WA, USA). A 4–5 cm 18 G insulated Tuohy needle (Cavitrap Tuohy, B. Braun, Bethlehem, PA, USA) connected to a nerve stimulator (Pajunk Vario, Tucker, GA, USA) was inserted approximately at the posterior border of the sternocleidomastoid muscle – 3 cm cephalad of the level of the 6th/7th cervical vertebrae. The needle was advanced using out-of-plane needle-probe orientation superficially into the middle scalene muscle until tissue displacement was observed just lateral to the two most superficial elements of the brachial plexus. At the 6th/7th cervical vertebral level, these correspond to the 5th/6th cervical roots or superior/middle trunks. The needle tip was then angled medially towards the two most superficial brachial plexus roots/trunks until a resultant medial movement was observed. Needle tip position was ultimately determined by the injection of dextrose 5% (10 ml) and observation of injectate spread immediately lateral to the target roots/trunks, or depending on operator preference, by elicitation of a sustained deltoid or biceps motor response at <0.5 mA. If a sustained motor response was present at <0.2 mA, the needle was manipulated until the response was eliminated.

A non-stimulating triple-orificed catheter was advanced blindly and then withdrawn such that 2–3 cm of the catheter remained past the original needle tip position. The catheter was finally fixed to the skin with a catheter-anchoring device (Lockit-plus®, Portex, Hythe, UK).

**Intraoperative management**

All patients were given a standardized light general anaesthetic (end-tidal minimum alveolar concentration = 0.8–1.0) using a laryngeal mask airway, desflurane anaesthesia, and spontaneous respiration. Ropivacaine 0.5% (30 ml) was administered via the catheter following the induction of general anaesthesia but before surgery. No long-acting opioid was administered; however, alfentanil 0.25 mg was administered PRN for a ventilatory frequency >25.

Randomization to the ‘mandatory + PRN bolus’ or ‘PRN only bolus’ group was implemented with a computer-generated random number previously delivered in pre-prepared sealed opaque envelopes with randomization performed by a research assistant away from the study procedures.

**Post-anaesthesia care unit protocol**

In the post-anaesthesia care unit (PACU), patients reporting a numerical rating pain score (NRPS) of more than 2 were given a bolus of lidocaine 1% (10 ml). If the NRPS subsequently remained more than 2, the catheter was withdrawn 1 cm and an additional lidocaine 1% (10 ml) was administered. If the NRPS still remained more than 2, the catheter was replaced. Patients receiving a replacement catheter received a repeat bolus of ropivacaine 0.5% (20 ml).

**Postoperative management**

All pumps were filled with ropivacaine 0.2%. The specific treatment protocol for each group is summarized in Table 1. Specifically, patients in each treatment group received ropivacaine boluses from the onset of operative
Mandatory boluses for continuous interscalene block

site pain and these continued as required every hour if the NRPS was >2. The ‘mandatory + PRN bolus’ group also received boluses ‘on the clock’ every 6 h irrespective of the NRPS from the onset of operative site pain. However, comfort permitting, patients slept through the night period (~11 p.m. to 6 a.m.) without a mandatory bolus. This protocol continued for at least 48 postoperative hours. The 6 h bolus interval was an arbitrary compromise between any potential therapeutic effect from mandatory boluses, patient inconvenience from having to manually activate the bolus device while also enabling a dose reduction in the mandatory bolus group (Table 1).

Acetaminophen (1 g every 6 h) and diclofenac slow release (75 mg every 12 h) were continued if any postoperative pain occurred. If the NRPS was more than 2 despite regular acetaminophen, diclofenac, and two consecutive ropivacaine boluses, tramadol slow release (100 mg every 12 h) was added. Discharge home occurred on the morning of postoperative day 1.

Patients were instructed to clamp off the infusion if, late on the afternoon of postoperative day 1, the hand was excessively numb or weak, or if the hand became excessively numb or weak after the initial primary block had begun to resolve. The written instructions handed out on the morning of day 1 reiterated these instructions albeit with more stringent stopping criteria: to clamp off the infusion ‘if you feel that you can’t move your hand at all or you don’t have any feeling in the arm and hand’ and to ‘unclamp it when you start to be able to move or feel the hand. Unclamp it also if you start to feel any discomfort in the shoulder’.

Data collection

The operating investigator recorded the needle endpoint used for the catheter placement and the number of alfentanil 0.25 mg boluses administered during surgery. A research assistant phoned all subjects on the afternoon of postoperative days 1 and 2 and questioned for ropivacaine bolus demands, supplemental tramadol consumption, NRPS (at rest, on movement, and ‘average’ pain but specifically excluding pain that was present in the recovery room), arm numbness/weakness (0–10; 0, no pain, numbness/weakness; 10, worst imaginable pain, numbness/weakness), the number of night awakenings, and whether the infusion had to be temporarily discontinued during the previous 24 postoperative hours. At 48 h, subjects were also questioned for dissatisfaction from the cumbersome nature of the elastomeric pump and for overall satisfaction with the technique (0–10; 0, no dissatisfaction, very unsatisfied; 10, worst dissatisfaction, very satisfied).

Blinding

The research assistant who questioned patients on days 1 and 2 for the main outcome data could be considered blinded to the treatment group at the start of patient interrogation. However, treatment group allocation would have become obvious after questioning. The operating investigators and patients were not blinded to the treatment group.

Statistical analysis

An independent statistician not otherwise involved in the study performed all calculations. Categorical outcomes were compared using the χ² test (tramadol requirement, day 2 night awakenings) or Fisher’s exact test (temporary infusion cessation, day 1 night awakenings). Ordinal outcomes (ropivacaine bolus consumption, numerically rated pain, numbness, weakness, dissatisfaction, and satisfaction) were compared using the Mann–Whitney U-test. P-values of <0.05 were considered statistically significant. Two-sided tests were used for all experimental outcomes.

Other data were summarized using appropriate descriptive statistics (mean, sd, and 95% confidence interval of the mean for normally distributed or symmetric variables; median and inter-quartile ranges for skewed variables; number and proportion for categorical variables). Because our primary interest was equivalence (non-inferiority) of the primary outcome (postoperative pain), 95% confidence intervals (of the mean) were presented for these data regardless of the data distribution. All statistical analyses were performed using SPSS Statistics 18.0.0 (SPSS Inc., Chicago, IL, USA).

The sample size calculation was based on the primary hypothesis that the ‘mandatory bolus/low background infusion’ technique would provide similar (not significantly inferior) analgesia to the ‘PRN only/high background infusion’ technique. Assuming an sd of 2.28 in each group based on the results from a recent study,9 a two-sided error protection of 0.05 and a power of 0.80, 80 patients would detect a difference in 1.65 points on the 11-point NRPS (StatMate 2.0; GraphPad Software, San Diego, CA, USA)—with a 15% adjustment for using the t-test when a subsequent non-parametric test was likely.

Table 1 Summary of treatment groups. PRN, pro re nata (for an NRPS >2 if 0, no pain, and 10, the worst pain imaginable). *On the clock* boluses were not administered during sleep hours. Calculated using an approximate time to first pain of 18 postoperative hours with mandatory boluses continuing for a minimum of 48 h

<table>
<thead>
<tr>
<th></th>
<th>Mandatory + PRN bolus</th>
<th>PRN only bolus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump name</td>
<td>PainBlister®</td>
<td>C-Bloc®</td>
</tr>
<tr>
<td>Reservoir volume</td>
<td>270 ml</td>
<td>400 ml</td>
</tr>
<tr>
<td>Background infusion</td>
<td>2 ml h⁻¹</td>
<td>5 ml h⁻¹</td>
</tr>
<tr>
<td>Bolus volume/followup</td>
<td>5 ml/60 min</td>
<td>5 ml/60 min</td>
</tr>
<tr>
<td>Bolus protocol</td>
<td>PRN and on the clock</td>
<td>PRN only</td>
</tr>
<tr>
<td>Minimum volume delivered</td>
<td>3 ml h⁻¹</td>
<td>5 ml h⁻¹</td>
</tr>
<tr>
<td>Maximum duration</td>
<td>120 h (5 days)</td>
<td>80 h (3.3 days)</td>
</tr>
<tr>
<td>possible from elastomeric device</td>
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</table>
Results

Eighty-seven patients presenting for rotator cuff surgery were enrolled during the study period: 43 patients were randomized to the mandatory + PRN bolus group and 44 patients to the PRN only bolus group. There were no differences in patient and surgical characteristics between the groups (Table 2). Six patients were excluded after randomization (Fig. 1). Thus, 81 patients completed the study according to protocol (‘intention to treat’). Intraoperative and PACU interventions are detailed in Table 3.

Table 2 Patient and surgical characteristics. Values are mean (sd), median (inter-quartile range), or n (%). PRN, pro re nata

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mandatory + PRN bolus (n=43)</th>
<th>PRN only bolus (n=44)</th>
</tr>
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<tbody>
<tr>
<td>Male sex</td>
<td>32 (74)</td>
<td>30 (68)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>56 (13)</td>
<td>56 (9)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>83 (14)</td>
<td>85 (10)</td>
</tr>
<tr>
<td>Duration preoperative pain (months)</td>
<td>12 (6–18)</td>
<td>10 (5.5–18)</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotator cuff repair</td>
<td>43 (100)</td>
<td>44 (100)</td>
</tr>
<tr>
<td>+ Total shoulder arthroplasty</td>
<td>3 (7)</td>
<td>4 (9)</td>
</tr>
</tbody>
</table>

Postoperative pain, night awakenings, and tramadol consumption were similar on both days 1 and 2 (Table 4) (Fig. 2): Group 2 ml h⁻¹ day 2 median (IQR) (95% CI of the mean) worst movement pain=4 (1.5–4) (2.8–4.7) vs 4 (2.5–5) (3.1–4.6) (P=0.99). Day 2 PRN ropivacaine bolus requirement was lower in the mandatory + PRN bolus group [median (inter-quartile range)=0 (0–1) vs 2 (1–3), P=0.002]. Numerically rated numbness and weakness were similar between groups on each day; however, nine patients (21%) in the PRN only bolus group vs only one patient (3%) in the mandatory + PRN bolus group had to temporarily stop the infusion because of side-effects (P=0.02) (Table 4). Of these 10 patients, eight patients stopped the infusion because of excessive hand numbness or weakness and two patients stopped the infusion because of mild dyspnoea. Neither dissatisfaction with the cumbersome nature of the device nor overall satisfaction differed between the groups (Table 4).

No patient demonstrated symptoms or signs of local anaesthetic toxicity in the recovery room, and there were no pneumothoraces evident clinically.

Discussion

In the context of continuous interscalene analgesia after rotator cuff repair, a delivery system incorporating a 2 ml h⁻¹ background infusion combined with 6 hourly mandatory (and PRN) boluses provided similar analgesia after rotator cuff repair. However, the mandatory + PRN bolus may be associated with a reduced need for PRN bolus infusions.

Fig 1 Patient flow through the study. 3 Three patients had no rotator cuff tear on diagnostic arthroscopy. 4 Two patients did not have catheters placed successfully. 5 One patient had a prolonged catheter disconnect on postoperative day 1.
cuff repair compared with a regimen delivering 5 ml h⁻¹
combined with PRN only boluses. The higher background
infusion regimen was associated with a significantly higher
proportion of patients experiencing side-effects (predomi-
nantly hand numbness or weakness).

These results are consistent with previous studies invol-
ving continuous sciatic and epidural block; compared with
a continuous infusion, an intermittent bolus regimen has
been shown to reduce local anaesthetic consumption and
improve analgesia.⁹⁻¹¹ It was postulated that boluses gener-
ate higher injection pressures than a slow infusion; in the
sciatic nerve area, this might overcome anatomical distances
between the catheter orifice(s) and nerve. In the epidural
space, experimental studies have confirmed the intermittent
bolus technique results in more uniform local anaesthetic
spread.¹² In the current study, despite the lower local anaes-
thetic dose administered in the mandatory bolus group,
algesia was similar to the higher dose, higher infusion
regimen. It is likely that similar to the sciatic area, the
higher pressures generated by the intermittent boluses facili-
tated spread to the appropriate roots/trunks (e.g. 5th/6th or
7th cervical nerve roots) of the brachial plexus. The reduction
in side-effects with this regimen is more difficult to explain,
but it is possible that total local anaesthetic dose is the
main determinant of extremity numbness and weakness as
evidenced by the higher proportion of patients having to
temporarily discontinue the infusion in the high background
infusion group.

We feel that a cautious historical comparison is warranted
in this instance. The current study is very similar to a recent
study by our group; the only difference being the addition of
two new operators and one surgeon. In the recent study,
ropivacaine 0.2% and 0.4% were compared when adminis-
tered via the same infusion regimen. No difference was
found in analgesic effectiveness between the groups; how-
ever, a significant number of patients experienced
moderate-to-severe breakthrough pain: day 2 worst pain on
movement had a median (inter-quartile range) of 5 (3–8).⁶
In contrast, in the current study, the median (inter-quartile
range) day 2 worst pain on movement was 4 (1–5). This
suggests that mandatory boluses are effectively minimizing
breakthrough pain, while the lower total local anaesthetic
dose administered also optimizes the infusion duration for
a given reservoir volume.

### Table 3: Intraoperative and PACU interventions. Values are n (%).

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Mandatory + PRN bolus (n=43)</th>
<th>PRN only bolus (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound needle endpoint</td>
<td>31 (72)</td>
<td>31 (70)</td>
</tr>
<tr>
<td>Alfentanil bolus ≥ 1</td>
<td>1 (3)</td>
<td>7 (16)</td>
</tr>
<tr>
<td>PACU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PACU catheter bolus only</td>
<td>0 (0)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>PACU catheter withdrawal + bolus</td>
<td>1 (3)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>PACU catheter replacement</td>
<td>1 (3)</td>
<td>3 (7)</td>
</tr>
</tbody>
</table>

### Table 4: Postoperative outcomes. Data expressed as n (%) or median (inter-quartile range). PRN, pro re nato; NRS, numerical rating score (0–10; 0, no numbness/weakness or not dissatisfied/satisfied; 10, very numb/weak or very dissatisfied/satisfied). *Total (mandatory + PRN) boluses. **PRN only boluses (mandatory boluses not included in this value).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mandatory + PRN bolus (n=38)</th>
<th>PRN only bolus (n=43)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal drool required</td>
<td>7 (18)</td>
<td>11 (26)</td>
<td>0.31</td>
</tr>
<tr>
<td>Day 1</td>
<td>16 (44)</td>
<td>19 (44)</td>
<td>0.99</td>
</tr>
<tr>
<td>Ropivacaine boluses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>1 (0–2)*</td>
<td>0 (0–1.5)</td>
<td>0.35</td>
</tr>
<tr>
<td>Day 2</td>
<td>0 (0–1)</td>
<td>2 (1–3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Numbness NRS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>9 (6–10)</td>
<td>9 (7–10)</td>
<td>0.99</td>
</tr>
<tr>
<td>Day 2</td>
<td>2 (0–5)</td>
<td>3 (1–6)</td>
<td>0.53</td>
</tr>
<tr>
<td>Weakness NRS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>8 (6–10)</td>
<td>9 (6–10)</td>
<td>0.63</td>
</tr>
<tr>
<td>Day 2</td>
<td>5 (2–6)</td>
<td>5 (3–7)</td>
<td>0.38</td>
</tr>
<tr>
<td>Cessation of infusion required</td>
<td>1 (0)</td>
<td>9 (21)</td>
<td>0.02</td>
</tr>
<tr>
<td>Night awakenings &gt;0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>3 (8)</td>
<td>5 (12)</td>
<td>0.72</td>
</tr>
<tr>
<td>Day 2</td>
<td>16 (41)</td>
<td>19 (44)</td>
<td>0.71</td>
</tr>
<tr>
<td>Pump dissatisfaction (cumbersome NRS)</td>
<td>2 (0–4)</td>
<td>2 (0–4)</td>
<td>0.76</td>
</tr>
<tr>
<td>Satisfaction NRS</td>
<td>10 (8–10)</td>
<td>10 (8–10)</td>
<td>0.40</td>
</tr>
</tbody>
</table>
For a more in-depth account of the pharmacology relevant to this treatment, readers are referred to a recent review.¹

A major strength of this study is the relative surgical procedure homogeneity: all included patients having had a rotator cuff repair; this is a unique attribute for dose-finding studies of this kind. A second strength was the inclusion of all catheters by four anaesthesiologists experienced in this procedure, thus further minimizing variability between the groups; although the inclusion of four operators should allow reasonable study generalizability.

A limitation arising from the use of two structurally different infusion devices and two different protocols for bolusing was that the study could not be blinded to either investigators or subjects. The pumps in this investigation are commonly used for ambulatory continuous peripheral nerve blocks; this was the primary reason for the choice of infusion rate. Consequently, investigator bias may have manifested at the time the verbal instructions were provided on the morning of postoperative day 1. In an attempt to minimize this bias, pre-prepared explicit written instructions were given to the patient detailing criteria for bolusing and temporarily suspending the infusion. Nevertheless, ideally, the results of this study should be confirmed with a blinded study using an electronic pump.¹¹⁻¹² Finally, we cannot be sure that the instructions given to patients by the investigators on the morning of postoperative day 1 were appropriately followed.

Despite the demonstrated advantages of the mandatory bolus group (reduced extremity numbness/weakness, prolonged infusion duration), the regimen is not without inconvenience. Anaesthesiologists/providers have to provide additional education on the bolusing regimen. Patients themselves also have to remember to activate the bolus button. The primary bolus dose of ropivacaine warrants comment. Ropivacaine 0.5% (30 ml) has been shown to be more than that required to prevent recovery room pain in ~95% of patients: a more appropriate dose for an ultrasound-guided anterolateral technique being approximately 20 ml 0.375%.⁶ There was a suggestion that this dose was associated with reduced motor block which may have accounted for the increase in patient satisfaction.⁶ However, for rotator cuff repair, where an emergence from general anaesthesia it can be clinically advantageous to have the entire upper extremity immobile in order to prevent the surgical repair, our current preference is to administer ropivacaine 0.75% (10 ml) diluted with lidocaine 1% (10 ml).

In summary, an ambulatory interscalene infusion at 2 ml h⁻¹ combined with 6-hourly mandatory (and PRN) boluses provides similar analgesia after rotator cuff repair compared with a regimen delivering 5 ml h⁻¹ with PRN only boluses. The lower background infusion regimen was associated with fewer patients experiencing side-effects and has the additional advantage of enabling a longer infusion duration for a given reservoir volume.

Acknowledgement
Mathangi Shanthakumar, MSc (Med Statistics), is thanked for performing the statistical analysis.
Conflict of interest

None declared.

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References

13. Barghi B, Facchini F, Agnelli V, et al. Pain relief and motor function during continuous interscalene analgesia after open shoulder surgery: a prospective, randomized, double-blind comparison between bupivacaine 0.25%, and ropivacaine 0.25% or 0.4%. Eur J Anaesthesiol 2006; 23: 1005–9
6.2. Discussion

6.2.1. Contribution and significance

The study in this chapter showed that for continuous interscalene analgesia after rotator cuff repair, an ambulatory pump delivering a 2 mL.hr\(^{-1}\) background infusion combined with 6 hourly mandatory intermittent 5 mL boluses provides comparable analgesia compared to a regimen delivering 5 mL.hr\(^{-1}\) combined with PRN only 5 mL boluses. The higher background infusion regimen was associated with a significantly higher proportion of patients experiencing side effects (predominantly hand numbness or weakness). This result is important because it identifies an infusion regimen that is less likely to cause side effects.

6.2.2. Limitations

As discussed in the published article, limitations to this study included the use of two structurally different infusion devices and two different protocols for bolusing. Thus, the study could not be blinded for both investigators and patients. Patient or investigator bias can therefore not be ruled out, although the former is unlikely given patients themselves would have no reason to favour one pump over the other. Ideally, the study should be conducted using a programmable electronic pump with full patient and investigator blinding. It was notable that the requirement for intraoperative alfentanil boluses was higher in the PRN only group (one-sided p value < 0.05). This raised the possibility that these catheters were not as accurately placed as the catheters in the mandatory group. This confounder may therefore have masked improved analgesia from the higher infusion.
Given these were ambulatory patients, the outcome “average pain” was used which referred to “average” pain over the previous 24 hours. The inherent lack of temporal precision may have masked a true between group treatment effect and use of a pain diary with regularly recorded scores may have overcome this limitation. However, previous use of such an instrument resulted in frequent missing data. \(^\text{118}\)

Finally, it would have been preferable to use the optimal primary bolus volume and concentration derived from the study in Chapter 4, however, the present study was started before the results from Chapter 4 were obtained.

To test the hypothesis that the two treatment regimens were ‘similar’ in analgesic effectiveness the study was essentially set up as a non-inferiority trial. It is important to recognize that such trials, although having advantages, have inherent weaknesses when compared to the traditional superiority design, and these weaknesses make them inherently less credible than superiority studies. \(^\text{93,174}\) Non-inferiority trials test whether a given treatment is not significantly inferior to an alternative. The motive for such trials arises from ethical issues around conducting ongoing placebo controlled trials, and from the desire to demonstrate incrementally smaller benefits for new treatments.

The biggest limitation of non-inferiority trials relates to the ability of such trials to demonstrate a difference if such a difference truly exist in the population. A superiority trial that demonstrates superiority can conclude that a difference exists. However, a blinded non-inferiority trial that demonstrates the effects are similar cannot definitively distinguish between a trial that was poorly conducted and failed to detect a difference due to imprecise data collection and increased data variability.

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For non-inferiority trials to be credible, the method of data collection must be sufficiently precise. Blinding has more relevance for non-inferiority trials. For a placebo controlled blinded superiority trial, investigator bias cannot feasibly influence data collection, however, for a blinded non-inferiority trial, a biased observer could conceivably aim to collect data such that there is minimal difference between groups. The sample size of non-inferiority trials generally needs to be larger than superiority trials. This is because the equivalence margin is set smaller than a similar placebo controlled superiority trial.

In conclusion, there always remains the possibility that for methodological reasons, a between group difference existed in the present study, but this was not detected.

6.2.3. Literature following

Few subsequent dose finding studies have been conducted for continuous interscalene block. Borgeat et al randomised 80 patients undergoing open rotator cuff repair to 0.2 or 0.3% ropivacaine administered at a rate of 14 mL.hr⁻¹. Not surprisingly, opioid consumption and sleep disturbance were improved in the 0.3% group. This study is difficult to generalise to the ambulatory setting where significantly lower basal infusions are used. Tariq et al showed that compared with 0.1%, a continuous ropivacaine 0.2% infusion at 5 mL.hr⁻¹ was associated with lower postoperative opioid requirements and pain scores.

Charrous et al. randomised volunteers receiving bilateral femoral catheters to a continuous ropivacaine 0.1% 5 mL/h basal infusion on one side, and hourly 5 mL bolus doses on the other side. The primary outcome was quadriceps muscle strength
(maximum voluntary isometric contraction) at 6 hours. Quadriceps muscle strength for ropivacaine 0.1% as a basal infusion reduced by a mean (SD) of 84(19)% compared with 83(24)% for those receiving 0.1% ropivacaine as repeated bolus doses (P = 0.91). The mean between group difference in quadriceps strength at 6 hours was -1.1% (95% CI -22.0-19.8%). There were similar marginal differences in the other secondary outcomes. In their publication, the authors concluded: “the study did not find evidence to support the hypothesis that varying the method of local anaesthetic administration – basal infusion versus repeated bolus doses – influences continuous femoral block to a clinically significant degree”. However, no mention was made of the study design with respect to the use of an end-hole perineural catheter rather than a multi-orifice design.

The demonstrated benefits of the intermittent bolus technique over the continuous technique (improved analgesia, reduced local anaesthetic requirement, and perhaps better differential sensory-motor block) are thought to be enhanced by multi-orifice flow; and thus, to maximise these benefits, a multi-orifice catheter is required. Flow pattern from a multi-orifice catheter depends on flow rate: below 80 mL.hr⁻¹, multi-orifice catheters function as single-orifice catheters; above 80 mL.hr⁻¹, they progressively function as multi-orifice catheters. Therefore, a continuous only regimen will likely only deliver single-orifice flow, while an intermittent bolus technique will likely deliver multi-orifice flow. Multi-orifice flow results in better epidural local anaesthetic spread, and it is this better spread that is thought to be responsible for the improved epidural block characteristics with the intermittent bolus technique: improved analgesia and reduced local anaesthetic consumption (for a given analgesic effect). Recent evidence also suggests that by enabling a local anaesthetic dose reduction through the use of the intermittent bolus technique, a
higher sensory-to-motor block ratio can be achieved (less motor block for a given analgesic effect).  Although some studies have demonstrated benefits using the intermittent bolus technique with end-hole catheters, the majority have incorporated a multi-orifice design. The conclusion from the Charrous study that: “it is doubtful that, when using continuous femoral block, varying local anaesthetic administration will provide an increased sensory-to-motor block ratio” therefore requires further study to be definitively concluded. Regardless of the results reported by Charous et al, the present chapter’s study results are still valid – one of the advantages of a low background infusion is that it enables patients to titrate analgesia to motor block. Even if a predominant bolus dose regimen is found to in fact have little effect on block quality, a low background infusion will still enable this titration, which may permit an overall reduction in motor block.

More recently, Yang et al randomised patients receiving continuous interscalene block to a ropivacaine 0.2% infusion of either 6 or 8 mL.hr⁻¹. Indices of block effectiveness did not differ between groups.

6.2.4. Future directions

The present study demonstrated that a mandatory bolus dose regimen may improve the analgesia to side effect balance. The most pressing need for future studies relate to evaluating the analgesic effectiveness of automated boluses for continuous interscalene block. This regimen has been shown to provide benefits for continuous sciatic nerve block and it remains to be seen whether these benefits apply to the interscalene area. Electronic pumps are now available that can deliver these automated boluses in the ambulatory setting (personal communication, Danny
Zanardo, Allied Medical Australia Ltd). A similar study to the present study but incorporating a low background infusion without mandatory boluses would also be desirable.
Part 4: Further Catheter Technique Advances

Chapter 7  Posterior versus anterolateral approach interscalene catheter placement: A prospective randomised trial

Chapter 8  Effect of catheter threading distance and orifice configuration

Chapter 9  Effect of catheter orifice configuration
Chapter 7. Posterior versus anterolateral approach
interscalene catheter placement: A prospective
randomised trial

7.1. Preface

As ultrasound-guided regional anaesthesia becomes more popular and practiced, a
plethora of research involving this relatively new modality is being published — to
the extent that the journal *Regional Anesthesia and Pain Medicine* recently added an
entire ultrasound-related section to every issue. However, the overwhelming majority
of these reports involve single-injection peripheral nerve blocks, rather than
perineural catheters. 185 Unfortunately, data from many of these publications cannot
be automatically inferred to perineural catheter placement for multiple reasons. First,
while the angle between the long axis of the placement needle and nerve is relatively
unimportant for single-injection blocks, it is critical for perineural catheter insertion
since catheters tend to exit the needle and traverse past any nerve that is
perpendicular to the needle itself. 186 Second, a major advantage of ultrasound
guidance for single-injection nerve blocks lies in the real-time repositioning of the
needle tip to maximise local anaesthetic spread, while perineural catheter bolus
and/or infusion is analogous to a single-point injection. 36 Third, unlike needles,
flexible perineural catheters rarely remain within a 2-dimensional ultrasound view,
making it difficult to observe catheter-tip placement relative to the target nerve. 187
Here, the practice of ultrasound guidance for perineural catheter placement
introduced in the previous thesis is further explored. The aim is to briefly review the
major ultrasound-guided catheter-insertion approaches along with their relative
strengths and weaknesses.
7.1.1. Ultrasound orientation

Before engaging in a discussion of ultrasound, commonly-accepted vocabulary introduced in Chapter 2 will be reviewed. A needle inserted with its length within a two-dimensional ultrasound beam is described as “in-plane,” while a needle inserted across a two-dimensional ultrasound beam is “out-of-plane.” A nerve with its long axis within the ultrasound beam is viewed in “long-axis,” compared with “short axis” when viewed in cross-section. 188

7.1.2. Needle in-plane, nerve in short-axis approach

For single-injection peripheral nerve blocks, the overwhelming majority of reports describe a short-axis view of the nerve because this view allows for easier identification and differentiation from surrounding structures. 188 When the needle is inserted within the ultrasound plane (“in-plane”), the needle tip location can be more-easily identified relative to the target nerve. If the initial local anaesthetic bolus is placed through the needle, the spread may be observed and adjustment of the needle tip made, if desired. Unfortunately, when the perineural catheter is inserted past the needle tip, it has the tendency to bypass the nerve given the perpendicular orientation of the block needle and target nerve, 3 although there are certain anatomic locations that will often allow a catheter to be passed and remain perineural. 124, 189 Some practitioners have advocated either passing the catheter a minimal distance past the needle tip, or advancing the catheter further initially and then, after needle removal, retracting the catheter such that its orifice(s) lie a minimal distance (<2 cm) past the original needle tip position 118 (although yet others have suggested this may result in a dislodged catheter tip as the needle is withdrawn over the catheter, especially by

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Some advocate the use of an extremely flexible perineural catheter in an attempt to keep the catheter tip in proximity to the target nerve if the catheter is inserted more than a minimal distance. Still others describe reorienting the needle to a more-parallel trajectory and inserting a stimulating catheter to better monitor catheter tip location.

Proposed benefits of the short-axis/in-plane technique include using the same basic technique for both single-injection and perineural catheter placement, simply adding the insertion of a catheter via the placement needle/angiocatheter; and its application in nearly all anatomic catheter locations, even for deeper target nerves. If a 17- or 18-gauge needle is used, the needle tip may be more-easily identified and remains within the ultrasound plane due to its rigidity compared with smaller gauge needles. While some have speculated that the use of a large needle is more painful, seven prospective studies reported a median catheter-insertion pain score of 0-2 on a 0-10 numeric rating scale (10=most pain imaginable) when the large needle track was first anaesthetised with lignocaine via a 25-27 gauge needle. In addition, the potential benefits of using a larger needle gauge (fewer needle passes given the relative ease of keeping a rigid, larger-gauge needle in-plane; less risk of undesired tissue contact due to misinterpretation of the needle shaft for the needle tip) must be weighed against the potential risks (increased patient discomfort; increased tissue trauma; increased injury if a vessel is punctured).

Disadvantages of the short-axis/in-plane approach include new needle entry sites relative to the nerve compared with more-traditional nerve stimulation modalities which typically use a parallel needle-to-nerve insertion; challenges keeping the needle shaft in-plane; difficulty with needle tip visualisation for relatively deep
nerves; and, as noted above, the catheter tip may bypass the target nerve given the perpendicular orientation of the needle and nerve. If an extremely flexible catheter is used in an attempt to minimise this issue, it is sometimes difficult to thread past the tip of the placement needle.

### 7.1.3. Needle out-of-plane, nerve in short-axis approach

One benefit of this approach is a generally familiar parallel needle-to-nerve trajectory used with traditional nerve stimulation techniques (and also vascular access). In addition, because the needle is parallel to the target nerve, the catheter theoretically may remain in closer proximity to the nerve, even when threaded more than a couple of centimetres past the needle tip. The main disadvantage of this technique is the relative inability to visualise the advancing needle tip, which some speculate increases the likelihood of unwanted contact with nerves, vessels, peritoneum, pleura, or even meninges. However, others have suggested that the consequent orientation of needle more along the long axis of the target nerve—as opposed to perpendicular—makes nerve penetration very unlikely, especially with a 17- or 18-gauge Tuohy needle. Practitioners often use a combination of tissue movement and “hydro-location” in which fluid is injected and the resulting tissue expansion infers the needle tip location (either with or without colour Doppler flow). Some have suggested that for superficial catheters (e.g., interscalene and femoral), the consequent “longitudinal” orientation of needle with nerve makes precise visualisation of needle tip less critical, as the needle tip tends to remain relatively close to the nerve if the needle tip is advanced beyond the ultrasound beam. However, for deeper nerves, this technique is not as straight-forward as guiding the
needle tip to a target nerve as in the in-plane technique described above, and may be more difficult to master (and, at times, nearly impossible). \textsuperscript{122, 195}

\textbf{7.1.4. Needle in-plane and nerve in long-axis approach}

Theoretically, this technique takes the benefits of both previously described approaches, and harbours few of the limitations. The nerve can be viewed along with the needle shaft/tip, and the catheter monitored as it exits the needle parallel to the target nerve. The problem is in the execution: keeping three structures (the needle, nerve and catheter) in the ultrasound plane is not only very difficult to learn, but difficult to execute even after mastery. \textsuperscript{199} Until now, evidence of this technique’s difficulties could be found only indirectly in the scarce published reports. \textsuperscript{199, 200}

\textbf{7.1.5. Summary}

Although proponents of the various approaches voice firm opinions based on their personal experience, few clinical data exist comparing aspects of any particular placement technique with another. Only by prospectively comparing various approaches will their relative benefits and drawbacks be truly revealed and the science of perineural infusion advanced. To this end, well-designed, randomised, controlled clinical trials are needed, allowing the development of an evidence-base for practice guidelines. More specifically and relevant to this thesis, the in-plane posterior and out-of-plane anterolateral approaches for interscalene catheter placement are both in common use, but have not been compared in a prospective randomised manner. That issue formed the basis for the work conducted in the current chapter.
The following section contains an unaltered reproduction of the article “Posterior versus Anterolateral Approach Interscalene Catheter Placement: A Prospective Randomised Trial” published in the journal *Regional Anesthesia and Pain Medicine*, Volume 36, Issue 2, Pages 125-133. In 2011, the journal had an impact factor of 4.079. All figures were generated as originals.
Background and Objectives: Two distinctly different approaches to interscalene catheter placement have been in common use for close to a decade. This prospective randomized study tested the hypothesis that interscalene catheters placed using the posterior approach would provide a more effective analgesia after shoulder surgery compared with catheters placed using the anterolateral approach.

Methods: A total of 110 patients presenting for elective shoulder surgery were randomly assigned to receive an ultrasound-guided posterior (n = 54) or anterolateral (n = 56) interscalene catheter with 20 mL of ropivacaine 0.375% administered preoperatively via the catheter before surgery under general anesthesia. Ropivacaine 0.2% at 2 mL/hour with on-demand hourly 5-mL boluses was continued for more than 48 hours with tramadol available as rescue. Patients were questioned in the recovery room, at 24 and 48 hours after surgery, for pain, ropivacaine bolus, and tramadol consumption.

Results: Patients were more frequently free of pain in the recovery room in the anterolateral group compared with the posterior group (mean, 91%; 95% confidence interval [CI], 84%–99% versus mean, 61%; 95% CI, 48%–74%; P = 0.005). Rescue tramadol consumption was higher for the posterior group during the first but not during the second 24 hours after surgery (day 1/day 2: 2.48% versus 2.77%, P = 0.101; 3.55% versus 3.27%, P = 0.02;). Postoperative pain, ropivacaine bolus consumption, numbness, weakness, neck discomfort, and satisfaction were similar between groups. Catheter threading difficulty was more common (33% versus 13%, P = 0.012), and catheter placement time was longer (median, 9 min; interquartile range, 7.5–10 min versus median, 6.5 min; interquartile range, 6.8–9 min; P < 0.0001) in the posterior group.

Conclusions: Anterolateral interscalene catheters perform more effectively and are procedurally more easily placed compared with catheters placed using the posterior approach.

Two distinctly different approaches to interscalene catheter placement have gained popularity during the last decade: anterolateral and posterior. Ultrasound-guided perineural catheter placement has added an additional consideration: the out-of-plane and in-plane needle-probe alignment techniques. At the interscalene level, the brachial plexus is imaged in the short axis: probe transverse or oblique transverse to the plexus. With the anterolateral approach, needle placement is cephalad of the probe, aligned out-of-plane of the ultrasound beam. With the posterior approach, needle placement is posterior to the probe, aligned in the plane of the beam.

More recently, further enthusiasm for the posterior approach has been expressed because of impressions of shorter procedural times, higher success rates,16–17 better catheter fixation (and therefore higher catheter retention rates),15–17 and a needle puncture site away from the external jugular vein or surgical field. However, despite almost 10 years of experience with both approaches, a prospective randomized controlled trial has not been reported to resolve any of these issues. A stated advantage of the posterior approach is that the needle shaft and tip are more easily visualized, which theoretically promotes more precise needle tip (and therefore catheter) positioning adjacent to the most appropriate elements of the brachial plexus, which, for shoulder surgery, corresponds to the fifth/sixth cervical nerve roots or superior/middle trunks.

Therefore, in a prospective randomized controlled trial, we sought to determine whether the posterior approach for interscalene catheter placement would improve catheter placement and block characteristics compared with the anterolateral approach when used for continuous interscalene anesthesia after shoulder surgery. Subjects underwent shoulder surgery under general anesthesia combined with an interscalene block administered via catheter. The primary outcome end point was the proportion of patients reporting recovery room pain. Secondary end points included operative site pain during postoperative days 1 to 2, subjectively assessed arm numbness, weakness, and indices of catheter placement difficulty.

METHODS

The local institutional review board (Northern Y Regional Ethics Committee, Hamilton, New Zealand) gave approval for the study, and the trial was prospectively registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12609000768291). We enrolled consecutive American Society of Anesthesiologists physical status I to II patients scheduled for elective shoulder surgery in the principal investigator’s practice from October 2009 to May 2010 at the Southern Cross Brightside Hospital. Exclusion criteria included interscalene block refusal, severe respiratory disease, known amide local anesthetic drug allergy, nonsteroidal anti-inflammatory drug intolerance, and preoperative opioid therapy administered for more than 1 month before surgery. Written informed consent for study procedures was obtained from all patients. Oral acetaminophen 1 g, diclofenac slow release 75 mg, and omeprazole 20 mg were administered 1 hr before surgery. In an area immediately adjacent to the operating room, intravenous sedation up to midazolam 2 mg and alfentanil 0.5 mg was
administered. The principal investigator, experienced in both approaches, performed all regional block procedures.

The following palpable landmarks were marked: sternomastoid posterior border, mastoid process, and ericoid cartilage. A “modified” superficial cervical plexus block was administered to facilitate catheter placement and ensure supraclavicular nerve(s) block. With a 22-gauge 2 in. (5-cm) B-Plax needle (Plexafix; B-Braun, Bethlehem, Pa.), 4 mL of lidocaine 1% + epinephrine 1:200,000 was infiltrated midway between the levels of the ericoid cartilage and the mastoid process on the sternomastoid muscle posterior border. Two milliliters was infiltrated subcutaneously along the sternomastoid posterior border approximately to the sixth cervical vertebral level. A further 2 mL was infiltrated in a similar caudal direction approximately 30 degrees posterior to the initial injection and 2 mL in the triangular area in between. A surgical clipper removed any excess neck hair at the anterolateral or posterior catheter fixation point.

After the superficial cervical plexus block, patients entered the operating room, and group allocation was revealed. Randomization to the anterolateral or posterior groups was implemented with a computer-generated random number previously delivered in prepared sealed opaque envelopes with randomization performed by a research assistant away from the study procedures.

The patient was transferred to the operating table, a pulse oximeter was applied, and appropriate aseptic technique was observed.

**Anterolateral Group**

Positioning was supine, and the head was turned to the contralateral side and supported with 1 to 2 pillows (Fig. 1). The scalene muscles and interscalene brachial plexus were imaged in the short axis at approximately the sixth/seventh cervical vertebral level using a 38-mm 13- to 16-MHz linear array transducer (SonoSite HFL/MicroMaxx, Bothell, Wash). A 4- to 5-cm 18-gauge insulated Tuohy needle (Contiplex Tuohy; B-Braun) attached to a 10-mL saline-filled syringe connected to a nerve stimulator (Pajunk Varix, Tucker, Ga) set at 0.2 mA (0.1 msec, 2 Hz) was inserted approximately 1 cm posterior to the sternomastoid muscle dorsal border approximately 3 cm cephalad of the sixth/seventh cervical vertebral level. Needle advancement was using out-of-plane needle-probe orientation superficially into the middle scalene muscle until tissue displacement was observed just lateral to the 2 most superficial brachial plexus elements. At the sixth/seventh cervical vertebral level, this corresponds to the fifth/sixth cervical roots or superior/middle trunks. The needle tip was angled medially toward the 2 most superficial brachial plexus roots/trunks until a resultant medial movement of the brachial plexus was observed.

**Posterior Group**

Positioning was lateral decubitus, with the bed tilted to a slightly reverse Trendelenberg position to drop the ipsilateral shoulder and therefore facilitate exposure of the supraclavicular fossa (Fig. 2A). The procedure was otherwise as for the

**FIGURE 1. Anterolateral approach: Needle-probe orientation. Needle is oriented in the direction of the brachial plexus; needle tip position is inferred by observation of tissue displacement and observation of injectate spread. Barrier drapes were omitted for clarity.**
FIGURE 2. A, Posterior approach: Needle-probe orientation. Barrier drapes were omitted for clarity. B, Posterior approach: axial section of the neck at the level of the sixth cervical vertebra. Needle is oriented perpendicular to the direction of the brachial plexus; needle tip position may be observed through in-plane needle imaging, with or without confirmatory observation of injectate spread.

anterolateral technique except that the needle entry point dorsal to the posterior aspect of the probe was based on achieving a needle orientation approximately parallel to the surface of the transducer: in lean patients, the needle entry point was further anterior and closer to the probe; in heavier patients, the needle entry point was further posterior and further away from the probe. This needle entry point was likely to be either directly through or immediately anterolateral to the levator scapulae muscle (Fig. 2B). Needle advancement was using in-plane needle-probe imaging into the middle scalene muscle until the needle tip was approximately 0.5 cm postero-lateral to the 2 most superficial brachial plexus elements. If the needle tip could not be precisely visualized, needle tip approximation was by injection of 1 mL of 0.9% saline aliquots.
In both groups, needle tip position was ultimately determined by the injection of 10 mL of 0.9% saline and observation of injectate spread immediately lateral to the target roots/trunks, or when a satisfactory brachial plexus ultrasound image could not be obtained, by elicitation of a sustained deltoid, biceps or triceps motor response at less than 0.5 mA. Regardless of needle end point (ultrasound or neurostimulation), if a sustained motor response was present at less than 0.2 mA, needle manipulation occurred (slight withdrawal, rotation) until the response was eliminated. A nonstimulating triple-orifice catheter (orifices approximately 0.9, 0.8, and 1.4 cm from catheter tip and radially oriented at the 12-, 4-, and 8-o’clock positions) was then advanced blindly via the (pink) needle-catheter guide, with the needle bevel facing the center of the shoulder, and then withdrawn such that 2 cm of the catheter remained past the original needle tip position.

The puncture site was sealed with 3 to 4 drops of topical medical cymaoclylate (Glustitch; Delta, British Columbia, Canada), and the catheter was fixed to the skin with a catheter-anchoring device (Lock-it-plus; Portex, Hylle, UK). A separate subcutaneous tunneling procedure was not performed.

Intraoperative Management
A standardized light general anesthetic was administered using a laryngeal mask airway, desflurane anesthesia, and spontaneous respiration (end-tidal minimum alveolar concentration, 0.8–1.0). Ropivacaine 0.375% 20 mL was administered via the catheter after general anesthesia induction but before surgery.19 No long-acting opioid was administered; however, alfentanil 0.25 mg was administered pre oper nata for a respiratory rate greater than 25 breaths per minute.

Post Anesthesia Care Unit Protocol
In the post anesthesia care unit (PACU), patients reporting a numerical rating pain score (NPRS, 0–10) higher than 2 were given a 10-mL lidocaine 2% bolus. If the NPRS remained higher than 2, the catheter was withdrawn 1 cm, and an additional 10-mL lidocaine 2% was administered. If the NPRS still remained higher than 2, the catheter was replaced. All such patients were retained on an intention-to-treat basis. Patients receiving a replacement catheter received a second ropivacaine 0.375% 20-mL bolus.

Postoperative Management
Ropivacaine 0.2% was administered via elastomeric pump delivering 2 mL/hr with patient-controlled boluses of up to 5 mL/hr (PainBuster; Surgical Synergies, Auckland, New Zealand). Patients depressed the ropivacaine bolus button if the NPRS increased to higher than 2. Acetaminophen (1 g every 6 hrs) and diclofenac slow release (75 mg every 12 hrs) were continued if any postoperative pain occurred. If the NPRS was higher than 2 despite regular acetaminophen, diclofenac, and 2 consecutive ropivacaine boluses, tramadol slow release (100 mg every 12 hrs) was added. Discharge home occurred either on the day of surgery, the morning of postoperative day 1 (all open procedures), or for total shoulder joint replacement, on postoperative day 2. This was a private practice setting where the hospital nursing staff and all patients understood they had 24-hr access to the mobile telephone of the principal investigator (and surgeon) for pain control problems. If analgesia was inadequate (NPRS > 5) despite tramadol supplementation, opioid rescue was available by telephone order (oral morphine for a NPRS < 5, intravenous morphine for a NPRS > 5).

Data Collection
Procedural time was recorded by the anesthesia assistant, which was defined as the time from the patient entering the operating room until the catheter-anchoring device was secured to the skin. The principal (operating) investigator recorded the needle end point used for catheter placement (ultrasound or neurostimulation) and whether there was any more than “moderate” resistance to catheter advancement. Moderate resistance was defined as the operator having to regrip the catheter a second time with the index finger and thumb because of resistance to advancement or buckling of the catheter distal to the index finger and thumb. The principal investigator also questioned the patient for procedural pain on an 11-point NPRS (0–10, 0 = no discomfort, 10 = worst discomfort imaginable). He also recorded the number of alfentanil 0.25-mg boluses administered during surgery. The patient’s primary PACU nurse recorded the emergence NPRS in the shoulder, arm, or elbow and details of catheter interventions. A research assistant telephoned all subjects at precisely 24 and 48 h after block placement and questioned for ropivacaine bolus demands, supplemental tramadol consumption, NPRS (at rest and on movement), and arm numbness/weakness (0–10, 0 = no pain, numbness/weakness, 10 = worst imaginable pain, numbness/weakness) during the previous 24 hrs after surgery (specifically excluding pain that was present in the recovery room). At 48 hrs, subjects were also questioned for catheter-related neck pain and overall satisfaction with the technique (0–10, 0 = no neck pain, very unsatisfied, 10 = worst imaginable neck pain, very satisfied).

Blinding of Treatments
Data recorded in the operating room by the principal investigator and his assistant were not blinded. The catheter fixation points for each technique are approximately 5 to 7 cm apart, and our institutional practice is to apply the final dressing in the PACU once catheter effectiveness has been confirmed. Therefore, the primary PACU nurse could have potential investigator also the treatment group. After PACU discharge, all data collection was observer blinded.

Statistical Analysis
An independent statistician not otherwise involved in the study performed all calculations. Twenty-five randomly selected patient data sheets were crosschecked with the electronic database for data entry errors. No errors were found. Categorical outcomes were compared using the chi-squared test (categorical data) or Fisher exact test (continuous data). Ordinal outcomes (procedural time, ropivacaine bolus consumption, numerically rated pain, numbness, weakness, and satisfaction) were compared using the Mann-Whitney U test. P < 0.05 was considered statistically significant. Two-sided tests were used for all experimental outcomes. No corrections were made for multiple comparisons.

Other data were summarized using appropriate descriptive statistics (mean and SD for normally distributed or symmetric variables, median and interquartile ranges for skewed variables, and number and proportion for categorical variables). All statistical analyses were performed using SPSS Statistics 18.0.0 (SPSS, Inc, Chicago, IL).

Sample size calculations were based on the proportion of patients reporting emergence pain. Previous studies using the anesthetist approach with a similar mix of surgeries but using ropivacaine 0.5% 30 mL reported recovery room pain free with a frequency ranging from 82% to 95%.16–21 For the purpose of
**TABLE 1. Patient and Surgical Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Posterior (n = 52)</th>
<th>Anterolateral (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>35 (67)</td>
<td>39 (70)</td>
</tr>
<tr>
<td>Age, yr</td>
<td>47 (15)</td>
<td>48 (15)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>85 (20)</td>
<td>85 (16)</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotator cuff repair (arthroscopic/open)</td>
<td>11 (21)</td>
<td>14 (27)</td>
</tr>
<tr>
<td>Stabilization</td>
<td>9 (17)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Arthroscopic acromioclavicular joint resection</td>
<td>7 (13)</td>
<td>6 (11)</td>
</tr>
<tr>
<td>Arthroscopic acromioplasty</td>
<td>7 (13)</td>
<td>8 (14)</td>
</tr>
<tr>
<td>Total shoulder joint replacement</td>
<td>2 (4)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2)</td>
<td>4 (7)</td>
</tr>
</tbody>
</table>

Values are n (%) or mean (SD).

this sample size calculation, we assumed a (conservative) recovery room pain free rate in the anterolateral group of 85% given the lower administered ropivacaine dose. Assuming 80% power and 2-sided 5% type 1 error protection, detection of a 14% increase in the proportion of patients pain free in the recovery room would require 50 patients in each group (X^2 test, StatMat 2.0; GraphPad Software, San Diego, Calif). To allow for dropouts, we recruited 110 patients. Post hoc power analysis was also performed for the main secondary outcome: postoperative pain with movement on postoperative day 1. The NRPS data from the relevant treatment arms of previous studies involving a similar heterogeneous shoulder surgery mix revealed a combined SD of 2.74.20,21 With this NRPS distributional assumption, 50 patients in each group would detect a shift of 1.6 points on the same 11-point NRP scale (80% power, 5% 2-tailed type 1 significance, unpaired t test, StatMat 2.0—with a 15% adjustment for using the t test when a subsequent nonparametric test was likely).22

**RESULTS**

One hundred ten patients presenting for elective shoulder surgery were enrolled during the study period: 54 patients were randomized to the posterior group and 56 patients to the anterolateral group. Two posterior group patients were excluded after enrolment (Appendix 1). Patient and surgical characteristics of the remaining 108 patients were similar between treatment groups (Table 1). Of these patients, 2 and 4 from the posterior and anterolateral groups respectively, necessitated a sustained motor response at less than 0.5 mM because of suboptimal brachial plexus ultrasound imaging (Table 2). Catheter threading difficulty was more common, and catheter placement time was longer in the posterior group (Table 2).

Patients were more frequently pain free in the recovery room in the anterolateral group compared with the posterior group (mean, 91%; 95% confidence interval [CI], 84%-99% versus mean, 61%; 95% CI, 48%-74%, P = 0.005; Table 3). Rescue tramadol consumption was higher for the posterior group during the first but not during the second 24 hrs after surgery (day 1/day 2: 48% versus 27%, P = 0.017 / 35% versus 27%, P = 0.27; Table 4). Postoperative pain, weakness, neck

**TABLE 2. Catheter Placement Details**

<table>
<thead>
<tr>
<th></th>
<th>Posterior (n = 52)</th>
<th>Anterolateral (n = 56)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>US needle end point</td>
<td>50 (96)</td>
<td>52 (93)</td>
<td>0.012</td>
</tr>
<tr>
<td>Difficulty threading catheter</td>
<td>17 (33)</td>
<td>7 (13)</td>
<td></td>
</tr>
<tr>
<td>Procedural time, min</td>
<td>9 (7.5-10)</td>
<td>6.5 (6-8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Insertion NRPS</td>
<td>2 (1-5)</td>
<td>3 (1-4)</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Values are n (%) or median (interquartile range).

NRPS indicates numerical rating pain score (0-10, 0 = no pain, 10 = worst imaginable pain); US, ultrasound.

**TABLE 3. Intraoperative and PACU Interventions**

<table>
<thead>
<tr>
<th></th>
<th>Posterior (n = 52)</th>
<th>Anterolateral (n = 56)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative alfentanil bolus ≥1</td>
<td>6 (12)</td>
<td>6 (11)</td>
<td></td>
</tr>
<tr>
<td>PACU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total interventions</td>
<td>20 (39)</td>
<td>5 (9)</td>
<td>0.005</td>
</tr>
<tr>
<td>Catheter bolus only</td>
<td>10 (19)</td>
<td>3 (5)</td>
<td></td>
</tr>
<tr>
<td>Catheter withdrawal + bolus</td>
<td>6 (12)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td>Catheter replacement</td>
<td>4 (8)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

Values are n (%).

**TABLE 4. Postoperative Outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Posterior (n = 52)</th>
<th>Anterolateral (n = 56)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol required</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>25 (48)</td>
<td>15 (27)</td>
<td>0.017</td>
</tr>
<tr>
<td>Day 2</td>
<td>18 (35)</td>
<td>15 (27)</td>
<td>0.27</td>
</tr>
<tr>
<td>Morphone required</td>
<td>4 (7.7)</td>
<td>1 (1.8)</td>
<td>0.19</td>
</tr>
<tr>
<td>Ropivacaine bolus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>2 (1-4)</td>
<td>1 (0-3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Day 2</td>
<td>3 (1-5)</td>
<td>3 (0-5)</td>
<td>0.61</td>
</tr>
<tr>
<td>Weakness NRS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>8 (5-8)</td>
<td>8 (5-9)</td>
<td>0.71</td>
</tr>
<tr>
<td>Day 2</td>
<td>4 (1-6)</td>
<td>5 (3-7)</td>
<td>0.15</td>
</tr>
<tr>
<td>Neck discomfort</td>
<td>1 (0-3)</td>
<td>1 (0-3)</td>
<td>0.35</td>
</tr>
<tr>
<td>Satisfaction NRS</td>
<td>8 (7-10)</td>
<td>9 (8-10)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Values are n (%) or median (interquartile range).

*R*This result should be interpreted with caution given there were no corrections for multiple comparisons and the large overlap in the interquartile range between groups.

NRS indicates numerical rating scale (0-10, 0 = no numbness/weakness or very unsatisfied, 10 = very numb/weak or very satisfied).

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Postoperative Pain

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worst Pain</td>
<td>9.3 ± 2.1</td>
<td>9.0 ± 2.1</td>
</tr>
<tr>
<td>Average Pain</td>
<td>6.2 ± 2.1</td>
<td>5.8 ± 2.1</td>
</tr>
</tbody>
</table>

FIGURE 3. Postoperative pain on days 1 and 2. “Worst pain” and “average pain” refer to the entire previous 24 hrs. Bars depict medians, boxes depict interquartile range, and whiskers are 90th centiles. Values are 95% CIs (of the mean).

discomfort, and satisfaction were all similar between groups (Fig. 3 and Table 4). There was weak evidence that day 2 numerically rated numbness was marginally higher in the anterolateral group.

No patient demonstrated symptoms or signs of systemic local anesthetic toxicity, and there were no pneumothoraces evident clinically. One patient developed dyspnea after hospital discharge resulting in a brief admission to another hospital (Appendix 1).

**DISCUSSION**

To our knowledge, this is the first study comparing the anterolateral and posterior interscalene catheter approaches prospectively; all other aspects of the technique controlled. The results support the anterolateral approach in several key outcomes, importantly, early analgesia after surgery.

We can only speculate on the reason for the lower success rate in the posterior group, but it may have been a consequence of imprecise positioning of either needle or catheter. The study protocol dictated an identical intended target needle tip position for the 2 groups—immediately (0.5 cm) posterosilateral to the 2 most superficial brachial plexus elements at the level of the sixth/seventh cervical vertebrae (fifth/sixth cervical roots or superior/middle trunks), but it is possible that the needle tip in the posterior group was not placed as precisely as intended. After penetration of the middle scalene muscle posterior fascia, in some patients, needle negotiation of the middle scalene muscle required “short sharp thrusts” to traverse the muscle; the plexus moving away from the needle on advancement. This resulted from the large-caliber (18-gauge) blunt (Tuohy) needle traversing the lax middle scalene muscle across the long axis of the muscle fibers (the neck muscles are lax in contrast to the thigh muscles, for example, which are taut). Consequently, placing the needle tip near the plexus with these short sharp needle movements was, at times, challenging. Some might question using a Tuohy needle given this problem and might advocate a long bevel needle to facilitate muscle penetration. However, Boezaart and Franco and Boezaart highlighted the fact that sharp needles were avoided around the neuroaxis because dural cuffs can extend along the nerve roots at this level: Tuohy needles providing some protection from penetrating these cuffs with consequent subarachnoid block, or worse, intracranial injection.

Needle shaft visualization was another challenge. In line with the experience of other investigators, despite a needle orientation almost parallel to the surface of the transducer, and rotation of the needle (tip), in some patients, needle shaft/tip imaging was difficult. In these patients, jiggling the needle back and forth and injection of saline aliquots were necessary to verify needle tip position. Third, and most important, in some patients, keeping the needle exactly within the plane of the beam while at the same time not moving the isonaxion angle was challenging—even for an experienced operator. At the sixth/seventh cervical vertebrae level, the fifth and sixth cervical roots often descend into the neck at different angles and are therefore often both only imaged at 1 narrow probe angle. The 3 aforementioned reasons for loss of precision with needle tip positioning are not as critical with in-plane single-injection techniques; block success with single-injection techniques requires the operator visualize only the injected local anesthetic spread, which is usually less challenging than precisely visualizing the needle tip—critical for accurate catheter placement.

Two possibilities exist for catheter imprecision. First, despite only 2 cm of catheter being left beyond needle tip in both groups, the posterior approach catheters possibly buckled or kinked, as suggested by the difficulty with catheter feeding in this group. Catheter advancement across the orientation of the muscle fibers of the scalene muscles was the most likely reason. Second, catheters may have traversed across the roots into the anterior scalene muscle. The anterolateral catheters, with their alignment more in line with the direction of the plexus/roots and adjacent muscle fibers, likely stayed near the roots.
as suggested by the minimal catheter threading difficulty using this approach.

One potential study bias source is that the operating investigator, who placed all catheters, had more previous experience using the anterolateral catheter technique. However, the operator did have substantial experience using the posterior interscalene technique and was also particularly experienced using in-plane perineural catheter techniques. A randomized trial comparing these 2 techniques would ideally incorporate operators having equal experience using each approach and, to maximize generalizability, would incorporate variously experienced operators. However, the technically challenging nature of continuous interscalene analgesia has prevented it gaining widespread acceptance, suggesting that thoracic surgeons develop a single-approach preference. Therefore, a randomized trial would have to enable operator randomization. Such study methods are logistically almost impossible for most operating room settings. Another limitation was the surgical procedure heterogeneity, which meant we had to use recovery room pain as the primary outcome and postoperative pain as a secondary outcome.

Historically, the tested hypothesis was debated anecdotally, or by comparison of the large prospective studies of Borgeat et al.13 and Boezaart et al.6 Despite the single-operator limitation, the present study represents the strongest evidence conducted to date, for the relative effectiveness of the anterolateral and posterior interscalene catheter techniques. Some will inevitably question the success rate of the posterior group of the present study; however, the success rate should be interpreted in the context of the local anesthetic dose administered (ropivaine 0.375% 20 mL followed by ropivaine 0.2% 2 mL/hr t hourly 5-mL boluses), which is the lowest dose reported for both the posterior14-17,24,26 and anterolateral6-5,28 techniques. Previous reports of the ultrasound-guided posterior approach catheter technique have used bolus doses of approximately ropivaine 0.5% 40 mL.16,17 Further, we did not specify a high body mass index exclusion criterion,16,17 and in fact, several posterior group failures had high body mass indices.

It should be recognized that the ultrasound-guided posterior technique used in the present study might not share the same block characteristics as the "continuous cervical paravertebral" technique; the results may not therefore be generalizable to that technique. For both techniques, the block needle approaches the roots (or trunks) tangentially from behind the patient through or alongside the neck extensors. The latter uses the sixth cervical vertebra short-transverse process bone landmark,6,12,26 the former uses ultrasound but with the needle entering the neck more laterally toward the nerve roots/trunks.6,12-17

Established posterior approach teaching was for a motor-sparing effect,6,26 which was explained anatomically: the posterior (sensory) and anterior (motor) rootlets arising from the spinal cord had not fused to form the spinal nerves (anterior rami or brachial plexus roots) at the level of the block was performed. However, the anterior and posterior rootlets have fused proximally to exiting the intervertebral foramina,26 making it conceptually difficult to explain on anatomic grounds. The current studies lack of posterior group motor-sparing effect is in keeping with this anatomy.

Other therapeutic options were not assessed by the study but might warrant a reappraisal of the posterior technique. In particular, precise placement of the catheter under real-time direct ultrasound imaging (eg, between the appropriate nerve roots) is possible. Similarly, observation of injectate administered via the catheter can be used as an indirect marker of catheter-plexus proximity. To date, reports of both methods have been limited to two small case series12,25 and 1 small randomized trial.12 It was noted in one of the case series that, "the catheter may or may not be visualized in its entirety depending on its orientation to the ultrasound beam," and the consensus view of the authors of the editorial accompanying the small randomized trial was that, "perineural catheters rarely remain within a 2-dimensional view, making it difficult to observe catheter tip placement relative to the target nerve." This suggests that the true value of catheter (or catheter injectate) visualization is, at present, unknown. The catheter placement technique used in the current study has been previously widely described and used in a large number of patients with well-documented success; it relies on the assumption that a multi-orificed catheter (orifices 0.4, 0.9, and 1.4 cm from catheter tip) placed 2 cm beyond the target needle tip position (orifices 0.6, 1.1, and 1.6 cm from needle tip position) will retain appropriate perineural proximity. Nevertheless, a technique incorporating ultrasound confirmation of accurate catheter placement may have merit and should be subject to further study, ideally a randomized trial.

Finally, 0.9% saline was used to assist needle tip visualization and to "distant" the perineural space before catheter threading. Saline was preferred over dextrose 5% because “rescue” neurostimulation was expected to be required only rarely, and saline is more readily available in our setting. Dextrose 5% might be a more appropriate solution for practitioners who use neurostimulation more routinely.

In summary, in this study, interscalene catheters placed using the anterolateral approach provided more effective analgesia after shoulder surgery compared with catheters placed using the posterior approach. The anterolateral catheters were also placed more efficiently and with less difficulty.

ACKNOWLEDGMENT

The authors thank Mathangi Shanthakumar, MSc (Med Statistics), for performing the statistical analysis.

REFERENCES


**APPENDIX 1**

**Patient Exclusions, Protocol Deviations, and Complications**

Unless stated, data collection was on an intention-to-treat basis.

**Posterior Group**

No. 42: The patient emerged from anesthesia with a NRPS of 8 despite upper extremity block. Enquiry revealed chronic intermittent opioid therapy that had not been disclosed at the preoperative consultation. All postrandomization data were excluded from analysis.

No. 9: The initial catheter could not be advanced past needle tip; hence, it was left at this position. Resistance to injection via the catheter was high; therefore, a replacement posterior catheter was sited. Pain in the PACU necessitated catheter replacement as per protocol, and given the presence of severe pain and 2 unsuccessful posterior approach catheters, an anterolateral catheter was placed. The subject was subsequently removed from the study.

No. 88: A surgeon-nurse miscommunication resulted in unintentional catheter removal on the morning of day 1. Uneventful reinsertion using the posterior approach occurred within 1 hr.

No. 53: A dressing-induced contact allergy necessitated catheter removal at 30 hrs and subsequent cessation of data collection.

Nos. 71 and 87: Both patients removed their catheters on the afternoon of day 1 because of local anesthetic leakage and concern over effectiveness of the device.
Anterolateral Group

No. 84: Catheter placement was under general anesthesia because of intolerance of the procedure under sedation alone.

No. 90: A 63-year-old woman with a body mass index of 29 kg/m² developed dyspnea on the morning of day 2. Chest radiograph at the local emergency department confirmed a raised hemidiaphragm. Cessation of the infusion occurred for 90 mins with resolution of symptoms.

No. 95: A 48-year-old woman with a body mass index of 37 kg/m² developed orthostatic dyspnea associated with ipsilateral subscapular burning pain during the first few hours after surgery, which was completely relieved by sitting erect. Chest radiograph showed an elevated ipsilateral hemidiaphragm. Tramadol slow release 100 mg and gabapentin 600 mg provided minimal relief. Symptoms resolved at 12 hrs. She experienced no shoulder pain during this time.
7.2. Discussion

7.2.1. Contribution and significance

This was the first study to compare the in-plane posterior and out-of-plane anterolateral approaches for interscalene catheter placement. The results support the superiority of the out-of-plane anterolateral approach over the in-plane posterior approach in terms of ease of catheter placement and catheter effectiveness for analgesia. Interscalene catheter placement is well recognised as being technically challenging\(^{53}\) and these findings may assist with the future uptake of the technique.

7.2.2. Limitations

First, although the present study supports the anterolateral approach, the study did not address whether one technique is easier to learn or teach. This may be relevant given the operator had substantial experience with both techniques. Second, out-of-plane approaches require the operator generate a three dimensional image of the needle shaft and tip,\(^{123}\) which is then confirmed by observation of tissue displacement and/or visualisation of injectate spread. Therefore, extrapolating the results of this study to other block techniques may not be appropriate. Generating a three dimensional image may not be problematic for the superficial interscalene brachial plexus where inadvertent needle advancement beyond the ultrasound beam will still result in the needle tip staying relatively close to the nerve, but it can be an issue for deep structures which require the needle to approach the nerve more perpendicularly (typically 30-45 degrees) e.g. the femoral nerve.\(^{196}\) Further, out-of-plane femoral nerve catheter placement adjacent to the posterior surface of the nerve...
has the added challenge of requiring a ‘rotatory’ needle motion. Out-of-plane interscalene catheter placement, on the other hand, just requires walking the needle tip down to the required depth and then angling the needle tip medially toward the appropriate nerve roots. Finally, with the in-plane technique, a common problem even for experienced operators is keeping the needle shaft within the plane of the beam. In the future, new needles and ultrasound technology may minimise this problem.

A catheter placement technique was used which involved blind catheter advancement a short distance beyond the needle tip. This is not the only way to accurately place perineural catheters. The results may therefore not be applicable for other techniques. For example, other previously used techniques involve confirmation of appropriate catheter position using electrical stimulation (‘stimulating catheter’), direct ultrasound visualisation of the catheter, or indirect confirmation of catheter position through observation of catheter injectate spread. Catheter visualisation either directly or indirectly has not been commonly reported possibly because the effectiveness of this approach has not been validated to the level of a randomised controlled trial. Furthermore, published evidence suggests catheter visualisation is not possible in at least 25% of patients. The present study results may also not apply to techniques involving flexible type catheters, which might advance differently through the tissues when aligned longitudinal or perpendicular to the nerve, the adjacent muscle fibres and fascia.
7.2.3. Literature following

Wang and colleagues \(^{202}\) performed a well-designed randomised, observer-masked study demonstrating the difficulties of the long axis, in-plane approach. Fifty patients had a femoral perineural catheter placed using ultrasound-guidance with an in-plane needle shaft. Half of the subjects had the nerve imaged in the long axis as well, while the remainder had the nerve imaged in short-axis. For the long-axis view group, catheters were advanced approximately 7 cm along the femoral nerve; for the short-axis view group, catheters were advanced 2 cm past the needle tip, but then withdrawn 2 cm following needle removal leaving the catheter tip at the original needle tip perineural position. For the long-axis treatment group, the investigators had great difficulty in keeping the nerve, needle, and catheter all within the ultrasound plane, and “could not advance the catheters with real-time ultrasonographic visualisation in the majority of the patients.” \(^{202}\) They “had to resort to some manoeuvres including changing the position and direction of the ultrasound probe, tilting the probe, shaking and partial withdrawal of the catheter, and injecting 2 to 5 mL saline to find the tip of the catheter.” \(^{27}\) Even with these manoeuvres, 10% of catheters could not be placed within 30 minutes, and the mean (SD) time for all insertions was 21 (8) min vs. 12 (3) min for the comparison group (p<0.01). A difference of 9 min for placement was not only statistically significant, but would be clinically significant in many, if not most anaesthesiology practices. When combined with the increased variability (SD of 8 vs. 3 min), this would often prevent perineural catheter insertion based simply on time constraints. There are additional limitations of the long-axis approach that preclude its use in multiple circumstances. To view the nerve in long-axis, the nerve itself must be relatively straight; and there can be only one target nerve as opposed to multiple trunks or cords as found within the
brachial plexus. All of these issues combine to make the needle in-plane, nerve in long-axis technique the most challenging of the three approaches discussed in the preface of this chapter. However, this balance may change with advances in catheter and/or ultrasound technology in the future. \(^{28}\) It is likely that the study by Wang et al is more an investigation of the difficulty imaging the nerve in long-axis, rather than of needle orientation per se. It confirmed a commonly held view that nerve imaging is easier with the probe aligned in short-axis.

When using short-axis nerve imaging, no other randomised study has been published that compared the in-plane and out-of-plane approaches for either perineural catheter placement, or single injection blocks. However, a study performed by our group and published during the course of this thesis found little difference between the out-of-plane and in-plane approaches for femoral catheter placement. \(^{203}\) Anatomical factors could explain the contrasting findings between that study and the present chapter’s study. Interscalene catheter placement requires the targeting of multiple neural elements (C5-7 roots or superior and middle trunks), compared with femoral catheter placement, which requires the targeting of a single large nerve. These anatomical differences may be relevant if one speculates on the likely catheter position when using the in-plane/short-axis technique and blind catheter advancement. The femoral nerve is typically 1.5 cm in width, \(^{204}\) which would allow a catheter placed transversely to lie with all orifices adjacent the nerve surface, as the most proximal orifice is 1.4 cm proximal to catheter tip. An interscalene catheter advanced transversely would be unlikely to lie adjacent multiple nerve roots or trunks because adjacent roots/trunks are typically aligned in a sagittal (anterior-posterior) orientation. The fascial plane anatomy in the interscalene area may also be a factor in that transverse positioning of a catheter between two adjacent roots may require
penetration of two fascial layers (medial fascia of the middle scalene muscle then lateral fascia of the anterior scalene muscle). For the femoral nerve, once the fascia lata and iliaca have been penetrated lateral to the nerve, no such fascial penetration is necessary near the nerve.

Three subsequent studies described small series of patients undergoing interscalene catheter placement using an in-plane/posterior approach. Although the techniques were described as successful, they provide little insight into whether this approach offers any advantage over the anterolateral approach because the studies were not randomised.

Two studies are worthy of extra discussion and analysis. 170 patients undergoing shoulder surgery were randomised to “conservative” or “aggressive” needle placement for single injection interscalene block. The aggressive (intra-plexus) technique involved advancing the needle in between the two most superficial roots/trunks, and if local anaesthetic spread was incomplete, further needle manipulation to ensure adequate spread. For the conservative (peri-plexus) technique, the needle was advanced no further than the medial border of the middle scalene muscle before local anaesthetic deposition. Local anaesthetic for both groups was 15-30 mL bupivacaine 0.5% depending on patient weight. Although the intra-plexus blocks had a slightly longer duration, there was no difference between groups in block onset or quality. This was the first study in the interscalene area to evaluate the relative merit of injecting local anaesthetic at a single point just lateral to the plexus, or more aggressively (and deeply) between adjacent nerve roots/trunks. The aggressive technique requires a distinct fascial pop to penetrate the fascia on the medial border of the middle scalene muscle. Other investigators have subsequently
reproduced the same results. What is becoming clear from these and other studies, is that a multi-injection technique provides little benefit for brachial plexus blocks, but significant benefit for the blockade of single large nerves e.g. the popliteal sciatic nerve. These studies also provide support for the anterolateral out-of-plane approach over the posterior in-plane technique for interscalene catheter placement. The more conservative anterolateral approach relies on simply positioning the catheter alongside the plexus, while the posterior approach often involves more aggressive needle positioning through the fascia on the medial border of the middle scalene muscle to a position between adjacent roots. There is also limited evidence that it is preferable to position the needle adjacent the C6 root rather than the C5 root, which could be related to the anatomical fact that the nerves innervating the shoulder joint (see Chapter 2) arise from not only the C5 and C6 roots, but also the C7 root.

Finally, Hanson et al performed an observational study in 50 patients undergoing interscalene block, which was designed to characterise the position of the long thoracic and dorsal scapular nerves. Two investigators sonographically mapped the positions of both nerves, both of which were confirmed with neurostimulation. In 90% of subjects, the position of one or both nerves was confirmed: a mean 1.1 cm deep to the skin and 0.7 cm lateral (posterior) to the brachial plexus. Depth to the skin was similar to the C6 nerve root. This study provides further evidence in support of the anterolateral (over the posterior) approach for both single injection interscalene block and in particular, interscalene catheter placement. With the anterolateral approach, the probe is orientated transverse to the plexus and needle-skin puncture is approx. 3 cm cephalad. Using the walk down technique, the needle tip is advanced, immediately lateral to the plexus, down to approx the C6 root depth.
Consequently, the paths of both the long thoracic and dorsal scapular nerves are avoided. The anterolateral approach is also several centimeters away from the phrenic nerve. With the posterior approach, both nerves lie in the path of the advancing needle. The clinical relevance of making contact with these nerves is uncertain, as being small nerves, they are most likely to be pushed away by an advancing blunt needle. The posterior approach is still a relatively new approach; time will tell whether long thoracic/dorsal scapular nerve neuropathy is a clinical issue.

7.2.4. Future directions

The study published in this chapter was initially rejected, but underwent successful rebuttal that led to publication. The issue investigated is highly controversial and inevitably attracted strongly positive and negative reviews. Peer review suggested that many practitioners are still strong advocates of the posterior/in-plane approach because of the ability to visualise the needle tip. Similar studies in different centres and by both trainees and experienced practitioners are therefore needed to confirm or refute this study’s findings. The hypothesis raised in the present study, that part of the problem with the posterior technique was excessive resistance to needle advancement using a blunt needle could be tested in future studies. For example, the issue could be satisfactorily addressed with a randomised study of sharp versus blunt needles for the posterior approach.
Chapter 8. Effect of catheter threading distance and catheter orifice configuration

8.1. Preface

The literature review in Chapter 2 identified several procedural issues relevant to interscalene catheter placement that are yet to be resolved. One was the optimum distance to thread an interscalene catheter beyond needle tip. Early description of the technique involved non-stimulating catheters threaded at least 5 cm beyond needle tip. These studies were associated with high ‘secondary’ catheter failure rates (i.e. local anaesthetic primarily injected through the needle successful, but the catheter infusion unsuccessful). This resulted in clinician scepticism about the value of the technique. Subsequently, practitioners started advancing the catheter less than 5 cm beyond the needle tip which corresponded with higher success rates. However, the optimum catheter threading distance remained unknown. Theoretically, by minimising catheter deviation, threading the catheter 1-2 cm would increase the success rate, while up to 5 cm would reduce the risk of inadvertent removal. Therefore the study presented in this chapter was conducted primarily to evaluate the optimum distance to thread a non-stimulating catheter beyond an anterolaterally orientated needle for interscalene catheter placement.

The following section contains an unaltered reproduction of the article “Catheter Orifice Configuration Influences the Effectiveness of Continuous Peripheral Nerve Blockade” published in the journal *Regional Anesthesia and Pain Medicine*, Volume 36, Issue 5, Pages 470-475. The journal covers research in the fields of regional anaesthesia and pain medicine, and in 2011, had an impact factor of 4.079.
Catheter Orifice Configuration Influences the Effectiveness of Continuous Peripheral Nerve Blockade

Michael J. Fredrickson, FANZCA, MD, * Craig M. Ball, MD† and Adam J Dalgleish, MD‡

Background and Objectives: We investigated perineural catheter threading distance and orifice configuration during continuous intercostal analgesia.

Methods: One hundred fifty-three patients receiving an analgesic intercostal intercostal catheter (catheter needle and nerve) in a similar alignment for elective shoulder surgery were randomized to 1 of 3 groups; following ultrasound guidance the needle tip in the same direction, is a simple, well described and tested technique and supported by prospectively collected data from more than 5000 patients—with generally excellent results. However, controversy exists regarding the optimal catheter plate configuration. Distances less than 1.5 or more than 3 cm are most commonly advocated.1,2,5,6,7,8

A second determinist pinned catheter success not previously investigated is catheter configuration: end-hole versus multiflucula Multiflucula catheters in this study performed better in terms of spread with intermittent bolus regimens, and provide alternative flow channels if one orifice obstructs. However, they may result in “multifluomaternal” placement with a resulting segmental (patchy) block10,11,12 and may also increase the intravascular absorption risk.13,14 Although these orifice configurations have been studied in the setting of epidural analgesia, no studies are available for peripheral nerve blocks, despite both configurations being in widespread use for more than a decade.

We therefore designed a prospective randomized trial to investigate primarily the impact of catheter threading distance on the effectiveness of continuous peripheral nerve blockade, in this instance, anterolateral approach intercostal analgesia. We hypothesized that catheter threading distance would have little effect on catheter performance. As a secondary consequence of this design, the study also assessed the effect of catheter tip configuration.

METHODS

The local institutional review board (Northern Y Regional Ethics Committee, Hamilton, New Zealand) approved the trial, and prospective registration was with the Australian and New Zealand Clinical Trials Registry (ACTRN12010000219077). Oral and written informed consent was obtained from all patients; the study was in accordance with the Declaration of Helsinki, and we followed the CONSORT recommendations for reporting randomized clinical trials. Consecutive American Society of Anesthesiologists physical status 1 to 3 patients, aged 16 to 75 years, scheduled for elective shoulder surgery under the care of one of the principal investigators from May 2010 through February 2011 at the Southern Cross Private Hospital were recruited. A research assistant mailed initial invitation for participation, but definitive recruitment was by the principal investigator. Exclusion criteria included intussusception block failure, severe respiratory disease, known allergy to local anesthetic drug allergy, transdermal anti-inflammatory drug intolerance, and preoperative opioid therapy administered for more than 1 month before surgery. The design was a single-center, prospective, randomized, observer-blinded trial.

Randomization and Blinding

One hundred fifty-three patients were randomly assigned to 3 groups. Randomization to the 3 groups was performed by a

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research assistant away from the study procedures and implemented with a computer-generated random number in blocks of 20. Randomization was not stratified by procedure. Group concealment was by 153 prepared sealed opaque envelopes, opened immediately after the superficial cervical block, but just before catheter placement. Data recorded in the operating room by the principal investigator were not blinded. All subsequent data collection was patient and observer blinded.

**Study Interventions**

Random assignment was to blind catheter advancement 0.5, 2.5, or 5 cm past the interscalene catheter needle tip (groups 0.5, 2.5, and 5, respectively). A triple-orifice catheter was used for groups 2.5 and 5. The triple-orifice catheter orifices are at approximately 0.5, 1, and 1.5 cm from the catheter tip and radially oriented at 12-, 4-, and 8-o’clock positions. Thus, in groups 2.5 and 5, the middle orifice was positioned approximately 1.5 and 4 cm distal, respectively, to the needle tip. The presence of the proximal orifice 1.5 cm proximal to the tip of the triple-orifice catheter meant that an end-hole catheter had to be used in the 0.5 cm group. The multiorifice catheter used for groups 2.5 and 5 was the standard triple-orifice catheter supplied with the Contiplex Tuohy kit (B/Braun, Bethlehem, Pa). The end-hole catheter (group 0.5) was prepared by cutting with a surgical blade and a 90-degree square cut, the triple-orifice catheter just proximal to the most proximal orifice (ie, 1.5 cm proximal to the catheter tip). All catheters were also cut at the proximal end to a length of 30 cm.

**Study End Points**

The primary end point was the proportion of patients reporting recovery room pain. The main secondary end points were time to first pain, numerically rated pain, and tamudol consumption during the first 24 hrs.

**Anesthesia and Analgesia**

A standardized technique was used. A multimodal oral analgesic regimen consisting of oral acetaminophen 1 g, diclofenac slow release 75 mg, and onaprazole 20 mg was started 1 hr before surgery.

Intravenous sedation up to midazolam 2 mg and alfentanil 0.5 mg was administered immediately outside the operating room. The principal investigator, who was experienced with this procedure, performed all blocks.

First, a “modified” superficial cervical plexus block was placed to facilitate catheter placement and ensure supraventricular nerve(ly) blockade.15 The following palpable landmarks were marked: sternomastoid posterior border, mastoid process, and cricoid cartilage. With a 22-gauge, 5-cm B-Plex needle (Plexfix; B/Braun), 4 mL lidocaine 1% + epinephrine 1:200,000 was infiltrated subcutaneously at a single point midway between the level of the cricoid cartilage and the mastoid process 1 cm posterior to the sternomastoid muscle posterior border. Two milliliters was infiltrated subcutaneously along the sternomastoid posterior border approximately to the sixth cervical vertebral level. A further 2 mL was infiltrated subcutaneously in a similar caudal/direction approximately 30 degrees posterior to the initial injection and 2 mL in the triangular area in between.12

Following the superficial cervical plexus block, patients were taken to the operating room and transferred to the operating table for subsequent catheter placement. A pulse oximeter was applied, and appropriate anesthetic technique observed. "Positioning was supine, the head turned to the contralateral side and supported with 1 to 2 pillows. The scalene muscles and inter-scalene brachial plexus were imaged in the short axis at approximately the sixth/seventh cervical vertebral level using a 38-mm, 15-6-MHz linear ultrasound probe (SonoSite HFL/ MicroMaxx; SonoSite, Bothell, Wash). A 4-cm, 18-gauge insulated Tuohy needle (Contiplex Tuohy; B/Braun) attached to a 1 mL saline-filled syringe connected to a nerve stimulator (Varin, Pajunk, Tuker, Gi) set at 0.2 mA (0.1 millisecond, 2 Hz) was inserted approximately 1 cm posterior to the sternomastoid muscle dorsal border approximately 3 cm cephalad of the sixth/seventh cervical vertebral level.14 Needle advancement was with the use of out-of-plane needle-probe orientation through the subcutaneous tissues into the middle scalene muscle (always associated with a “pop” as the prevertebral/scalenae fascia is penetrated) until tissue displacement was observed just lateral to the 2 most superficial brachial plexus elements. At the sixth/seventh cervical vertebral level, this corresponds to the fifth/sixth cervical roots or superior/middle trunks. The needle tip was angled medially to be immediately lateral to 2 most superficial brachial plexus roots/trunks (usually associated with brachial plexus medial movement). "Needle tip position was finally determined by the injection of 10 mL 0.9% saline and monitoring of injectate spread laterally to the target roots/trunks, or when a satisfactory brachial plexus ultrasound image could not be obtained, by elicitation of a sustained deltoid, biceps, or triceps motor response at less than 0.5 mA. If a sustained motor response was present at less than 0.2 mA, needle manipulation occurred until the response was eliminated."14

Following confirmation of correct needle tip position, with the needle bevel facing laterally, and the needle-catheter guide sited within the needle hub, a nonstimulating catheter was blindly advanced 3 to 7 cm beyond the needle tip and then, after needle withdrawal, until withdrawn 0.5, 2.5, or 5 cm of catheter remained past the original needle tip position.

The puncture site was sealed with 3 to 4 drops of topical medical cymoxanecyleate (Dermabond, Ethicon, San Angelo, Tex), and the catheter fixed to the skin with a catheter-anchoring device (Lockit-plus; Portex, Hythe, UK). A separate subcutaneous tunneling procedure was not performed.

**Intraoperative Management**

General anesthesia was also standardized using a larynged mask airway and spontaneous respirations (deeper end-tidal minimum alveolar concentration, 0.8–1.0). Following general anesthesia induction and approximately 10 mins after catheter placement, but before surgery, a 20-mL bolus of a 50:50 mixture of lidocaine 1% + ropivacaine 0.75% was administered via the catheter over approximately 2 to 3 mins (flow rate expected >400 mL/hr).13 No long-acting opioid was administered intraoperatively; however, alfentanil 0.25 mg was administered if the respiratory rate was greater than 25 breaths/min.

**Painesthesia Care Unit Protocol**

In the postanesthesia care unit (PACU), patients reporting a numerical rating pain score (NRPS, 0–10) of more than 2 were administered a 20-mL bolus of a 50:50 mixture of lidocaine 2% + ropivacaine 0.75%. If, 30 mins after this bolus, the NRPS remained more than 2, morphine 2 mg every 2 to 3 mins was administered to achieve an NRPS of 2 or less.

**Postoperative Management**

An electronic pump delivered ropivacaine 0.2% at 2 mL/hr with patient-controlled 5–10 mL boluses (flow rate 150 mL/hr) of up to 1 bolus every hour (PainBusser; Surgical Synergies).
Auckland, New Zealand). From the onset of shoulder pain until 48 hours postoperatively, patients deprived the ropivacaine bolus button “on the clock” (“mandatory”) every 6 hours irrespective of the NRPS. Additional 3-mL boluses were administered in between mandatory 6-hour boluses if the NRPS increased to more than 2. Multimodal analgesia was continued after surgery: acetaminophen (1 g every 6 h) and diclofenac slow release (75 mg every 12 h) if any postoperative pain occurred; tramadol slow release (100 mg every 12 h) if the NRPS increased to more than 2 despite regular acetaminophen, diclofenac, and 2 consecutive ropivacaine boluses. Discharge home occurred on the day of surgery; the morning of postoperative day 1 (all open procedures), or, for total shoulder joint replacement, on postoperative day 2.

Data Collection

The principal (operating) investigator recorded the needle end point used for catheter placement (ultrasound or neurostimulation). He also recorded whether there was difficult resistance to catheter advancement; defined as total obstruction to catheter passage from the nerve tip (usually associated with buckling of the catheter distal to the advancing index finger and thumb) requiring needle manipulation or an additional needle saline bolus. Positive aspiration of venous blood by the catheter was recorded. The principal investigator also recorded the number of alfentanil 0.25-mg boluses administered during surgery. The patient’s primary PACU nurse recorded the emergence NRPS in the shoulder, arm, or elbow details of PACU interventions (local anesthetic bolus, morphine rescue). A research assistant phoned all subjects at 24 and 48 postoperative hrs and questioned for ropivacaine bolus demands, supplemental tramadol consumption, time to first pain, NRPS (worst and “average” pain during the previous 24 hrs), and numbness/weakness—0 = no pain, numbness/weakness; 10 = worst imaginable pain, numbness/weakness)—during the previous 24 hrs (specifically excluding pain that was present in the recovery room). Patients were also asked whether “the booster button had stopped working as well as it had previously” (yes/no). At 48 hrs, subjects were also questioned for overall satisfaction with the technique (0 = very unsatisfied, 10 = very satisfied).

Statistical Analysis

An independent statistician (Richard White) performed all calculations. For the primary outcome (% reporting pain in the PACU), 95% confidence intervals (CIs) are reported, thus providing equivalence estimates with 95% confidence. The skewed NRPS data were logtransformed (to convert to an approximate Gaussian distribution) before CIs were calculated. Categorical outcomes were compared using the Fisher exact test (difficulty threading difficulty PACU interventions, “boosters button stopped working”). Non-normally distributed continuous variables (time to first pain and ordinal outcomes (triamodol consumption, ropivacaine bolus use, tenuously rated pain, hand numbness, hand weakness, and satisfaction) were compared using the Kruskal-Wallis test. We performed planned comparisons (with multiple-comparisons correction) between groups 2.5 and 0.5 and groups 2.5 and 5 using Dunn’s (95% CI) postest. P < 0.05 was considered statistically significant. Two-sided tests were used for all experimental outcomes. Other data were summarized using appropriate descriptive statistics (mean and SD or mean and range for normally distributed or symmetric variables; median and interquartile ranges for skewed variables; number and proportion for categorical variables). All statistical analyses were performed using R 2.12.1 (R Foundation, Vienna, Austria)

Sample size estimates were based on a demonstration of equivalence of the primary outcome: the proportion of patients reporting emergence pain. We considered a 15% difference as clinically significant. A previous study using the airtensional approach and a similar surgical mix but two 20-mL ropivacaine 0.375% reported a 90% pain-free recovery room rate. Assuming 80% power, detection of a 15% shift (9% increase; 9% decrease) in the proportion of patients pain-free in the PACU, with 95% confidence, would require 50 patients in each group (χ2 test, Statmate 2.0 GraphPad Software, San Diego, Calif.).

Given the evidence of primary outcome equivalence between multirofile groups 2.5 and 5, we performed post hoc power analysis for the main secondary outcome (“average pain” during the first 24 hrs) for these groups. SD values were 1.4 and 1.9 in groups 2.5 and 5, respectively; thus, allowing for a 15% adjustment for the use of the / test when a subsequent non-parametric test was expected, the study had 80% and 99% power to detect a difference of 1.1 and 1.7 NRPS points, respectively (Statmate 2.9).

RESULTS

One hundred thirty-four patients presenting for elective shoulder surgery were enrolled, 50, 50, and 53 patients were randomized to groups 0.5, 2.5, and 5, respectively. Patient and surgical characteristics were comparable between groups (Table 1).

Two patients were excluded following PACU discharge: 1 group 0.5 patient did not follow the mandatory bolus instructions correctly and 1 group 5 patient could not be contacted after hospital discharge; thus, 151 patients completed the study. Of 1 patient randomized to group 0.5 cm, high injection resistance prevented the initial intraoperative local anesthetic block. The problem resolved after catheter withdrawal to 2.5 cm at the end of surgery; the patient was retained in group 5. Three, 4, and 2 patients

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<th>TABLE 1. Patient and Surgical Characteristics</th>
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<td>Arthroscopic capsular release</td>
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<td>Total shoulder joint replacement</td>
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Values are mean (SD), mean (range), or n.
in groups 0.5, 2.5, and 5 cm, respectively, necessitated a sustained motor response at less than 0.5 mA because of subaxillary brachial plexus ultrasound imaging (Table 2). Ease of catheter threading was similar between groups (Table 2).

Pain was more frequent in the recovery room in the end-hole 0.5 cm group compared with the multifluid 2.5 and 5 cm groups (34% vs 6%, 9%; \( P = 0.0053 \); Table 2). Groups 2.5 and 5 demonstrated equivalence for this outcome (95% CI of difference between proportions, -7% to 15%). During the first 24 hrs, despite all patients leaving the ICU with effective analgesia, "average pain" (median = 3 vs 1, 2; \( P = 0.0044 \); Fig. 1), ropivacaine bolus, and tranudal consumption were higher in the end-hole 0.5 cm group (Table 3). Time to first pain (10 vs 17, 15 hrs) was also correspondingly shorter in the end-hole 0.5 cm group (Table 3). Neither group 2.5 or 5 cm demonstrated superiority in any outcome (Table 1).

There was no evidence of unintentional catheter vascular cannulation in any patient. No patient demonstrated symptoms or signs of systemic local anesthetic toxicity. No patient reported significant dysesthesia requiring more than simple reassurance, before or after hospital discharge.

**DISCUSSION**

The most notable finding from this study was the unexpected apparent finding that a multifluid perineural catheter produces superior intermittent bolus peripheral nerve blockade compared with end-hole catheters. A second finding, of lesser clinical importance, was the lack of any significant outcome benefits for multifluid catheters advanced 0.5 cm beyond needle tip compared with those advanced 5 cm (and vice versa).

The apparent benefit of the multifluid configuration over the end-hole design should be interpreted in the light of the slight difference in catheter orifice position in groups 0.5 and 2.5, the proximal and middle orifices of group 2.5 were approximately 1 cm and 1.5 cm beyond the needle tip—0.5 and 1 cm, respectively, to the position of the end-hole orifice of group 0.5. This discrepancy arose because the study was designed primarily to investigate the effect of catheter threading distance rather than orifice configuration. However, the absence of outcome differences between groups 2.5 and 5 suggests that this orifice position effect was unlikely to have contributed significantly to the difference in outcomes between groups 0.5 and 2.5, at least for the primary outcome. The significant between-group difference in the proportion of patients on day 2 who reported that "the booster button had stopped working as well as previously" raises the possibility of catheter migration in the 0.5 cm group. However, there was no difference in this outcome present on day 1; hence, this potential confounder was unlikely to have contributed to the observed day 1 outcome differences. Ideally, future studies should investigate the orifice configuration effect with catheter threading distance controlled.

The apparent orifice configuration effect is consistent with continuous epidural analgesia studies: multifluid epidural catheters have been shown to improve analgesia and reduce local anesthetic consumption compared with end-hole catheters. However, the benefits of the multifluid design may apply only under the conditions of intermittent local anesthetic bolus regimens. Intermittent bolus regimens represent the most efficient way of delivering local anesthetic14-20 and, compared with continuous only infusions, provide more effective analgesia, for both continuous epidural and continuous peripheral nerve blocks. In addition, “autoneuro” the bolus regimen, that is, delivering regular, preprogrammed boluses (electronic or patient initiated),

![Graph](image)

**TABLE 2. Catheter Placement and Intraoperative and PACU Interventions**

<table>
<thead>
<tr>
<th>Interventions</th>
<th>0.5 cm</th>
<th>2.5 cm</th>
<th>5 cm</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound needle end point</td>
<td>47 (94)</td>
<td>46 (92)</td>
<td>51 (86)</td>
<td>0.16</td>
</tr>
<tr>
<td>Difficulty threading catheter</td>
<td>6 (12)</td>
<td>6 (12)</td>
<td>6 (12)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Intraoperative alfentanil bolus ≥1</td>
<td>3 (6)</td>
<td>6 (12)</td>
<td>3 (6)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>PACU</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local anesthetic bolus</td>
<td>17 (34, 24-46)</td>
<td>3 (6, 2-14)</td>
<td>5 (9, 4-18)</td>
<td>0.0063</td>
</tr>
<tr>
<td>Meperidine bolus</td>
<td>7 (14)</td>
<td>1 (2)</td>
<td>3 (6)</td>
<td>5 (9)</td>
</tr>
</tbody>
</table>

Values are n (%) or n(median) (range). 90% CI: 90% CI provide equivalence estimates with 90% confidence.

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enhances those benefits.4,6,22,23 Similarly, the benefits of intermittent bolus regimens may apply only to multiorifice catheters.22,23

Flow from a multiorifice catheter has been shown to depend on the flow rate: below 90 mL/hr, multiorifice catheter function like single-orifice catheters.13 Therefore, the present results may not be generalizable to infusion-only regimens. With infusion-only regimens, orifice configuration is likely to have minimal impact on block characteristics because, with these regimens, multiorifice catheters will function as single-orifice catheters.13,22,23 In other words, to realize the benefits of the multiorifice design, flow rates greater than 100 mL/hr need to be achieved—flow rates that can be delivered only with intermittent bolus regimens. Extrapolating from in vivo experiments, the regimen used in the present study likely resulted in triple-orifice flow during the manual primary local anesthetic bolus (>400 mL/hr), double-orifice flow during on-demand boluses (150 mL/hr), and single-orifice flow during the background infusion (2 mL/hr).13

Most commercially available continuous peripheral nerve block catheter kits contain an end-hole-type catheter. For example, the Arrow Stimucath (Stittles Medical, Research Triangle Park, NC), the Purjek Plexolong (NanoLine and Sono, Stimulon Sono, and SonoLong NanoLine (Fujiki Medical, Norecos, Gu) kits all contain an end-hole catheter; the B/Braun Centiplex (Tulob, D and Sim) kits contain a multiorifice catheter; the Polymedic Polypoles kit (Medline Industries, Mundeléine, III) is available in both designs. Epidural catheters, on the other hand, are usually available in both an end-hole and multiorifice design; thus, a simple option for conceiving peripheral catheter kits containing an end-hole catheter to a multiorifice type would be to replace the end-hole catheter with a multiorifice epidural catheter.

We performed the present study in the interscalene area. Given the results are similar to those previously observed for epidural analgesia,24,25 it is not surprising that the benefits of the multiorifice design would apply to other areas such as the femoral and sciatic nerves; however, ideally, confirmatory studies should be conducted.

The demonstrated equivalence between groups 2.5 and 5 suggests that when the needle and interscalene brachial plexus are at approximate alignment such as when using the anterior lateral approach, blindly advancing a catheter 5 cm beyond needle tip does not apparently compromise catheter plexus proximity. However, it is noteworthy that 6 outcomes demonstrated a trend to superiority in group 2.5 compared with group 5 cm: recovery room pain, time to first pain, “average” pain, and ropivacaine bolus consumption during the first 24 hrs. Although each outcome difference was not statistically significant, the consistency of the direction of the trend makes statistical chance explanation unlikely. In other words, taken together, they suggest that group 2.5 was associated with improved orifice-plexus proximity.

We emphasize that the observed lack of a catheter threading distance effect may not be generalizable to approaches where the needle is aligned perpendicular to the nerve/plexus. Because, with tangential approaches, blind 5cm advancement of a non-flexible (or flexible)28 catheter is likely to result in the catheter deviating away from the nerve/plexus. We hypothesize that similar results may be found for other superficial locations where it is possible to approximate the needle angle in the direction of the target nerves such as the femoral and popliteal sciatic regions, but this remains to be studied.

Having all catheters placed by an experienced operator gave the study significant strength: the ability to control for differences other than orifice configuration and catheter threading distance relied, in part, on the catheters in each group being placed consistently in the same position. Confirmation of catheter positioning by direct catheter visualization or “invisibility” by observation of catheter injection spread has been previously used,1 and it could be argued that these methods made the current “blind” method redundant. However, these techniques have not been rigorously validated, in particular, with the strength of a randomized controlled trial. Furthermore, a recent controlled trial performed by 2 anesthesiologists with 2 years’ experience in ultrasound-guided regional anesthesia, revealed that catheter visualization (femoral area, in-plane technique) was not possible in 21% of patients.24 This issue would possibly be more of a problem with the out-of-plane technique as used in the present study. We prepared the end-hole catheter by cutting the standard multiorifice catheter with a surgical blade. Future studies should ideally incorporate a commercially produced catheter. Finally, the “success” (66%) of the end-hole group could seem inappropriately low for interscalene block suggesting that these catheters might not have been positioned satisfactorily. However, no previous studies have evaluated interscalene block “success” when performed using 20 mL of local anesthetic through an end-hole catheter.

In summary, this study suggests that the previously known performance benefits of epidural multiorifice catheters (when used with intermittent bolus regimens) also apply to peripheral nerve catheters. Furthermore, in the context of anterolateral approach interscalene analgesia (needle and plexus aligned in
ACKNOWLEDGMENTS

The authors thank Richard White, R. Math (Advanced Honors, Harvard School of Public Health, Harvard University, Boston, Mass) for performing the statistical analysis.

REFERENCES


8.2. Discussion

8.2.1. Contribution and significance

Following further reflection since this study was published, in part arising out of additional peer review, reorientation of the study findings is warranted. Input from both the thesis reviewers and the thesis supervisor brings the author to the conclusion that certain aspects of the conclusions made in the published paper are inappropriate. Specifically, inappropriate emphasis was placed on the possible effect of catheter orifice configuration, when it was impossible to exclude the effect of catheter threading distance in the 0.5 cm end-hole group. A more appropriate conclusion is that the study found that a "multi-orifice perineural catheter threaded 2.5 to 5 cm into the plexus region produces improved indices of catheter performance in the immediate post-operative period compared to a single orifice catheter threaded to 0.5 cm". There are two key components to this conclusion. First was the lack of any significant outcome benefits for multi-orifice catheters advanced 2.5 cm beyond needle tip compared to those advanced 5 cm (and vice versa). Secondly, was the inferior performance of the 0.5 cm end-hole group. Either reduced threading distance or the use of an end-hole catheter in this study group could explain this inferior performance.

For catheter placement techniques involving alignment of the catheter needle in the direction of the nerve or plexus, there has been controversy regarding the optimum blind distance to introduce a non-stimulating catheter. \(^2\) It was argued in the literature review in Chapter 2, \(^3\) that blindly advancing a non-flexible catheter placed via the anterolateral approach more than 3 cm beyond needle tip might
compromise the success rate of the technique. This recommendation was based on a historical observation that the success rate associated with continuous interscalene block increased from 1995 – 2005, which was paralleled by an observation in the relevant studies that the distance catheters were threaded past the needle tip reduced over the same time period. The present study does not support this contention, and illustrates the potential risk associated with making inference from apparent associations. The present results suggest that when the needle and interscalene brachial plexus are in approximate alignment using the anterolateral approach, blindly advancing a catheter 5 cm beyond needle tip will not significantly compromise catheter plexus proximity. That said, advancing the catheter beyond 5 cm is unlikely to offer further benefit in terms of reducing the risk of catheter dislodgement, and may in fact increase the risk of complications arising from catheter deviation.

8.2.2. Limitations

As previously discussed, the main limitation of this study was the introduction of two variables into the three treatment groups – catheter orifice configuration and threading distance. This confounder arose because the study was designed primarily to investigate the effect of catheter threading distance featuring a group threaded 0.5 cm beyond the needle tip. It was obvious that use of a triple office catheter in the 0.5 cm group would result in the proximal orifice being positioned proximal to the needle tip. The only logical solution was to convert this group to an end-hole catheter. However, the result was to introduce two variables to that treatment group – either or both variables may have contributed to the observed inferior performance of that group. Specifically, the proximal and middle orifices of group 2.5 cm were
approximately 1 and 1.5 cm beyond the needle tip – 0.5 and 1 cm distal respectively to the position of the end-hole orifice of group 0.5 cm. However, the absence of outcome differences between groups 2.5 cm and 5 cm was against this orifice position effect contributing significantly to the difference in outcomes between groups 0.5 and 2.5 cm; at least for the primary outcome. The significant between group difference in the proportion of patients on day 2 who reported that “the booster button had stopped working as well as previously” raises the possibility of catheter migration in the 0.5 cm group. No difference in this outcome was present on day one; hence this potential confounder was unlikely to have contributed to the observed day one outcome differences. Moreover, for the reasons outlined above, it seems logical to suggest that the outcome would have been no better for the 0.5 cm group if a multi orifice catheter had been used.

As stated in the article, cutting the catheter with a blade may have influenced the performance of the end-hole catheter. It is conceivable that the sharp edges produced by such a surgical blade could have affected how this catheter negotiated tissue planes compared with a factory-produced design incorporating round edges.

It is emphasised that these findings may not be generalised to approaches where the needle is aligned perpendicular to the nerve/plexus, because with tangential approaches, blind 5 cm advancement of a non-flexible catheter is likely to result in the catheter deviating away from the nerve/plexus. The results are, however, likely to hold true for other superficial locations such as femoral and popliteal sciatic catheterisation, where it is possible to align the needle more or less in line with the nerve.
An equivalence-based methodology was chosen because it provided the most
detailed (and the least likely to be misinterpreted) data results. If equivalence was not
proven, then secondary post-hoc analyses could be performed to identify trends (as
was done when comparing the 0.5 cm catheter to the 2.5/5 cm catheters). In contrast,
initially testing for non-inferiority (or superiority) could lead to stronger conclusions
than were warranted given the limited sample. To that end, the posthoc power
calculation warrants comment. The study had 80 and 99% power to detect a shift in
numerically rated pain of 1.1 and 1.7 points respectively. Clearly, these were not
prespecified but derived from the study data. A 2-point shift is often quoted as a
clinically relevant shift in acute pain. However, the “clinically relevant” figure is
largely arbitrary and depends on the logistics of incorporating the required practice
change. For example, incorporating ultrasound technology into an Anaesthetic
Department may be viewed as requiring a higher pain shift benefit compared with
using different catheter types.

8.2.3. Literature following

No further studies have been conducted related to perineural catheter threading
distance or orifice configuration.

8.2.4. Future directions

The obvious limitation to the present study was the inability to single out the effect
of catheter threading distance over orifice configuration. A randomised trial is
therefore needed to evaluate the effect of orifice configuration without the
confounding effect of catheter threading distance.
Chapter 9. Effect of catheter orifice configuration

9.1. Preface

The study conducted in the previous chapter showed that in the context of anterolateral approach interscalene analgesia (needle and plexus aligned in approximately in the same direction) there is little benefit either way to blind catheter advancement 2.5 or 5 cm beyond needle tip. That study also raised the possibility that the previously known performance benefits of epidural multi-orifice catheters (compared to end-hole catheters) also apply to peripheral nerve catheters. However, the study design prevented a separation of the effect of catheter threading distance and orifice configuration. Therefore, the study conducted in this chapter was performed to evaluate the relative effectiveness of an end-hole, triple hole or novel 6-hole catheter for continuous interscalene analgesia.

The following section contains an unaltered reproduction of the manuscript “Randomised Comparison of an End-hole, Triple-hole and Novel Six-hole Catheter for Continuous Interscalene Analgesia” which is currently under review for possible publication.
Randomised comparison of an end-hole, triple-hole and novel six-hole catheter for continuous interscalene analgesia

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SUMMARY

Epidural analgesia studies and a recent continuous peripheral nerve block study suggest multi-hole perineural catheters perform better than end-hole catheters. Confounding catheter positioning issues limit interpretation of the latter study. One hundred and fifty-six patients receiving an anterolateral interscalene catheter for elective shoulder surgery were randomised to three groups: following out-of-plane ultrasound confirmation of the needle tip immediately lateral to the C5/6 roots, an end-hole (n=52), triple-hole (n=51) or six-hole (n=51) non-stimulating catheter was positioned 3 cm beyond the needle tip. Ropivacaine 0.375% 15 ml was administered preoperatively via the catheter before surgery under general anaesthesia. A ropivacaine 0.2% 2 ml/hour infusion with mandatory six hourly, and on-demand one hourly, 5 ml bolus was continued for >48 hours with tramadol available as rescue. Patients were questioned in the recovery room, and at 24 hours for numerical rating pain score (0 to 10), ropivacaine bolus and tramadol consumption. The frequency of recovery room pain was similar between groups (P=0.75) and demonstrated strong evidence for equivalence at the 5% significance level. Neither time to first pain, “average” or “worst” pain during the first 24 hours, ropivacaine bolus or tramadol consumption significantly differed between groups. Catheter threading difficulty was more common for the square-tipped end-hole catheters (end-hole=16% versus triple-hole=6%, six-hole=0%, P<0.001). This study found no evidence to support catheter orifice configuration significantly affecting the quality of continuous peripheral nerve blockade. These findings are in contrast to epidural catheter studies, and suggest that anatomical factors have a significant bearing on whether multi-orifice catheters confer advantage over the single-orifice design.

Key Words: regional anaesthesia, regional blockade, perineural catheter

In a recent continuous interscalene analgesia study conducted by our group, it was suggested that multi-hole catheters are associated with improved catheter performance compared to end-hole catheters. This finding was consistent with studies of continuous epidural analgesia during labour in which, compared to end-hole catheters, multi-orifice catheters were associated with better analgesia. Possible explanations are that the better bolus injectate spread occurring from the multi-orifice configuration and alternative flow channels if one orifice obstructs. However, a significant limitation of the previous interscalene catheter study was that catheter threading distance was not standardised between the multi-hole and end-hole groups; therefore, catheter threading distance may have contributed to the findings. Also, the end-hole catheter in that study was prepared by cutting the standard multi-orifice catheter with a surgical blade and such a catheter could conceivably perform differently to a factory-prepared design.

The suggestion that orifice configuration influences the effectiveness of continuous regional analgesia has gained further relevance because of the recent commercial introduction of novel six-hole epidural/perineural catheters. Therefore, performed a prospective, randomised study to compare an end-hole, triple-hole and novel six-hole catheter for continuous interscalene analgesia after shoulder surgery.

METHODS

The local institutional review board (Northern Y Regional Ethics Committee, Hamilton, New Zealand) approved the trial and prospective registration was with the Australian and New Zealand Clinical Trials Registry (ACTRN12612000118422). Oral
and written informed consent was obtained from all patients, the study was in accordance with the Declaration of Helsinki, and I followed the Consolidated Standard of Reporting Trials (CONSORT) recommendations for reporting randomised clinical trials.

Consecutive American Society of Anaesthesiologists physical status 1 to 2 patients, aged 16 to 80 years, scheduled for elective shoulder surgery under the care of the principal investigator from January through December 2012 at the Southern Cross Brigham Hospital were recruited. A research assistant made the initial invitation for participation, but definitive recruitment was by the principal investigator. Exclusion criteria included interscalene block refusal, severe respiratory disease, known amide local anaesthetic drug allergy, non-steroidal anti-inflammatory drug intolerance and preoperative opioid therapy administered for >1 month prior to surgery. The design was a single centre, prospective, randomised, observer-blinded trial.

**Randomisation**

One hundred and fifty-six patients were randomly assigned to three groups. Randomisation to the three groups was performed by a research assistant away from the study procedures and implemented with a computer-generated random number in blocks of 20. Randomisation was not stratified by procedure. Group concealment was by 156 pre-prepared sealed opaque envelopes, opened just before catheter placement.

**Study interventions**

Random assignment was to an end-hole, triple-hole or six-hole catheter (groups 1, 3, 6). All were 20G polyamide catheters manufactured by B Braun Ltd (Bethlehem, PA, USA). The triple-orifice catheter was the standard triple-orifice catheter supplied with the Contiplex Tuohy® kit. The end-hole catheter was the standard end-hole catheter incorporated into the Contiplex D® kit — the rest of that kit was discarded. The six-hole catheter was a new, individually supplied, six-hole polyamide catheter featuring a soft polyurethane outer coating and a 4 cm tapered tip (Perifix ONE® catheter). The polyurethane coating is said to increase catheter tip flexibility. The triple-hole and six-hole catheter orifices are located approximately 0.5, 1 and 1.5 cm from the catheter tip and radially orientated at 12, 4 and 8 o’clock; the six-hole orifices are a similar size and arranged with the same configuration as the triple-hole design in pairs at the three locations. All catheters were also cut at the proximal end to a length of 25 cm to minimise the flow pressure gradient between each catheter’s proximal end and orifice(s).

**Catheter placement**

The principal investigator, who was experienced with this procedure, performed all catheter placements as previously described in several publications and described at (accessed March 17, 2013). Catheter placement first involved a modified superficial cervical plexus block, an out-of-plane ‘antecubital’ approach and specifically:

1. A 4 cm 18G insulated Tuohy needle (Contiplex Tuohy®) ‘unelled’ subcutaneously such that 4 cm of needle was under the skin.
2. Concomitant neurostimulation (0.8 mA, 2 Hz) necessitating a brief deltoit, biceps or triceps motor response to confirm the target nerve roots/ trunks. Sustained motor responses at <0.5 mA were only sought when sonographic imaging of the roots was suboptimal.
3. Injection of 10 ml dextrose 5% via the needle immediately before catheter advancement.
4. Blind catheter advancement 5 to 7 cm beyond the needle tip and then after needle removal, catheter withdrawal until 3 cm remained past the original needle tip position (catheter fixed 4+3=7 cm at the skin).
5. All interscalene local anaesthetic administered via the catheter.

**Anaesthesia and Analgesia**

A standardised technique was used. Intravenous sedation, up to midazolam 2.0 mg and alfentanil 0.5 mg, was administered before catheter placement. Intraoperative multimodal analgesia consisted of intravenous paracetamol 40 mg and dexamethasone 8.0 mg.

**Intraoperative management**

General anaesthesia was also standardised using a laryngeal mask airway and spontaneous desflurane respirations (end-tidal minimum alveolar concentration 0.8 to 1.0). Following general anaesthesia induction and approximately 10 minutes after catheter placement, but before surgery, ropivacaine 0.375% 15 ml was administered via the catheter over approximately two to three minutes (flow rate expected >400 ml/hour). This combination of local anaesthetic volume and concentration was chosen as a compromise between a dose low enough to realistically detect a difference between groups for the primary outcome (pain on emergence) and a dose high enough to avoid unacceptable recovery room pain. No long acting opioid was administered intraproperatively; however, alfentanil 0.25 mg was given if the respiratory rate was >25.

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PACU protocol

In the post-anesthesia care unit (PACU), patients reporting a numerical rating pain score (NRPS, 0 to 10) of more than two were given a bolus of lignocaine 1.5% 15 ml via the catheter and intravenous fentanyl 25 μg pro re naea every one to two minutes. If pain persisted 30 minutes after this bolus the catheter was replaced with the same catheter type, and a further 15 ml of ropivacaine 0.375% was given via this catheter.

Postoperative management

An elastomeric pump was used for the first six months of the study (PainBuster® pump, Surgical Synergies, Auckland, New Zealand), but because of supply issues with that device, an electronic pump was used for the last 6 months (ambIT® pump, Summit Medical Products, South Sandy, UT, USA). Both were set to deliver ropivacaine 0.2% at 2 ml/hour with patient-controlled 5 ml boluses (bolus flow rate=100 to 150 ml/hour) of up to one bolus every hour. From the onset of shoulder pain until 48 hours postoperatively, patients were instructed to activate the ropivacaine bolus button “on the clock” every six hours irrespective of the NRPS. Additional 5 ml boluses were administered in-between mandatory six-hourly boluses if the NRPS increased to more than two. Multimodal analgesia was continued after surgery: paracetamol (1 g every six hours) and slow release diclofenac (75 mg every 12 hours) if any postoperative pain occurred; slow release tramadol (100 mg every 12 hours) if the NRPS increased to >2 despite regular paracetamol, diclofenac and two consecutive ropivacaine boluses within three to four hours. Discharge home occurred either on the day of surgery or the morning of postoperative day one (all open procedures).

Study endpoints

The primary endpoint was the proportion of patients reporting pain in the PACU. The main secondary endpoints were time to first pain, numerically rated pain and tramadol consumption during the first 24 hours.

Data collection and blinding

The principal (operating) investigator recorded the needle endpoint used for catheter placement (ultrasound or neurostimulation). He also recorded whether there was “extensive” resistance to catheter advancement defined as marked resistance to catheter advancement beyond the needle tip despite a 1 to 2 mm needle retraction. The principal investigator also recorded the number of alfentanil 0.25 mg boluses administered during surgery. The patient’s primary PACU nurse recorded the emergence NRPS in the shoulder, arm or elbow and details of PACU interventions (local anaesthetic bolus, fentanyl rescue). A research assistant phoned all subjects at 24 postoperative hours and questioned for ropivacaine bolus demands, supplemental tramadol consumption, time to first pain, NRPS (worst and “average” pain during the previous 24 hours), numerically rated numbness/weakness and satisfaction (0 to 10, 0=none, numbness/weakness, very unsatisfied; 10=worst imaginable pain, numbness/weakness, very satisfied) during the previous 24 hours (specifically excluding pain that was present in the recovery room). Data recorded in the operating room by the principal investigator was not blinded. All subsequent data collection was patient and observer-blinded.

Statistical Analysis

An independent statistician performed all calculations. Categorical outcomes were compared using Fisher’s exact test (catheter threading difficulty, intraoperative alfentanil boluses, pain in the PACU and breathlessness). Time to first pain was compared using the log-rank test for survival data. Ordinal outcomes (NRPS outcomes, tramadol consumption,....
and ropivacaine bolus use) were compared using the Kruskal-Wallis test. \( P \) values \(<0.05\) were considered statistically significant. Two-sided tests were used for all experimental outcomes.

Other data were summarised using appropriate descriptive statistics (mean and standard deviation or mean and range for normally distributed or symmetric variables, median and interquartile ranges for skewed variables, number and proportion for categorical variables). All statistical analyses were performed using R 2.12.1 (R Project, Institute for Statistics and Mathematics, Vienna, Austria).

Sample size estimates were based on a hypothesis of no difference between groups and therefore, demonstration of equivalence of the primary outcome: the proportion of patients reporting emergence pain. I considered an arbitrary 15% difference as clinically significant. A previous study using the anterolateral approach and a similar surgical mix but using ropivacaine 0.375\% 20 ml reported a 90% pain-free recovery room rate. Assuming 80% power, detection of a 15% shift (9% increase; 19% decrease) in the proportion of patients pain-free in the PACU, with 95% confidence, would require 50 patients in each group (\( \chi^2 \) test, Statmate 2.0; GraphPad Software, San Diego, CA, USA).

We also performed three post hoc equivalence tests for the primary outcome by calculating the 90% confidence interval for the difference between the proportion of patients reporting emergence pain for each group compared with the other two groups. These limits provide estimates for which equivalence can be concluded at the 5% significance level.

RESULTS

One hundred and fifty-six patients presenting for elective shoulder surgery were enrolled: 52, 53 and 51 patients were randomised to the groups 1, 3 and 6 respectively. Patient and surgical characteristics were comparable between groups (Table 1). Eight patients were not contactable on day one and were thus excluded (4, 2 and 2 patients in groups 1, 3 and 6 respectively). Thus, 148 patients completed the study per protocol. Two patients in the end-hole group necessitated a sustained motor response at \(<0.5\) mA because of suboptimal brachial plexus ultrasound imaging.

Difficulty with catheter threading was more common in the end-hole group (end-hole=19\%; versus triple-hole=6\%, six-hole=0\%), \( P=0.001 \) (Table 2).

The frequency of recovery room pain was similar between groups (end-hole=12\%, triple-hole=15\%, six-hole=10\%, \( P=0.75 \); Table 2), and demonstrated strong evidence for equivalence: 90\% confidence intervals for the difference between proportions was within the 15\% pre-specified limit for the end-hole versus triple-hole (-15, 8) and end-hole versus six-hole (-8, 12), and only marginally outside the limit for the triple-hole versus six-hole (-6, 16).

These limits are the estimates for which equivalence can be concluded with 95\% confidence. Neither time to first pain, “average” pain during the first 24 hours, “worst” pain during the first 24 hours, nor the other catheter function-related secondary outcomes were significantly different between groups (Table 3).

There was no evidence of inadvertent catheter vascular cannulation in any patient. No patient demonstrated symptoms or signs of systemic local anaesthetic toxicity. No patient reported significant dyspnoea, requiring more than simple reassurance, before or after hospital discharge.

DISCUSSION

This study showed no major differences between an end-hole, triple-hole and novel six-hole catheter when used for continuous interscalene analgesia after shoulder surgery. These results are in contrast to our previous study suggesting benefit from the multi-orifice design and from previous epidural catheter studies.

There is one notable difference between the current and previous study, which might explain

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Catheter Placement, Intraoperative and PACU Interventions.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1: end-hole (n=52)</td>
</tr>
<tr>
<td>Difficulty threading catheter</td>
<td>10 (19)</td>
</tr>
<tr>
<td>Interscalenealfentanil bolus 1</td>
<td>2 (4)</td>
</tr>
<tr>
<td>PACU</td>
<td></td>
</tr>
<tr>
<td>Local anaesthetic bolus (pain)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>Catheter replacement</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Values are n (%). PACU=post-anesthesia care unit.

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MULTI-ORIFICE VERSUS END-FOLE PERINEURAL CATHETERS

Table 3

<table>
<thead>
<tr>
<th>Postoperative Outcomes</th>
<th>1: end-hole (n=52)</th>
<th>3: triple-hole (n=53)</th>
<th>6: six-hole (n=53)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to first pain (h)</td>
<td>23 (20–24)</td>
<td>22 (13–24)</td>
<td>22 (14–24)</td>
<td>0.60</td>
</tr>
<tr>
<td>Average pain NRS</td>
<td>1 (0–3)</td>
<td>1 (0–2)</td>
<td>1 (0–2)</td>
<td>0.94</td>
</tr>
<tr>
<td>Worst pain NRS</td>
<td>3 (1–5)</td>
<td>1 (0–4)</td>
<td>3 (0–5)</td>
<td>0.87</td>
</tr>
<tr>
<td>Tramadol consumption</td>
<td>0 (0–1)</td>
<td>0 (0–1)</td>
<td>0 (0–1)</td>
<td>0.86</td>
</tr>
<tr>
<td>Repriacaine boluses</td>
<td>2 (1–3)</td>
<td>2 (0–4)</td>
<td>2 (0–4)</td>
<td>0.79</td>
</tr>
<tr>
<td>Hand numbness NRS</td>
<td>8 (5–10)</td>
<td>8 (5–10)</td>
<td>8 (5–10)</td>
<td>0.37</td>
</tr>
<tr>
<td>Hand weakness NRS</td>
<td>8 (5–10)</td>
<td>8 (5–10)</td>
<td>7 (5–8)</td>
<td>0.76</td>
</tr>
<tr>
<td>Breathless*”Can't take deep breath”</td>
<td>19 (40)</td>
<td>18 (35)</td>
<td>21 (49)</td>
<td>0.60</td>
</tr>
<tr>
<td>Satisfaction NRS</td>
<td>10 (8–13)</td>
<td>10 (8–10)</td>
<td>9 (8–10)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Values are n (%) or median (interquartile range). NRS values refer to the entire previous 24 hours. h=hours. NRS= numerical rating score (0 = no pain/numbness/weakness or very unsatisfied; 10 = very pain/numb/weak or very satisfied).

Previous epidural analgesia studies in labouring patients have shown multi-orifice catheters are associated with a reduction in unilateral block, missed segments, and ultimately improved analgesia with a reduced requirement for catheter manipulations. Anatomical factors could explain the contrasting findings with the present study. Epidural block, being a compartmental block, is known to be influenced by the presence of septae and inadvertent catheter advancement outside the epidural compartment via the intervertebral foramina. Multi-orifice catheters, therefore, have good reason to perform better than single orifice catheters under these unique anatomical conditions.

The study design warrants comment. Given continuous nerve blocks are used to control pain during the first few days after surgery, the logical primary outcome would be 24 or 48 hours postoperative pain. However, I used recovery room pain (yes/no) as the primary outcome in order to maximise detection of a catheter orifice-related treatment effect. First, our previous research experience with this (local anaesthetic via catheter only) technique has suggested any catheter-related effect is most likely to manifest as a difference in the proportion of patients reporting pain in PACU, while 24-hour outcomes (pain, ropivacaine bolus and tramadol consumption) will only manifest for larger effects. Second, the highest catheter flow rate/pressure (>400 ml/hour) occurred during administration of the primary local anaesthetic bolus. The primary local anaesthetic bolus would therefore have had the highest chance of resulting in differential local anaesthetic spread from an orifice configuration-related effect — manifesting as a between group difference in PACU.
pain. Similarly, the primary local anaesthetic dose (15 ml 0.375%) was deliberately selected to be just below the estimated catheter administered ED50 for volume and concentration to prevent PACU pain (20 ml 0.375%). Fifteen ml of 0.375% was thought to be low enough to detect a between-group difference in PACU pain, while also associated with an acceptable incidence of PACU pain (10% to 15%). When interpreting this apparently high incidence of PACU pain, it is important to note that all but one patient (96.4%) became pain-free after a supplementary 15 ml bolus in PACU and were thus deemed to have had a successfully placed catheter.

My preferred catheter placement technique involves blind catheter positioning a short distance beyond the ultrasound-confirmed needle tip. However, an alternative technique involves confirming catheter position by direct catheter visualisation or ‘indirectly’ by observation of catheter injectate spread4; although neither direct nor indirect catheter confirmation has been validated with a randomised trial4. Regardless, the catheter placement technique was consistent across groups and was further strengthened by being performed by an experienced operator: the ability to control for factors other than orifice configuration relied in part, on the catheters in each group being consistently placed in the same position.

Catheter threading difficulty was more common for the six-hole catheters. Furthermore, although there was no difference in threading difficulty between the triple and six-hole catheters as defined by marked threading resistance despite a 1 to 2 mm needle retraction, my observation was that catheter threading was easier for the new six-hole catheter. The end-hole catheter tip has a square shape; the triple-hole catheter has a curved ‘bullet’ shape tip, while the six-hole catheter has a 4 cm ‘tapered’ tip. The six-hole catheter also has a polyurethane coating, which is said to increase catheter tip flexibility. Either the catheter tip shape or flexibility or both might have contributed to these observed differences in catheter performance and further study is suggested to definitively test these observations.

I performed the present study in the interscalene area. It is likely the results would apply to other areas such as the femoral and sciatic nerves. However, ideally, confirmatory studies should be conducted.

CONCLUSION
In summary, this study found no evidence to support the contention that catheter orifice configuration (end-hole, triple-hole or six-hole) significantly affects the quality of continuous interscalene analgesia. These findings are in contrast to epidural catheter studies, and suggest that anatomical factors have a significant bearing on whether multi-orifice catheters confer advantage over the single-orifice design.

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REFERENCES
9.2. Discussion

9.2.1. Contribution and significance

The current study found no major differences between an end-hole, triple-hole and novel 6-hole catheter when used for continuous interscalene analgesia after shoulder surgery. The present study suggests, that for perinueral catheters, there is little performance advantage by increasing orifice number.

9.2.2. Limitations

As stated in the publication, a possibility for the lack of orifice effect in the present study is that the ambulatory pump boluses were not delivered at a high enough pressure or flow to result in adequate multi-orifice flow from the multi-orifice catheters. However, if local anaesthetic spread differed enough between the 1, 3 or 6 orifice catheters to significantly affect block quality, this would have almost certainly manifested as a difference in the frequency of recovery room pain given the relatively low volume and concentration used for the primary local anaesthetic bolus (15 mL ropivacaine 0.375%), and its administration at > 400 mL.hr\(^{-1}\).

Although not a limitation, the high catheter success rate (99.4%) warrants comment. All our previous interscalene catheter studies which have used ultrasound guidance for catheter placement, have been associated with a catheter success rate < 95%. The current study introduced a practice modification of always confirming the visualised roots by eliciting a brief appropriate motor response. The hypothesis was that previous catheter failures were the result of erroneous ultrasound image
interpretation: i.e. what was thought to be the C5 or C6 root was in fact a different root or a non-neural structure.

9.2.3. Literature following

No further studies have compared orifice configuration in the setting of either continuous epidural or peripheral nerve blocks.

9.2.4. Future directions

Further studies are indicated to evaluate whether the present results apply to other anatomical areas such as the femoral and sciatic nerves. Although unlikely, it is also possible the absence of effect demonstrated in the present study was in part due to the ambulatory pump delivering an inadequate flow rate and pressure. A follow up study using a pump delivering higher flow rates and pressures would address this potential limitation. The effect of manual catheter cutting compared to a factory prepared product would also be worthy of future study.

Finally, the impression of a higher success rate in this study compared with historical controls warrants further study because of the suggestion that this was in part due to the routine use of neurostimulation to confirm the appropriate nerve roots.
Part 5: Interscalene Block Related Complications

Introduction

Chapter 10  Neurological and neuraxial complications related to interscalene block

Chapter 11  Minor neurological symptoms after interscalene and other regional blocks

Chapter 12  Deliberate intraneural injection

Chapter 13  Superficial cervical plexus neuropathy

Chapter 14  Performing interscalene block in unconscious patients

Chapter 15  Avoiding neurological complications
Introduction

It has been asserted that the introduction of the interscalene block by Alon P Winnie in 1970 revolutionised pain management after shoulder surgery, particularly for its most painful intervention – rotator cuff repair. The subsequent development of brachial plexus catheterisation allowed further prolongation of the beneficial effects of the block: randomised studies summarised in Chapter 2 have confirmed that CISB significantly improves pain control after major shoulder procedures for up to three days; the studies presented in this thesis were designed to further optimise this block.

Before the introduction of CISB, opioid administration for several days was not uncommon after shoulder surgery, and with that opioid requirement came the inevitable side effects of sedation, nausea, vomiting and pruritus, and the consequent requirement for ongoing hospitalisation. Large, prospective studies now totalling > 2 thousand patients have confirmed that in experienced hands, CISB has an excellent safety profile. However, like general anaesthesia and opioid analgesia, if performed incorrectly, both single-injection and continuous interscalene block have the potential to pose a significant risk to patient safety.

This section of the thesis reviews the potential complications of CISB with particular emphasis on neurological complications, aspects of their causation, and how they may be prevented. Major and minor neurological and neuraxial complications are reviewed in addition to the potential relevance of deliberate intraneural injection, which has been recently proposed as an acceptable practice. Finally, evidence related to perineural catheter infection and its importance (or lack of) is reviewed.
Chapter 10. Major neurological and neuraxial complications related to interscalene block

Only a year after Winnie’s description, bilateral epidural block, and two years later total spinal anaesthesia were reported following SSISB – all fortunately without lasting adverse effects. In 1980, Barratell reported the first permanent upper limb neurological deficit, presumably related to injection directly into a nerve, nerve root or the spinal cord, and since then there have been at least four further cases of permanent neurological deficit probably related to this mechanism. One of the reports describing four cases of permanent spinal cord damage led in part to a recommendation by the American Society of Regional Anesthesia (ASRA) that interscalene block be placed in a separate category of peripheral nerve blocks, and the decree that these blocks: “should not be performed in anaesthetised or heavily sedated adult or paediatric patients”. The assumption was that the awake or lightly sedated patient would report the pain and paraesthesia that may accompany needle entry and injection into neural tissue. The notion that interscalene blocks are potentially more dangerous than other peripheral nerve blocks is supported by Auroy’s data on the incidence of complications from >250 000 nerve blocks studied prospectively: the overall incidence (for all block types) of nerve damage was around 1:5000; for interscalene blocks it appears to be about 1:3 500. Is this block truly more dangerous than all others, and if so, why?

All blocks carry with them the generic risks of regional anaesthesia: failure, nerve damage, local anaesthetic toxicity, bleeding, infection and damage to surrounding structures. The anatomical proximity of the brachial plexus roots to critical structures makes inadvertent injection into the neuraxis, a vessel or pleural puncture
possible, and many anaesthetists rightfully regard the anterior triangle of the neck as “tiger country”. There has also been speculation that a relatively high incidence of abnormal nerve function after interscalene block (up to 15% within the first 10 days in one study) results from the high ratio of neural to connective tissue in the cervical nerve roots, and their relative immobility as they emerge from the spine. Nerve root immobility increases the likelihood of needle impalement, while the relative lack of nerve root connective tissue may increase the risk of neurological dysfunction if intraneuronal injection occurs. It is possible that this relatively high incidence may in part be related to the fact that patients are more likely to identify abnormal sensation in the hands than the feet.

Of greatest concern is the potential threat to the neuraxis. Alon Winnie’s original description of the block recommended a needle orientation aimed directly towards the neuraxis: “perpendicular to the skin in all planes, that is, mesiad, dorsad, and slightly caudad”. Further, he advised that if it was not possible to elicit paraesthesia, the needle should be advanced until a transverse process is contacted, and then “walked” along the process until paraesthesia is evoked. Research using MRI imaging and cadavers has suggested that the needle angulation originally described by Winnie is such that if the needle is inserted too far, entry through an intervertebral foramen and into the spinal canal becomes possible. How far is too far?

Of the 20 published reports (in 24 patients) of total spinal, epidural or permanent neuraxial injury following SSISB, excessive needle depth can be implicated in all on the basis of needle contact with the transverse process, a needle depth ≥2.5 cm, contralateral paraesthesia, or failure to report needle depth (Table 10.1). Studies have
confirmed that in the vast majority of patients, an insertion depth >2.0 cm is unnecessary when using the Winnie approach, which is the needle trajectory that creates the shortest distance between the skin and the brachial plexus.

Another key safety factor for neuraxial complications is the needle insertion angle. In 1997, Meier\textsuperscript{110} described a variation of the Winnie technique specifically to facilitate interscalene catheter placement. The approach has been popularised by Borgeat,\textsuperscript{34} who termed it the ‘modified lateral’ approach, while others have used the term ‘anterolateral.’\textsuperscript{227} A key safety feature of this approach is not only a needle orientation more in line with the direction of the plexus, but also, and importantly, avoidance of medial orientation. Thus, the needle trajectory is more parallel to the neuraxis and may even be directed away from it. A more caudally directed needle means that a needle so inserted is much less likely to head towards the neuraxis, and even if encroaching on the vertebral column, is less likely to pass through an intervertebral foramen into the spinal canal.\textsuperscript{107, 108}
Table 10.1. Case Reports of Interscalene Block Related Neuraxial Complications

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>Case number</th>
<th>Complication</th>
<th>LOC</th>
<th>Needle type</th>
<th>Needle approach</th>
<th>Remarks</th>
<th>Contributing Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kumar 1971</td>
<td>Anesthesiology</td>
<td>1</td>
<td>Epidural block (bilateral)</td>
<td>Deep sedation</td>
<td>22G 3.8 cm</td>
<td>Winnie</td>
<td>C6 TP contacted then “walked” caudally</td>
<td>Needle too deep</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>Epidural block (unilateral)</td>
<td>Sedation</td>
<td>Not reported</td>
<td>Winnie</td>
<td>C6 TP contacted then “walked” caudally</td>
<td>Needle too deep</td>
</tr>
<tr>
<td>Ross 1973</td>
<td>Anesthesiology</td>
<td>1</td>
<td>Total spinal</td>
<td>Conscious sedation</td>
<td>5 cm</td>
<td>Winnie</td>
<td>Needle depth 1”</td>
<td>Needle too deep</td>
</tr>
<tr>
<td>Cobcroft 1976</td>
<td>Anesthesiology</td>
<td>1</td>
<td>Epidural block (bilateral)</td>
<td>Not reported 19G</td>
<td>5.5 cm</td>
<td>Winnie</td>
<td>Needle depth 1”</td>
<td>Needle too deep</td>
</tr>
<tr>
<td>Edde 1977</td>
<td>A&amp;A</td>
<td>1</td>
<td>Total spinal + cardiac arrest</td>
<td>Conscious sedation</td>
<td>6 cm</td>
<td>Winnie</td>
<td>Needle too deep (not reported)</td>
<td></td>
</tr>
<tr>
<td>Scammell 1979</td>
<td>AIC</td>
<td>1</td>
<td>Epidural block (bilateral)</td>
<td>Not reported 22G</td>
<td>5 cm</td>
<td>Winnie</td>
<td>Needle too deep (not reported)</td>
<td></td>
</tr>
<tr>
<td>Butterill 1980</td>
<td>Anesthesiology</td>
<td>1</td>
<td>Total spinal/permanent neurological arm deficit</td>
<td>No sedation</td>
<td>22G 9 cm</td>
<td>Winnie</td>
<td>Worsening “sharp” paresthesia on LA inject</td>
<td>Needle too deep (not reported)</td>
</tr>
<tr>
<td>Lombard 1983</td>
<td>Anesthesiology</td>
<td>1</td>
<td>Bilateral block</td>
<td>No sedation</td>
<td>17G over-the-needle cannula</td>
<td>Winnie</td>
<td>Paresthesia in contralateral arm during block</td>
<td>Needle too deep (contralateral paraesthesia)</td>
</tr>
<tr>
<td>Cook 1991</td>
<td>BJA</td>
<td>1</td>
<td>Epidural block (bilateral)</td>
<td>Deep sedation</td>
<td>2G</td>
<td>Winnie</td>
<td>Catheter advanced 12 cm beyond cannula</td>
<td></td>
</tr>
<tr>
<td>McGlade 1992</td>
<td>AIC</td>
<td>1</td>
<td>Total spinal</td>
<td>Conscious sedation</td>
<td>23G hypodermic</td>
<td>Winnie</td>
<td>Catheter over advanced</td>
<td></td>
</tr>
<tr>
<td>Baraka 1992</td>
<td>Anesthesiology</td>
<td>1</td>
<td>Total spinal</td>
<td>Sedation</td>
<td>22G</td>
<td>Winnie</td>
<td>Needle depth 2.5 cm until C6 TP contacted</td>
<td></td>
</tr>
<tr>
<td>Tetzlaff 1994</td>
<td>Reg Anesth</td>
<td>1</td>
<td>Total spinal</td>
<td>Conscious sedation</td>
<td>25G 2 cm</td>
<td>Winnie</td>
<td>Needle too deep (not reported)</td>
<td></td>
</tr>
<tr>
<td>Dutton 1994</td>
<td>Anesthesiology</td>
<td>1</td>
<td>Total spinal</td>
<td>No sedation</td>
<td>22G 2.5 cm short bevel (Plexafix)</td>
<td>Winnie</td>
<td>Needle depth 2.5 cm, motor response 0.2 mA</td>
<td></td>
</tr>
<tr>
<td>Passamonte 1996</td>
<td>A&amp;A</td>
<td>1</td>
<td>Total spinal/permanent neurological arm deficit</td>
<td>GA</td>
<td>24G 7.6 cm B-bevel</td>
<td>&quot;Caudal/posterior&quot;</td>
<td>Intraneural injection</td>
<td></td>
</tr>
<tr>
<td>Iocolano 1997</td>
<td>Nursing journal</td>
<td>1</td>
<td>Total spinal</td>
<td>Sedation</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Needle too deep (not reported)</td>
<td></td>
</tr>
<tr>
<td>Norris 1996</td>
<td>CJA</td>
<td>1</td>
<td>Total spinal</td>
<td>Deep sedation</td>
<td>22G short bevel</td>
<td>“Slightly dorsal/caudal”</td>
<td>Needle-depth 2 cm, contralateral arm paresth during block</td>
<td>Needle too deep (contralateral arm paraesthesia)</td>
</tr>
<tr>
<td>Bemmefd 2000</td>
<td>Anesthesiology</td>
<td>1</td>
<td>Cervical cord injection/permanent deficit</td>
<td>Deep sedation</td>
<td>22G 3 cm short bevel (stimuplex)</td>
<td>Not reported</td>
<td></td>
<td>Needle too deep (syinx)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>Cervical cord injection/permanent deficit</td>
<td>GA</td>
<td>22G 3 cm short bevel (stimuplex)</td>
<td>Not reported</td>
<td></td>
<td>Needle too deep (syinx)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>Cervical cord injection/permanent deficit</td>
<td>GA</td>
<td>25G 3.8 cm</td>
<td>Not reported</td>
<td></td>
<td>Needle too deep (syinx)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>Cervical cord injection/permanent deficit</td>
<td>GA</td>
<td>22G 3 cm short bevel (stimuplex)</td>
<td>Not reported</td>
<td></td>
<td>Needle too deep (syinx)</td>
</tr>
<tr>
<td>Walter 2005</td>
<td>Anaesthetist</td>
<td>1</td>
<td>Total spinal from catheter</td>
<td>No sedation</td>
<td>19G 5 cm</td>
<td>Meier</td>
<td>Catheter 6 cm beyond tip. Phrenic stimulation</td>
<td>Excessive catheter advancement</td>
</tr>
<tr>
<td>Faust 2006</td>
<td>A&amp;A</td>
<td>1</td>
<td>Epidural block (unilateral) from catheter</td>
<td>Light sedation</td>
<td>5.5 cm</td>
<td>Not reported</td>
<td>Catheter 5 cm beyond tip</td>
<td>Inappropriate needle approach (not reported)</td>
</tr>
<tr>
<td>Feasca 2007</td>
<td>Ann Fr Anesth</td>
<td>1</td>
<td>Total spinal from catheter</td>
<td>Deep sedation (pain during initial LA injection)</td>
<td>18G 5.5 cm</td>
<td>Winnie</td>
<td>Catheter 3.5 cm beyond tip. However manipulation was necessary due to resistance during drug administration</td>
<td>Inappropriate needle approach</td>
</tr>
<tr>
<td>Gans 2011</td>
<td>Anesthesiast</td>
<td>1</td>
<td>Epidural block (contralateral) from catheter</td>
<td>GA</td>
<td>18G 5 cm</td>
<td>Winnie</td>
<td>Catheter 5.5 cm beyond tip</td>
<td>Inappropriate needle approach</td>
</tr>
</tbody>
</table>

**Key:**
- **AIC=Anaesthesia and Intensive Care; A&A=Anesthesia and Analgesia; BJA=British Journal of Anaesthesia; GA=General Anaesthesia; LA=Local anaesthetic; LOC=Level of consciousness; TP=Transverse process;**

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As noted above, placement of interscalene catheters to provide continuous interscalene analgesia has become popular in many centres. However, plexus catheterisation is not without its dangers, particularly if performed incorrectly. Of the five published reports of complications resulting from catheterisation, four involved catheter placement using a Winnie-type medial needle angulation or the approach was not specifically described. One report of neuraxial blockade involved catheter advancement >5 cm beyond the needle tip. The optimal distance to which a catheter should be passed beyond the needle tip remains a controversial issue. However, concerns exist that excessive catheter advancement might increase the likelihood that the catheter may pass into the epidural space, through a dural cuff into the subarachnoid space, or at the very least towards a less desirable anatomical location. Consequently, most experienced clinicians insert catheters no more than 3 – 5 cm beyond the tip of the introducing needle. Indeed, the study conducted in Chapter 8 confirmed there is little to be gained by advancing the catheter 5 cm beyond the needle tip, so advancing any further will only potentially increase complications. When inserting interscalene catheters, many anaesthetists inject local anaesthetic through the needle rather than through the catheter to maximise the chances of primary block success. Maximising primary block success may be relevant when the block is to be used for surgical anaesthesia, and some also argue for this approach on the basis that it is most likely to ensure effective analgesia during the first 12 – 18 hours after surgery when pain is at its most intense. However, another common approach when surgery is performed under general anaesthesia is to inject the first local anaesthetic bolus through the catheter rather than the needle.
This provides valuable confirmation of satisfactory catheter placement when the patient awakes in recovery pain-free. It is also common and intuitively correct practice to inject the first local anaesthetic bolus through the catheter when the patient is in a closely monitored environment so that accidental intravascular or neuraxial injection can be readily identified and rapidly treated.

Ultrasound guidance for block performance and catheter placement is becoming popular in developed countries. One of the main advantages of this technology when compared to neurostimulation-assisted landmark techniques is that it provides useful information regarding appropriate needle depth. However, like the paraesthesia technique and neurostimulation, it too is limited by false negatives: nerve root and needle tip visualisation is not always possible, so the same needle depth and orientation principles described above also apply for ultrasound-guided techniques. Similarly, catheter (or catheter injectate) visualisation can be technically challenging. However, it is encouraging that there has as yet been no neuraxial complication reported that has resulted from an interscalene block performed under ultrasound guidance.

The interscalene brachial plexus block is by its very nature a block performed close to the neuraxis, and therefore a high index of suspicion should be maintained about the possibility of injection into the neuraxis. The local anaesthetic drugs injected through the needle or catheter can on occasion gain access to the epidural or subarachnoid spaces – left untreated, respiratory arrest and even death can occur. Single-shot blocks and the first injection down the catheter (or the start of an infusion) should arguably only be performed in an environment that allows the ready identification and rapid management of any resulting complications.
Regardless of the complications described in this account, it is important to note the fact that no analgesic regimen with any drug or any drug combination and by any route is without significant complications. In particular, the leading competitor to continuous regional analgesia, intravenous patient-controlled opioid analgesia, has likely been associated with many serious complications (including death) since its introduction. 214 Further, scrupulous attention to detail in the performance of the block and catheterisation, and careful postoperative management of the catheter infusion, will allow the provision of excellent analgesia at an acceptably small – but never zero - incidence of serious complications. It might be appropriate to state at this point, that in the 798 patients receiving CISB as part of the studies reported in this thesis, there were no reported major neurological or neuraxial complications. However, using the “times 3” rule, the upper 95% confidence interval for significant complications could still be a high as 0.04%.
Chapter 11. Minor neurological symptoms after interscalene and other regional blocks

Anaesthesiologists are often alarmed by studies documenting the frequency of neurological symptoms occurring after interscalene block: up to 20% of patients will report vague symptoms in the first few days after surgery\textsuperscript{225} a figure very similar to the frequency determined in one of the studies conducted in the first thesis.\textsuperscript{150} On the surface, this might seem disturbingly high; however, more critical review of the relevant studies is reassuring.

First, in studies reporting relatively high “complication” rates, interrogation for symptoms typically occurred during the first two weeks after surgery.\textsuperscript{34, 106, 150, 169, 225, 246} The natural history of these symptoms, which typically include mild numbness and tingling, is for rapid resolution within a few weeks.\textsuperscript{34, 106, 150, 169, 225, 246} Second, most symptoms are minor: they may be reported when patients are prompted during interrogation, but they may not be bothersome enough to be volunteered otherwise.\textsuperscript{150} When assessing the significance of these minor symptoms, it is important to note that many patients undergoing regional block are undergoing surgical procedures that require months of rehabilitation. A minor symptom (e.g. patchy numbness) resolving within a couple of weeks may therefore be inconsequential in the context of the surgical rehabilitation. Third, minor symptoms may be unrelated to the block. Many large prospective series have been conducted documenting the incidence of neurological complications following regional anaesthesia and surgery.\textsuperscript{34, 150, 153, 225} However, inadequate study has been conducted to document the frequency of postoperative neurological symptoms occurring following surgery \textit{without} regional block, at least to allow a reliable comparison. Therefore the relative impact of the
block versus other causes is not known. In fact, studies have shown that most postoperative neurological symptoms have causes unrelated to the block.\textsuperscript{150, 224}

Caution should also be exercised comparing postoperative neurological complication rates between large prospective studies. The rarity of prolonged neurological complications reported in previous studies renders the 95\% confidence intervals so wide that one needs to be cautious making any sort of comparison between studies. Furthermore, there are other major limitations to making between study comparisons. First, the study protocols of large prospective studies differ in their definition of what constitutes a complication (or symptom): the threshold criteria for significant sensory symptoms ranges from simply “altered sensation”,\textsuperscript{34, 150} to “non-resolving paraesthesia”,\textsuperscript{224} to “sensory deficit with clinical or electrophysiological evidence of a peripheral site of injury”\textsuperscript{222, 223} to the extreme of the continuum, “neurological deterioration, allodynia or severe pain”\textsuperscript{153}. Second, there is the inescapable reality of reporting bias.\textsuperscript{247} A “neurological complication” in the eyes of one investigator can be insignificant to another investigator. In fact, there has been at least one recent prospective study involving hundreds of patients, claiming a neurological rate of zero despite direct patient interrogation in the first two weeks after surgery.\textsuperscript{248} Third, large prospective studies vary in their level of follow up. Very large, multicenter studies inevitably have lower follow up rates.\textsuperscript{222-224} Single institution and/or single operator studies, on the other hand, typically have high (>95\%) follow up rates,\textsuperscript{34, 150, 153} and it is an unlikely coincidence that these high follow up rates are associated with high neurological complication rates.

The aforementioned limitations are reflected in the marked disparity in the short-term neurological complication rates between studies. As previously stated, in the very
early postoperative period (< 2 weeks), neurological complications have been reported to occur with a frequency of 0.02%, 0.2%, 0.5%, 8% and 11%; rates that are statistically very different (p < 0.0001). These differences can all be explained on the aforementioned limitations in study design.

Such limitations make the literal comparison of one series against another imprecise at best. When these limitations are combined with the issue of very low historical baseline neurological rates and very wide confidence intervals, all that can be concluded is that the neurological complication rate from a particular series is not markedly higher than similar previous studies. Regardless of this issue, minor neurological symptoms do not represent a threat to life or functional capacity, but patients should be warned of the possibility during informed consent.
Chapter 12. Deliberate intraneural injection

Intraneural injection was previously regarded as a strong predictor of prolonged neurological deficit following peripheral nerve blocks, and consequently, the prevailing teaching for many years was to do all possible to avoid injecting local anaesthetic inside nerves. However, there have been several reports of so-called "intraneurally" injected local anaesthetic confirmed by ultrasound that did not result in subsequent neurological deficit. 127, 249-253 This has been in association with both low 249-251 and high 127, 252, 253 local anaesthetic volume. This has led to the suggestion that the injection of small volumes of local anaesthetic beneath the epineurium but outside the perineurium is an acceptably safe practice. 249

The most influential of these reports was a prospective series of axillary nerve blocks, 249 where a traditional (non-ultrasound guided) technique was used to place the needle, but the subsequent local anaesthetic injection was monitored with ultrasound. A high proportion of injections were, in fact, intraneural. If intraneural injection was observed, local anaesthetic injection was aborted after a few mL had been injected. None of the patients in the study demonstrated persistent neurological symptoms (> several months). Further studies conducted at the popliteal sciatic nerve level have reported similar findings – even when a large volume of local anaesthetic has been injected. 253, 254

One needs to view these results cautiously. Peripheral nerves consist of axons surrounded by endoneurium, which are assembled into fascicles. A tough connective
tissue layer, the perineurium, envelops the fascicles, which are themselves organised into peripheral nerves – the nerve is surrounded by the epineurium.

Intraneural injection is widely accepted as hazardous and strongly associated with prolonged neurological deficit. Current ultrasound technology cannot distinguish between intraneural and extraneural injection, and it is highly likely that previous reports of intraneural injection involved extraneural injection. At the axillary level of the brachial plexus and the popliteal level of the sciatic nerve, the nerves have a relatively high proportion of connective tissue, which probably resulted in intraneural injection remaining extraneural. The same findings may not apply to proximal nerves such as the interscalene brachial plexus and the subgluteal sciatic nerve, where the proportion of connective tissue within the nerve is much lower. For the axillary brachial plexus study, early follow up was not conducted, therefore, transient neurological symptoms lasting less than a few months were likely missed. Finally, controversy exists regarding the fascial lining of the sciatic nerve at the popliteal level. What may have been believed to be subepineural injection (i.e. intraneural), was almost certainly a subfascial but extraneural injection as the sciatic nerve at this level is surrounded by a complex fascial sheath.

A consequence of intentional intraneural injection that is often overlooked is the trauma that occurs to a nerve when the epineurium is breached regardless of whether local anaesthetic is injected. It has been shown that the intentional intraneural placement of very fine (28-32G) electroneurography needles is associated with subsequent electrophysiological conduction disturbances, but symptoms are reported in only about 10% of patients. These symptoms typically persist for 3-7 days but can very occasionally persist for several weeks. Regarding the effects of
intraneurally placed (larger calibre) nerve block needles without an associated injection, it has been shown that those needles used for regional anaesthesia produce a proportionately greater degree of axonal injury than microneurography needles when fascicles are accidentally impaled. Long bevelled needles inserted with the bevel transverse to the long axis of the nerve fibres, also cause more fascicular damage than those inserted longitudinally to the fibres. These observations all point to a likely greater disruption of nerve integrity with larger calibre needles placed intraneurally compared with electroneurography needles. More frequent and more severe symptoms might therefore be expected.

Short bevelled needles are preferred to long bevelled needles – a practice that is often based on animal studies showing that short bevelled needles are less likely to penetrate both the epineurium (intraneural) and perineurium (intrafascicular). However, if a short bevelled needle penetrates a fasciculus, it has been shown that this results in more axonal damage than a long bevel needle. Regardless of bevel type, when nerve impalement occurs, all needle types have been associated with axonotmesis and interruption of the myelin sheath.

On the basis of these arguments, most practitioners avoid intraneural injection. It is thought the purported advantage of a more rapid block onset does not justify the potential increased risk of prolonged neurological deficit. If rapid onset surgical anaesthesia is needed, an option is to place supplementary blocks, or administer a light general anaesthetic. The sciatic nerve deserves special comment. For popliteal sciatic block, the fascia surrounding the nerve needs to be penetrated. Such needle placement has been previously described as "intraneural" or "subepineurial", however, it is more correctly a (extraneural) “subfascial” injection.
Deliberate intraneural injection has been a controversial subject during the conduct of this thesis. But, is it relevant to CISB? CISB does not warrant the possible increased risk associated with intentional injection. CISB is used primarily for postoperative analgesia rather surgical anaesthesia, therefore, the sometimes stated justification for intentional intraneural injection – rapid block onset – has little relevance in the context of this treatment.
Chapter 13. Superficial cervical plexus neuropathy

Superficial cervical plexus block is a valuable regional anaesthetic adjunctive technique to interscalene block for shoulder surgery, by anaesthetising the needle puncture site during anterolateral interscalene catheter placement, and for providing anaesthesia/analgesia to the skin of the shoulder. It is also useful for thyroid surgery and carotid endarterectomy. Superficial cervical plexus block can be performed easily and rapidly using a blind infiltration technique. Nerve stimulation has limited applicability due to the sensory only nature of the constituent nerves, while ultrasound has not been shown to provide significant clinical benefit.

Few complications have been reported directly attributable to the superficial cervical plexus block. With written consent, a patient is reported who developed superficial cervical plexus neuropathy following a superficial cervical plexus block (and interscalene catheter placement), which manifested as chronic pain – the most serious complication reported to date from this procedure.

A 50-year old female with a 4-year history of shoulder pain, but taking only simple oral analgesics, presented for arthroscopic acromioplasty. She had temporarily responded to several steroid injections. Following intravenous midazolam 2 mg and alfentanil 0.5 mg, a superficial cervical plexus block was placed using a well-accepted technique. With a 1.6 cm 25G regular-bevel hypodermic needle (PrecisionGlide, BD, Franklin Lakes, NJ), 8 mL lignocaine 1% was infiltrated on the posterior border of the sternomastoid muscle midway between the levels of the mastoid process and cricoid cartilage (i.e. at “Erb’s point” – where the nerves of the superficial cervical plexus are likely to “fan-out” within the subcutaneous tissues).
There was some procedural discomfort consistent with local anaesthetic infiltration in a patient with chronic pain, but the block was otherwise uneventful. An anterolateral interscalene catheter was then placed with the needle entry point approximately 3 cm cephalad of the level of the cricoid cartilage just posterior of the sternomastoid muscle. Surgery proceeded uneventfully under general anaesthesia with the patient emerging without pain. Her immediate postoperative course was also uneventful, and she obtained good pain relief from her catheter; however, at 1 month she reported lateral neck numbness with pain radiating to the angle of the mandible and chin. Neurological examination was unremarkable. MRI showed mild foraminal narrowing at the C5/6 level but was otherwise normal. Nerve conduction studies were also normal. Her neck pain persisted beyond 1 year and was characterised by daily spasms (VAS 58/100) on top of a background ache (VAS 18/100). Tramadol, nortriptyline, and gabapentin were trialled briefly but stopped due to side effects.

Needle induced superficial cervical plexus neuropathy has only recently been recognised as a clinical entity. Christ et al prospectively interrogated 273 patients who had undergone an isolated anterolateral approach interscalene block for symptoms in the distribution of the superficial cervical plexus: symptoms were reported in 7.7% of patients at 24 hours, 1.8% at one month; with all resolving by 6 months. All patients reporting symptoms reported “hypoesthesia” (diminished sensation) but none reported numbness or pain. The history of the patient reported here was unique in that her symptoms included numbness and pain and persisted beyond one year. Concurrent with this patient presenting with pain, there were, over the course of 4 months, six other patients reporting neck numbness. Consequently, two technical aspects of the superficial cervical plexus block procedure were changed. The regular-bevel hypodermic needle was switched to a short-bevel needle
Plexufix, B|Braun, Bethlehem, PA), 261, 262 while the traditional superficial cervical plexus block described above was changed to a “modified” technique. The modification aimed to avoid needle puncture at Erb’s point, where the nerves of the superficial cervical plexus pass from deep to superficial just posterior to the posterior border of the sternomastoid muscle. 267 A secondary aim was to inject local anaesthetic more specifically towards the supraclavicular nerve(s) that pass caudally and laterally. Similarly, the catheter needle entry point was moved 1 cm posterior to the posterior border of the sternomastoid muscle. The procedure is described in Chapter 7 in full. In the ensuing year after abandoning the previously described superficial cervical plexus block technique, no patient had voluntarily reported significant neck symptoms at the postoperative surgical consultation (> approximately 250 patients). Furthermore, initial observations suggest that the success of the superficial cervical plexus block has not been significantly compromised by the change in technique.

Limitations to this report include the potential confounding effect of the patient’s preoperative chronic pain; the absence of definitive numerator and denominator data allowing reliable calculation of its incidence; the possibility that the catheter needle was responsible for the pain, or there was just a random cluster of cases unrelated to the existing block technique. It was thought the latter factor was unlikely given that following the described practice change, there does not seem to have been a problem in several hundred cases. Lastly, uncertainty exists regarding which procedural change contributed to the outcome change (or indeed if there was an outcome change): the needle bevel or needle insertion site(s). Ideally, a focussed prospective study such as that conducted by Christ et al should be conducted to more accurately identify possible associations.
Chapter 14. Performing interscalene block in unconscious patients

Traditional teaching as featured prominently throughout educational material has focused on procedure related pain as being indicative of needle-nerve impalement or intraneural injection. Thus, the theoretical advantage of performing interscalene block in an awake patient is that local anaesthetic injection will be suspended in response to the patient’s reporting of pain. However, this teaching is supported only by a limited number of case reports (albeit partly because of the medico-legal implications of reporting such cases). In a review of severe chronic pain syndromes following presumed intraneural injections, all eight patients retrospectively reported severe procedure related pain. In two large prospective series, of seven patients who developed nerve related symptoms after block resolution, five had pain associated with the procedure. Finally, in two other case reports of severe block related neuropathies, severe pain was said to have been present during the injection phase of the block procedure. Other prolonged neuropathies have occurred without any significant procedure related pain. Complicating the interpretation of procedure related pain as an indicator of intraneural needle placement/injection is the range of thresholds patients have for reporting procedural pain. For example, the author’s experience is that patients who complain about pain during IV cannula placement and local anaesthetic infiltration frequently report significant pain during dextrose/LA injection and catheter advancement. Thus, non-block related procedural pain might be useful in clinically assessing the significance of reported pain during dextrose/LA injection or catheter advancement.
Because pain on injection does not always occur with intraneural injection, and many patients with block related procedural pain are clearly not undergoing intraneural injection, anaesthesiologists are increasingly reappraising the necessity for patient consciousness during these procedures. Regardless, patients who complain of procedure related pain, it could be argued, should be suspected of sustaining needle-nerve impalement or intraneural injection.

Interscalene block is often singled out as a block where it is imperative to have patients conscious throughout the procedure. This is because of several case reports of permanent neurological deficit secondary to intracordal local anaesthetic injection during interscalene block performed under general anaesthesia. However, such complications are probably related to poor technique rather than performing the block under awake vs. general anaesthesia per se. In particular, a needle orientation that reduces the likelihood of the needle traversing an intervertebral foramen is important as previously discussed.

For these reasons, many practitioners argue for only performing peripheral blocks in responsive patients, and all central neuraxial blocks awake or under light sedation. However, recently published literature has confirmed the ongoing practice of performing interscalene block under deep sedation or general anaesthesia. Torrillo et al, reported a patient with Huntington’s Chorea who had an interscalene catheter placed under general anaesthesia without complication. The patient was said to only be able to tolerate the procedure asleep. Misamore reported 951 patients who underwent interscalene block under general anaesthesia, with a long-term neurological symptom rate of 0.8% – comparable to that reported for the rate when performed under sedation.
In the present studies, based on the arguments above, blocks were performed whenever possible under light sedation. Block placement under deep sedation or general anaesthesia was allowed for patients who refused to undergo the procedure awake, or when the procedure was deemed to be impossible because of inadequate patient cooperation. All patients who underwent interscalene catheter placement under deep sedation or general anaesthesia avoided significant block related complications.
Chapter 15. Avoiding neurological complications during continuous interscalene block

15.1. Avoiding block related neurological complications during CISB involves:
1. Avoiding nerve trauma secondary to repeated needle-nerve contact.
2. Avoiding intraneural needle placement and/or injection.
3. Avoiding central neuraxial needle placement/injection.
4. Avoiding drug errors.

15.2. Avoiding nerve trauma secondary to repeated needle-nerve contact

Recent animal studies have shown that repeated needle-nerve contact results in histological nerve changes consistent with nerve trauma.\(^{276}\) The clinical significance of these histological changes are unclear, but they would probably manifest as short-lived minor neurological symptoms e.g. numbness +/- tingling. Therefore, the argument could be made for the use of ultrasound needle guidance to minimise needling and repeated needle-nerve contact even though there is currently no clinical data supporting this notion.

15.3. Avoiding intraneural injection

Despite recent evidence showing that intraneural injection of small local anaesthetic volumes does not invariably result in prolonged neurological deficit,\(^ {249}\) the most widely held view is that intraneural injection should be avoided. This is because,
regardless of needle tip configuration or needle trajectory, intraneural needle placement causes disruption to a nerve’s structural integrity. Furthermore, \textit{intrafascicular} local anaesthetic injection strongly correlates with prolonged neurological deficit. Fine bore needles can certainly be inadvertently placed within nerve fascicles.

None of the currently available systems for guiding insertion of block needles can reliably rule out intrafascicular needle placement/injection. For example, modern ultrasound machines can easily detect intraneural injection, but they do not have the resolution to identify intrafascicular vs. extrafascicular needle placement. Current nerve stimulator technology has a very high positive predictive value. That is, if a motor response is present at stimulation thresholds of $< 0.2$ mA (without any dextrose injected prior to stimulation), intraneural needle placement is almost certain. However, the absence of a motor response at high stimulation thresholds (upwards of 1.0 mA), does not rule out an intraneural needle location. One explanation is that the needle may be adjacent sensory neurons but distant to motor neurons. Recently, injection pressure monitoring has been suggested as protecting against local anaesthetic injection related nerve injury: low injection pressures supposedly ruling out harmful intrafascicular injection. However, this technology also has its limitations as other factors unrelated to intrafascicular injection may result in high injection resistance e.g. needle/catheter orifice obstruction by fascia. Furthermore, recent evidence suggests that intrafascicular injection may not invariably be associated with high injection pressures.

How can these arguments be interpreted? Neither ultrasound, nerve stimulation or injection pressure monitoring can eliminate intrafascicular (nor intraneural) injection.
An unexplored therapeutic technique is the routine use of an 18G (or larger) Tuohy needle. The needle’s calibre is such that it is simply not possible to place inside a nerve fascicle, and with the exception of the sciatic nerve, its diameter and tip configuration virtually precludes it from being placed inside a nerve. Further protection could theoretically be afforded by needle orientation so it approaches the nerve along its long axis (rather than perpendicular), which should protect against nerve impalement (the so called “spearing the sausage” analogy).

That said, ultrasound, nerve stimulation and injection pressure monitoring might all be useful in providing additional operator reassurance regarding appropriate extraneural injection.

15.4. Avoiding central neuraxial needle placement

Complications related to central neuraxial needle placement have been some of the most devastating and include not only epidural, subdural and total spinal block, but also permanent neurological deficit, hemiplegia (secondary to injection related syrinx formation) and death (see Chapter 10). As discussed extensively in Chapter 10, interscalene block can be implicated for one unique reason: interscalene block (and deep cervical plexus block) is the only peripheral nerve block where it has been common practice to angle the needle directly towards the neuraxis. It has been suggested that an intracordal syrinx can form secondary to intraneural nerve root injection with subsequent proximal tracking of the local anaesthetic into the spinal cord. On the basis of the previously presented concepts for avoiding interscalene block related complications, the following practice is supported:
1. Use of an anterolateral needle approach, which makes intervertebral foramen penetration virtually impossible.

2. Limiting needle tip depth to one half the distance from the skin to the vertebral column (< 1.25 cm in most but certainly < 2.5 cm).

3. Use of a blunt large calibre needle (e.g. an 18G Tuohy), which makes nerve root impalement and dural puncture unlikely.

4. If a catheter is placed, advancement of the catheter no further than 3-4 cm beyond the needle tip.

Although these were the principles adhered to in the reported studies, they are not necessarily specifically supported by the work here (e.g. point 3).

15.5. Avoiding drug errors

This subject is beyond the scope of this thesis. Of particular relevance to regional anaesthesia is the recent practice of emptying a drug ampoule into a pot on the regional block tray for the anaesthesiologist to aspirate into a syringe. This practice may increase the risk of inadvertently injecting alcoholic chlorhexidine around nerves or into the epidural space.
Chapter 16. Infectious complications during continuous interscalene block: How clinically significant are they?

Recommendations for aseptic technique are often based on “what is probably a good idea” or “what is hard to criticise”. In the case of peripheral perineural catheters, historical recommendations for aseptic technique are often extrapolated from the widely accepted standards for epidural and central venous catheterisation. Infection of the latter poses a completely different risk to patients.

When one attempts to extract the best available evidence to support practice, there is a notable lack of evidence to support the notion that perineural catheter infection is an important clinical issue. First, following more than a decade of experience with perineural catheters worldwide, there have been only four case reports of catheter related infection. These reports were all notable for their absence of persistent patient morbidity. Second, high quality large prospective studies might have shown that colonisation of perineural catheters is relatively common, but with the exception of catheters used for trauma, in ICU and for prolonged periods, progression to clinically significant infection is exceedingly rare. Interestingly, the aseptic technique was not described in two of these latter studies, suggesting that it did not involve ‘full’ barrier precautions. Complicating the interpretation of these data, local inflammation is often labelled as infectious when it could feasibly represent foreign body induced chemical inflammation. Crucially, superficial perineural catheter related infection is eminently treatable, with all infectious events in large prospective series resolving within a few days. This
contrasts with the potentially catastrophic sequelae related to epidural space infection.

Because of these reassuring data, many anaesthesiologists hold the view that superficial (interscalene, supraclavicular, axillary, anterior femoral and perhaps sciatic) perineural catheters are less invasive than a peripheral intravenous cannula. If a peripheral intravenous cannula becomes colonised and/or clinically infected, a bacteraemia can result with possible secondary seeding to a recently implanted joint prosthesis. In the event of infection of a perineural catheter, micro-organisms are likely to be contained within the surrounding subcutaneous tissue as a result of non-communication of catheter with blood stream. The exception to this hypothesis, are (deep) psoas compartment catheters, which have been associated with transient bacteraemia. 284

Popular in many settings is the routine sheathing of ultrasound probes. Both radiologists and more recently, anaesthesiologists 289 have shown that unsheathed probes are not a vector for nosocomial infection during minimally invasive procedures, provided the probes are thoroughly wiped between patients and disinfected at the end of the day. 290 Pre-procedure antibiotic administration has been invariably absent in previous large prospective studies; however, perioperative antibiotics have been shown to reduce perineural catheter colonisation/inflammation. 153, 285 If antibiotics are to be given perioperatively, it is prudent to have them within the tissue at the time of catheter placement consistent with surgical prophylaxis. 291

So what is the downside to observing full barrier precautions for peripheral catheter techniques? First, donning a gown, fully draping the area and sheathing an
ultrasound probe has a consumable item cost. It will also have an inevitable impact on the environment. Most importantly it takes time. Providers are under increasing pressure to manage operating throughput efficiently so as to contain healthcare costs.

In the private sector, where anaesthesiologists often work alone and therefore have to simultaneously place blocks and administer monitored anaesthesia care, the time factor is a frequent reason stated by anaesthesiologists for not placing perineural catheters for painful surgery. It is also a common reason reported by surgeons for their reluctance to support these techniques. 292

For many practice models, an appropriate aseptic technique for the placement of peripheral perineural catheters intended for short term ambulatory use may involve an alcohol hand rub, sterile gloves, alcohol/chlorhexidine skin preparation, ‘limited’ draping, a clean sheathed or unsheathed probe and a ‘no-touch’ technique similar to urinary catheterisation, with particular attention paid to that part of the catheter likely to penetrate the skin. Using a similar technique, and routine pre-procedure antibiotics, there was one very minor superficial infection from 720 peripheral ambulatory catheters (unpublished data from the large prospective study reported in the previous thesis). 150 However, it should be noted that aseptic technique for a proficient, busy, private practitioner placing perineural catheters that are intended for brief ambulatory use is probably not appropriate technique for a junior resident placing a nerve catheter in a multitrauma intensive care patient. 153, 286

Stringent recommendations for aseptic technique have already appeared in influential national documents. Chapter <797> of the United States Pharmacopoeia recommends that ambulatory local anaesthetic pumps be filled in the pharmacy under a laminar flow hood. The motives for such documents are to protect patients from
substandard care. However, their relevance for low risk treatments such as short-term ambulatory infusions is questionable. Filling ambulatory pumps in the pharmacy might not be difficult to institute in large academic teaching centres, but would have significant implications for small stand-alone ambulatory facilities that don’t have a pharmacy equipped with such a hood. Even though institutions and providers do not necessarily have to follow the <797> guidelines, anaesthesiologists in these centres could understandably just not offer ambulatory infusions to their patients if it means non-compliance with the <797> recommendations. This illustrates how inappropriately extrapolating procedural guidelines to procedures having different risk profiles can hinder ongoing practice advancement. 293
Part 6: Summary, Discussion and Conclusions

Chapter 17  Summary

Chapter 18  Discussion

Chapter 19  Conclusions
Chapter 17. Summary

The work contained in this thesis is a continuation of research started 10 years ago aimed at advancing the technique of ultrasound-guided continuous brachial plexus block for ambulatory anaesthesia after shoulder surgery. By conducting a series of evaluative studies, further refinements have been made in the postoperative pain management of patients receiving continuous brachial plexus blockade for analgesia after this surgery.

Prior to commencement of the current interventional studies, a literature review was conducted in relation to the regional anaesthetic techniques used for analgesia after shoulder surgery. The aim of this review was to critically assess the evidence for the effectiveness of these techniques and to identify important unrecognised gaps in the knowledge base. Despite its common use, subacromial/intra-articular local anaesthetic infiltration was identified as performing only marginally better than placebo, and because the technique has been associated with catastrophic chondrolysis, it was concluded that it could no longer be recommended for this surgery. All single injection nerve blocks were found to be limited by a short effective duration. Nevertheless, single injection blocks possibly remain the most commonly used analgesic technique after this surgery. Suprascapular nerve block was found to reduce postoperative pain and opioid consumption following arthroscopic surgery, but provides inferior analgesia compared with single injection interscalene block. CISB incorporating a basal local anaesthetic infusion and patient controlled boluses was confirmed to be the most effective analgesic technique following both major and minor shoulder surgery.
Several key clinical questions were identified that required answering to advance the CISB technique. First, what is the optimum primary bolus dose of interscalene ropivacaine to prevent recovery room pain and minimise motor block? Second, does local anaesthetic volume and concentration influence block duration? Third, what is the relative efficacy of patient initiated mandatory boluses compared to PRN only boluses during use of a CISB? Fourth, what is the preferred approach for interscalene catheter placement: anterolateral or posterior? Fifth, what is the optimum distance to thread a non-stimulating catheter past the needle tip during use of the anterolateral approach, and finally, does catheter orifice configuration significantly affect block quality?

To answer the first clinical question, a 3-stage study was conducted to estimate the volume and concentration of interscalene ropivacaine that would prevent recovery room pain following shoulder surgery under general anaesthesia. In stages one and two, the initial interscalene catheter ropivacaine dose was adjusted in a 10% incremental up-down sequential manner depending on the presence of recovery room pain in the previous patient. During stage 1, the volume of ropivacaine 0.5% was varied from 30 mL. During stage 2 the concentration of ropivacaine 20 mL (the ED(volume)95 estimate from stage 1) was varied from 0.45%. During stage 3, subjects were randomly assigned to receive ropivacaine 0.5% 30 mL (‘conventional dose’) or 0.375% 20 mL (the estimated ED(volume+concentration)95 from stages one/two). A postoperative ropivacaine 0.2% 2mL.hr⁻¹ infusion was administered via an elastomeric pump. Grip strength was measured in the recovery room and time to first pain was noted at 24 hours. During stage 1 (n=34) the ropivacaine 0.5% ED(volume)50/ED(volume)95 (95% CI) estimates were 2.7/20.5 mL (2.4-9.5/17.3-25.8). During stage 2 (n=29), the ropivacaine 20 mL
ED(concentration)$_{50}$/ED(concentration)$_{95}$ (95% CI) estimates were 0.15/0.34% (0.13-0.30/0.29-0.43). The ED(dose)$_{50}$ was similar for stages one and two (13.5 vs. 30 mg) but the ED(dose)$_{95}$ was higher for stage 1 (102.5 vs. 68 mg). During stage 3 (n=40), satisfaction (0-10) was modestly higher for the new/lower dose [median (IQR) = 10 (10-10) vs. 9 (8-10), p=0.007]. Pooled data regression analysis showed that increasing ropivacaine concentration increased grip weakness but not block duration. It was concluded that ropivacaine interscalene block requires a threshold volume and concentration, with concentration primarily determining motor block. When combined with continuous blockade, supra-threshold ropivacaine doses do not significantly prolong primary block duration but may compromise patient satisfaction.

The subsequent randomised study investigated the ropivacaine volume and concentration effect on interscalene block duration. 185 patients were randomised to five ropivacaine volume/concentration combinations (0.75% 5, 10 and 20 mL; 0.375% 20 and 40 mL) administered preoperatively via an interscalene catheter before shoulder surgery under general anaesthesia. A ropivacaine infusion via an elastomeric pump commenced at the onset of pain. Patients were questioned at 24 hours for the primary outcome: time to first pain. Group 5 mL was excluded posthoc because of an unacceptably high block failure rate. Multivariate Cox regression was used to assess the effect of volume and concentration (each corrected for the other) on the primary outcome. Probability of pain as a function of time was associated with not only dose, but also volume corrected for concentration, and concentration corrected for volume: hazard ratio (95% CI) for dose = 0.992 (0.987, 0.997) / p=0.002, volume = 0.959 (0.937, 0.982) / p=0.001, concentration = 0.852 (0.743, 0.976) / p=0.021. Increasing the volume of ropivacaine 0.375% from 10 to 40 mL
was estimated to increase median (quartiles) block duration from 10.0 (9.5-11.5) to 15.0 (10.75-21) hours. Similarly, increasing the concentration of 20 mL ropivacaine from 0.375% to 0.75% was estimated to increase median (quartiles) block duration from 10.75 (9.75-14.0) to 13.75 (10.5-21.0) hours. In conclusion, block duration is influenced by both local anaesthetic volume and concentration; a finding of increasing relevance with the current trend to lower volumes for ultrasound guided regional anaesthesia.

The third study reported in the thesis evaluated the effect of patient initiated mandatory boluses over PRN only boluses with respect to postoperative analgesia and side effects. This was a prospective, randomised study, which tested the hypothesis that a reduced dose CISB incorporating a low background infusion with mandatory boluses would provide similar shoulder surgery analgesia compared to a dose regimen incorporating a higher dose, higher background infusion. Patients undergoing rotator cuff surgery received via an interscalene catheter, one of two elastomeric pumps, each having a 5-mL/60 min bolus function and a 2 mL.hr⁻¹ (n=38) or 5 mL.hr⁻¹ (n=43) ropivacaine 2 mg.hr⁻¹ infusion. Boluses commenced from the onset of pain and continued for > 48 hours as required (PRN) up to every hour for a NRPS (0-10) > two. Group 2 mL.hr⁻¹ received mandatory 6 hourly boluses irrespective of the NRPS. Patients were questioned on postoperative day one and two for treatment effectiveness and side effects. Postoperative pain was similar between groups [Group 2 mL.hr⁻¹ day two median (IQR) [95% CI of the mean] worst movement pain = 4 (1-5)[2.8-4.7] vs. 4 (2-5)[3.1-4.6], p=0.99], as were night awakenings and rescue tramadol consumption. Numerically rated numbness and weakness were similar between groups; however, nine patients (21%) in the 5 mL.hr⁻¹ group vs. one (3%) in the 2 mL.hr⁻¹ group required a temporary infusion cessation.
due to side effects (predominantly hand numbness) (p=0.02). It was concluded that continuous interscalene ropivacaine 0.2% 2 mL.hr\(^{-1}\) with mandatory 6 hourly (and PRN) boluses provides similar analgesia after rotator cuff repair but with reduced side effects compared to 5 mL.hr\(^{-1}\) with PRN only boluses.

In the next investigation, the aim was to identify the optimal anatomical needle approach for interscalene catheter insertion. A prospective, randomised study, was conducted which tested the hypothesis that interscalene catheters placed using the posterior approach would provide more effective analgesia after shoulder surgery compared with catheters placed using the anterolateral approach. A total of 110 patients presenting for elective shoulder surgery were randomly assigned to receive an ultrasound guided posterior (n=54) or anterolateral (n=56) interscalene catheter with ropivacaine 0.375% 20 mL administered preoperatively via the catheter prior to surgery under general anaesthesia. Ropivacaine 0.2% 2 mL.hr\(^{-1}\) with on demand hourly 5 mL boluses was continued for > 48 hours with tramadol available as rescue. Patients were questioned in the recovery room at 24 and 48 postoperative hours for pain, ropivacaine bolus and tramadol consumption. Patients were more frequently pain free in the recovery room in the anterolateral group compared with the posterior group [% (95% CI): 91(84-99)% vs. 61(48-74)%, p=0.005]. Rescue tramadol consumption was higher for the posterior group during the first, but not second 24 postoperative hours (day one / day two: 48% vs. 27%, p=0.017 / 35% vs. 27%, p=0.27). Postoperative pain, ropivacaine bolus consumption, numbness, weakness, neck discomfort and satisfaction were similar between groups. Catheter threading difficulty was more common (33% vs. 13%, p=0.012) and catheter placement time was longer [median (IQR) = 9 (7.5-10) vs. 6.5 (6-8) min, p < 0.0001] in the posterior group. It was concluded that anterolateral interscalene catheters perform more
effectively and are procedurally more easily placed compared with catheters placed using the posterior approach.

The fifth clinical study aimed to evaluate the effect of interscalene catheter threading distance. The effect of this design attribute had not been previously investigated despite the technique being in use for over a decade. A total of 153 patients receiving an anterolateral interscalene catheter (catheter needle and nerve/plexus in a similar alignment) for elective shoulder surgery were randomised to one of three groups: following out-of-plane ultrasound confirmation of the needle tip immediately lateral to the 5th-6th cervical roots, a non-stimulating catheter was blindly advanced 0.5 cm (end-hole; n=50), 2.5 cm (multi-orifice; n=50) or 5 cm (multi-orifice; n=53) beyond needle tip. Ropivacaine 0.75%+lignocaine 1% (50:50) 20 mL was administered preoperatively via the catheter before surgery under general anaesthesia. A ropivacaine 0.2% 2 mL.hr$^{-1}$ infusion via elastomeric pump with mandatory 6 hourly (and on demand) 5 mL boluses was continued for > 48 hours with tramadol available as rescue. Patients were questioned in the recovery room, at 24 and 48 hours for NRPS (0-10), ropivacaine bolus use and tramadol consumption. Patients were more frequently pain free in the recovery room in the multi-orifice 2.5 and 5 cm groups compared with the end-hole 0.5 cm group (94%, 91% vs. 66%, p<0.001). During the first 24 h, the 0.5 cm end-hole group demonstrated an earlier time to first pain (median, 10 vs. 17, 15 h, p<0.001), higher “average pain” (median, 3 vs. 1, 2, p=0.004), and more ropivacaine bolus (median, 5 vs. 3, 3, p<0.001) and tramadol consumption (p=0.01). Groups 2.5 and 5 cm did not significantly differ in any outcomes. These results showed that there is no difference in efficacy between a threading distance of 2.5 cm or 5 cm for the multi-orifice catheter. Although the paper in which the work was published drew conclusions about the efficacy of
catheter orifice configuration, upon reflection, it was decided that further work would be required to evaluate this issue.

Because conclusions about the influence of orifice configuration could not be definitively made in the previous study, the final study aimed to evaluate the effect of catheter orifice configuration controlled for threading distance. 156 patients receiving an anterolateral interscalene catheter for elective shoulder surgery were randomised to 3 groups: following out-of-plane ultrasound confirmation of the needle tip immediately lateral to the C5/6 roots, an endhole (n=52), triple hole (n=53) or 6-hole (n=51) non-stimulating catheter was positioned 3 cm beyond the needle tip. 15 mL ropivacaine 0.375% was administered preoperatively via the catheter before surgery under general anaesthesia. A ropivacaine 0.2% 2 mL.hr⁻¹ infusion with mandatory 6-hrly and on demand 1-hrly 5 mL boluses was continued for > 48 hours with tramadol available as rescue. Patients were questioned in the recovery room, and at 24 hours for numerical rating pain score (NRPS, 0-10), ropivacaine bolus and tramadol consumption. The frequency of recovery room pain was similar between groups (p=0.75), and demonstrated strong evidence for equivalence at the 5% significance level. Neither time to first pain, “average” or “worst” pain during the first 24 hours, ropivacaine bolus or tramadol consumption significantly differed between groups. Catheter threading difficulty was more common for the square-tipped end-hole catheters (end-hole=19% vs. triple-hole=6%, 6-hole=0%, p<0.001). These results show that catheter orifice configuration does not significantly affect the quality of continuous peripheral nerve blockade. These findings are in contrast to epidural catheter studies, and suggest that anatomical factors have a significant bearing on whether multi-orifice catheters confer advantage over the single-orifice design.
Chapter 18. Discussion

Pain relief after surgery is important for many reasons beyond the ethical duty to minimise pain and suffering. The physiological insult of surgery is lessened, recovery and general patient wellbeing may be improved with patients returning to normal activities faster, and the incidence of chronic pain is reduced. Despite widespread understanding of these principles there are frequent impediments to implementing high quality pain relief. Current practice emphasises “multimodal analgesia”. Although this is commonly understood to mean using a range of drugs, appropriate use of local anaesthetic is frequently an important part of a multimodal approach to pain relief after surgery.

The peripheral application of local anaesthetics has increased dramatically in recent years through the increased use of interventional regional anaesthesia/analgesic techniques. While this change has been due in part to the perceived complexity and complications of epidural blockade, and to developments in the available analgesic agents, two technological breakthroughs have played a key role. These are ultrasound guidance for nerve localisation and perineural catheters for providing extended peripheral nerve blockade. Both technologies emerged in the late 1990’s, and have been progressively incorporated into routine clinical practice over the last decade.

Advances in ultrasound technology make it commonplace to have high quality portable ultrasound machines in the operating suite, which are capable of nerve localisation for local anaesthetic deposition. In addition to allowing visualisation of nerves and plexuses, real-time ultrasound guidance has, for the first time, enabled visualisation of: important adjacent structures; the advancing needle and subsequent
local anaesthetic spread. Evidence from randomised controlled trials suggests a reduction in needle passes, small reductions in procedure related pain, and a reduction in procedural time when ultrasound is compared to traditional nerve localisation techniques. However, ultrasound has not been shown to unequivocally increase block success rates, as success rates were already high with blocks performed by experienced practitioners using existing techniques. Intuition would suggest that real-time needle guidance should translate into a reduction in iatrogenic needle related complications; however, to date this has only been demonstrated with respect to inadvertent vascular puncture, although a recent retrospective study suggested neurological complications were reduced after a department’s introduction of ultrasound technology. The most feared complication of peripheral nerve blocks, iatrogenic nerve injury, is fortunately very rare so it is unlikely to ever be demonstrated, in a randomised study, whether real-time ultrasound needle guidance has any impact on this complication. Although the evidence of reduced risk is somewhat equivocal, ultrasound has resulted in more patients receiving perioperative peripheral nerve blockade.

While ultrasound technology has attracted most of the attention over the last 5 years, it is perineural catheters, or continuous peripheral nerve blocks that have had the greatest positive impact on the perioperative experience of orthopaedic patients. The management of pain after shoulder surgery has exemplified this development. As recent as 2003, it was not uncommon for patients having rotator cuff surgery to require a two night hospital admission for intravenous opioid. Now, with our ability to accurately and safely place catheters at the appropriate position along the brachial plexus, together with the availability of affordable ambulatory local anaesthetic delivery systems, prolonged brachial plexus blockade can be provided in the
ambulatory setting (typically 3-5 days), thereby extending potent postoperative analgesia while avoiding opioid related side effects. The technique has been shown to be well tolerated and associated with high patient satisfaction. Consequently, rotator cuff procedures can now be performed as overnight or even day stay procedures. Similar results have been achieved for a wide range of painful peripheral limb surgery and promising results have been reported for major knee surgery. 301, 302

In the previous body of work, it was concluded that ambulatory continuous brachial plexus block was an effective analgesic treatment following shoulder surgery, and had an acceptable risk profile. The treatment was found to be feasible for anaesthetists who managed shoulder surgery patients on a regular basis. The neurostimulation-based technique had a false negative motor response rate of over 50%, which was higher than single injection tangential needle approaches i.e., in over 50% of subjects, despite the interscalene catheter needle being in contact with the brachial plexus, a motor response was not elicited. Interscalene catheters were shown to be effectively placed with ultrasound only guidance; however, a subset of patients existed in whom the use of nerve stimulation was an essential tool for accurate catheter placement. The size of this subset may be dependent on the operator’s level of experience with ultrasound. Compared with the neurostimulation technique alone, the addition of ultrasound guidance for interscalene catheter placement reduced needle passes, procedural pain and, following shoulder surgery, resulted in a reduction in local anaesthetic and supplemental opioid consumption. The previous work also addressed a key aspect related to CISB pharmacology. With

http://www.library.auckland.ac.nz/thesis (search field, Fredrickson MJ)
ropivacaine 0.2% administered at 2 mL.hr⁻¹. A significant proportion of patients undergoing rotator cuff repair/total shoulder joint replacement experienced moderate to severe breakthrough pain. This was not improved by doubling the concentration to 0.4%. Ambulatory continuous brachial plexus block was found to improve analgesia and reduce opioid consumption after not only major shoulder surgery, but also minor arthroscopic procedures. Finally, an acceptable and effective strategy for the management of patients requiring more than 72 hours of continuous brachial plexus block via an elastomeric pump was to simply refill the pump. The current work described in this thesis and summarised in Chapter 16 has built on the knowledge base obtained from this previous work.

Several studies by other authors have further assessed the issue of ultrasound vs. nerve stimulation. These studies essentially support the findings from the studies conducted in the first thesis – that ultrasound guidance confers significant benefit over traditional neurolocalisation techniques. McNaught conducted an up-down dose finding study for interscalene block for shoulder surgery using either ultrasound or nerve stimulation guidance. The ultrasound method was associated with a lower minimum effective local anaesthetic volume to prevent recovery room pain, in addition to a reduction in needle passes. ³⁰³ In Thomas et al’s randomised study of ultrasound vs. neurostimulation guidance for single injection interscalene block, the ultrasound method was associated with reduced block procedural time and faster block onset. Indices of block effectiveness were not significantly different between groups. ³⁰⁴ Danelli et al compared ultrasound and nerve stimulation guidance for interscalene catheter placement and found that ultrasound guidance reduced procedural time, needle passes and inadvertent vascular puncture. ³⁰⁵
prospective studies continue to support the safety of the ultrasound guided technique in trainees and experienced practitioners alike.  

Inevitably, several studies were published after the literature review reported in Chapter 2, but are relevant to its conclusions. An independently conducted systematic review published subsequent to our review, found that continuous nerve blocks as a whole were associated with reduced pain and opioid consumption, in addition to reduced nausea and improved patient satisfaction.  

Taninshi compared a low volume (10 mL) interscalene block with no block. All patients received general anaesthesia. The interscalene group demonstrated reduced pain and analgesic consumption during the first few hours after surgery. These results were essentially reproduced by Cho et al. Goebel et al compared a single injection interscalene block with the continuous technique for open shoulder surgery. As expected the continuous technique patients required less rescue analgesic medication.  

Lee et al compared single injection interscalene block with combined single injection suprascapular and axillary (circumflex) nerve blocks. The study also featured a control group incorporating no block (general anaesthesia only). Interscalene block was associated with the lowest pain scores; the suprascapular/axillary group provided better analgesia than the group incorporating no block. These results are easily explained by the anatomical fact that the suprascapular and axillary nerves are not the only nerves innervating the shoulder.  

DeMarco randomised patients undergoing shoulder surgery with a postoperative subacromial ropivacaine infusion to either a bupivacaine interscalene block or saline (sham) block. The interscalene group demonstrated reduced pain scores and analgesic consumption at 6 hours. Koltka randomised patients having arthroscopic
rotator cuff repair to a patient controlled continuous interscalene or subacromial levobupivacaine infusion. Analgesic requirements were lower, and patient satisfaction was higher in the interscalene group. 313

In addition to the proven effectiveness of CISB for postoperative pain control following shoulder surgery, recent prospective studies have suggested the technique may be useful for treating complex regional pain syndrome of the shoulder. 56 Such patients with refractory shoulder pain unresponsive to alternative treatments were followed for 12 months after a one-week continuous interscalene block. Pain scores and indices of shoulder function improved over the ensuing months suggesting a treatment effect from the block and rehabilitation. Clearly, randomised trials are needed to confirm or refute this treatment for these patients. 314 Single injection interscalene block has also been used to treat shoulder, chest and scapula pain arising from the cervical spine (cervical radiculopathy). 315 Finally, ongoing reports have emerged of the potential role of ultrasound in detecting previously undiagnosed pathology such as a malignant thyroid cyst during interscalene block. 316

Several issues relevant to the current body of work have arisen and warrant further elaboration and discussion. For example, local anaesthetic as introduced in chapter 2, local anaesthetic adjuvants may prolong block duration – a quality central to the effectiveness of single injection peripheral nerve blocks for early postoperative analgesia. Single injection blocks have the advantage over continuous techniques in their relative technical simplicity. A recent tightly controlled laboratory study of the isolated rat sciatic nerve has suggested that dexamethasone, at concentrations exceeding that used clinically, had no effect on the time course of recovery from
lignocaine-induced block of both A-delta and C-fibres. This supports the hypothesis that its analgesic effect is mediated systemically.

Recent studies investigating potential local anaesthetic adjuvant neurotoxicity for dexamethasone have raised concerns. Although there is little clinical evidence for neurotoxicity, recent laboratory studies in rats have raised the possibility of dexamethasone neurotoxicity at clinical doses. In isolated rat sciatic nerves, dexamethasone at a concentration of 133 mcg/mL in the immediate perineural milieu (corresponding to a perineural injection of approx. 4 mg), increased ropivacaine induced neurotoxicity as evidenced by the tryptan blue assay for neuronal death. Dexamethasone has also been shown in animals to reduce blood flow. Furthermore, some dexamethasone preparations contain known neurotoxins such as benzyl alcohol, a vehicle such as polyethylene glycol and insoluble particulate matter.

It should also be noted that regardless of the route of administration, dexamethasone possesses not only beneficial analgesic and antiemetic effects, but also adverse effects such as insomnia, hyperglycaemia in diabetic patients, and possibly immunosuppression related increase in the wound infection risk.

An additional consideration for perineural dexamethasone as an adjuvant for brachial plexus blocks is the finding that it also increases upper limb motor block. Studies have suggested an association between upper limb motor block and patient dissatisfaction, and it is possible, therefore, that any dexamethasone induced motor block might manifest as an increase in patient dissatisfaction. On balance, it would appear from these studies that there is insufficient evidence for the routine
administration of interscalene dexamethasone. Future studies are needed to evaluate potential neurotoxicity, and to definitively answer whether there is sufficient advantage in administering dexamethasone perineurally rather than systemically.

A hotly debated but unresolved controversy over the last decade relates to the anterolateral \(^7, 8, 10, 11, 14\) (or ‘modified lateral’) \(^3, 14\) versus posterior (or ‘cervical paravertebral’) approaches \(^3, 14\) to placement of an interscalene catheter. \(^1, 2, 3, 4\) It has been said the posterior approach can reduce motor block (or ‘dead feeling’), \(^3, 14\) and the anterolateral approach can cause transient acute neuropathic upper limb pain. \(^3, 14\) Consequently, it was thought necessary to perform a prospective randomised controlled trial to address these issues. The study conducted during this work (Chapter 7) found no evidence to support the former hypothesis; however, some might question the specific posterior approach used in the present study; in particular, that it is fundamentally different to the ‘continuous cervical paravertebral’ approach that had been in common use for over a decade. In other words, the continuous cervical paravertebral and more recently described “ultrasound-guided posterior approach continuous interscalene catheter” approaches might be seen to represent different techniques; the terms being used synonymously, almost inappropriately. Apart from the concomitant use of ultrasound, it is generally accepted that these techniques are similar: \(^3, 14\) the needle approaching the roots (or trunks) tangentially from behind the patient through or alongside the neck extensors. The former uses the 6\(^{th}\) cervical vertebra short transverse process bony landmark; \(^3, 14\) the latter utilises ultrasound but with the needle entering the neck more laterally towards the nerve roots. \(^8, 11, 14\)
Other methodological options were not assessed by the study in Chapter 7 but might warrant a reappraisal of the ultrasound guided posterior approach. These include (1) thinner but still sufficiently blunt, more echogenic needles (2) very flexible catheters, and (3) the precise placement of the catheter between the roots under direct vision assisted with a mechanical transducer holder or assistant. With respect to such a holder, in the setting of a busy operating room or when the nerve roots are closely approximated, our experience is that this is not always practical.

Additional issues should be considered when deciding on the interscalene catheter approach. With the anterolateral approach, the needle is directed away from the neuraxis, which introduces a safety factor. With the posterior approach, if practitioners inadvertently move anterolaterally around the neck and consequently adopt a more tangential needle approach in relation to the cervical spine, and lose sight of the needle tip, they risk entering an intervertebral foramen, with the associated risks. The dorsal scapular and long thoracic nerves both pass through the middle scalene muscle. Therefore, both may be subject to needle trauma when the posterior approach is used. This may cause serratus anterior muscle paralysis. Similarly, the superficial cervical plexus and external jugular vein are close to the needle puncture point of the traditional anterolateral approach. As stated before, a large calibre Tuohy tipped needle orientated along the long axis of a nerve almost eliminates the possibility of intraneural needle placement. The anterolateral approach is a more superficial technique as the plexus is situated closer to the front than the back of the neck. Therefore, in the very unlikely event of catheter related deep space infection requiring surgical drainage, a posterior approach catheter may require a more invasive surgical procedure. Anterolateral catheters are more difficult to fixate due to the superficial nature of the brachial plexus at this
location and the mobile overlying skin. However, when at least 3-4 cm of block needle is tunnelled under the skin usually cephalad towards the mastoid process before the catheter exits the skin, and followed by tincture of benzoin skin preparation, combined with a purpose designed catheter fixation device, the author’s experience is that premature catheter dislocation is very rare.

Several reviews, observational studies and case reports published during the writing of this thesis have provided new insights for performing interscalene block, particularly those patients with respiratory disease. First is an evidence based review of the perioperative strategies for minimising respiratory compromise in patients with lung disease having shoulder surgery. The review’s findings support regional blocks for postoperative analgesia, and if interscalene block is chosen, to minimise phrenic block, use of a low volume and low concentration of local anaesthetic administered as caudal/lateral (“supraclavicular”) as possible and/or adjacent to the C7 root. Perioperative management of these patients is a significant problem. Unfortunately, the conclusions from the review are not completely supported by the data: the authors conclude that interscalene block should be limited to a single injection, which is based on two studies that demonstrated a 100% incidence of phrenic block after 24 hours of a > 5 mL.hr\(^{-1}\) infusion. However, this conclusion overlooks one of the main advantages of all catheter techniques: the ability to titrate analgesia to side effects (without the all or nothing problem of single injection techniques). The conciseness of the review also precluded a discussion of the various options for surgical anaesthesia in patients with severe respiratory disease: general anaesthesia only (with planning for elective postoperative ventilation), interscalene block only, general anaesthesia with interscalene block, or general anaesthesia with other regional techniques. Although level 1 evidence is at present lacking, the review
supports the use of the “shoulder block” in these patients for postoperative analgesia: i.e. blockade of the suprascapular and axillary nerves. Another approach to these patients, which is supported by the review, and is indeed our preferred approach, is for a preoperative single injection suprascapular block combined with either an axillary nerve block or infraclavicular block. Surgery can be conducted under light general anaesthesia using a laryngeal mask airway. An interscalene catheter can be placed before surgery but without local anaesthetic. Postoperatively, a patient controlled interscalene infusion can be connected but kept off until required for pain (2 mL.hr⁻¹ background infusion; 5 mL bolus; lockout 60 min). Supplementary nurse controlled intravenous opioid can be available as required. Nurses can be instructed to turn the interscalene infusion off if there is any suggestion of increasing respiratory compromise.

Other studies published during the writing of this thesis included an observational study of 146 patients undergoing interscalene block. In this study, anatomical variations were common (49% of patients), however, these variants did not appear to have a major influence on block performance. Interscalene block with catheter placement could be successfully performed in a patient with severe facial and cervical deformities due to previous radiotherapy. A cadaver study reported the presence of a previously unrecognised muscle, the cleidoatlanticus muscle passing over the typical site of needle placement. The authors speculate that this muscle may lead to misrepresentation of the interscalene sonographic image. Further study of the muscle’s relevance is necessary. Muhly et al’s cadaver and clinical correlation study confirmed the presence of arterial branches of the subclavian artery passing directly through the area of the interscalene brachial plexus in 86% of patients. This vessel may put the patient at risk of inadvertent intravascular injection.

187
The increasingly relevant comorbidity of obesity in patients presenting for shoulder surgery is attracting research attention. A retrospective database review of a single institution's experience with interscalene block found that obesity was associated with prolonged block procedural time and higher postoperative opioid requirements and nausea. Despite these problems, it is recognised that these patients still benefit from interscalene block. Further research is required to optimise block success in these patients. Finally, a novel technique for the early identification of block success or failure involves perfusion index and plethysmographic variability. This may be useful in predicting block failure in patients perceived to be at risk of block failure, however the clinical utility of the technique remains uncertain.

Three recent reports have highlighted a new complication related to interscalene catheter placement – perineural entrapment or catheter adhesion formation resulting in difficulty with removal. Interestingly, all patients in whom this complication occurred received a stimulating type catheter that typically incorporates a wired mesh tip. Such complications have not been reported with soft polyamide (non-stimulating) catheters. Other complications reported during the writing of this thesis include pleural effusion and atelectasis presenting as chest discomfort while the interscalene infusion was running, and prolonged dyspnœa in association with a single injection block, that following investigation, was found to be due to undiagnosed Addison’s disease.

Finally, risks associated with the beach chair position commonly used for shoulder surgery are beyond the scope of this thesis, but a recent large prospective study deserves mention. Rohrbaugh et al reported a retrospective case series of over 15,000
patients who underwent shoulder surgery in the beach chair position under single injection interscalene block and sedation. There was one ischaemic stroke presenting 24 hours after surgery. The series provided support for the safety of this technique when performed under interscalene block and sedation. 347
**Chapter 19. Conclusions**

On the basis of the studies contained within this body of work, the following conclusions are supported:

1. Subacromial/intra-articular infiltration provides little, if any clinically important benefit in terms of reduced postoperative pain (especially for open and/or rotator cuff procedures), and may be associated with irreversible chondrotoxicity.

2. There is insufficient evidence from randomised trials, at present, to support the addition of an axillary (circumflex) nerve block to suprascapular nerve block; however, prospective observational data exists to support its use. Suprascapular nerve block with or without a concomitant axillary (circumflex) nerve block may be the preferred technique when an interscalene block is contraindicated (e.g. moderate-to-severe respiratory disease) or where the absolute avoidance of distal extremity motor block is important. The addition of a suprascapular nerve block to interscalene block cannot be recommended.

3. Interscalene block provides more effective analgesia than ‘1’ and ‘2’ following most shoulder procedures; however, it is an invasive procedure, having been associated with rare but serious procedure related complications.

4. Continuous interscalene block represents the most effective modality for postoperative analgesia following both major and minor, open and arthroscopic shoulder surgery. It provides better analgesia than a single injection interscalene block (which in turn provides better analgesia than both suprascapular nerve
block and subacromial (bursal)/intra-articular infiltration). However, like its single injection counterpart, it remains an invasive procedure and may cause serious procedure related complications. Despite advances in the methods used to facilitate catheter placement, it remains technically challenging.

5. Ropivacaine interscalene block requires a threshold volume and concentration, with concentration primarily determining motor block. The dose finding studies in this thesis support a primary bolus dose of 20 mL ropivacaine 0.375%. When combined with continuous blockade, supra-threshold ropivacaine doses do not significantly prolong primary block duration but may compromise patient satisfaction. In the context of a single injection interscalene block, block duration is dependent on both local anaesthetic volume and concentration.

6. After rotator cuff repair, continuous interscalene ropivacaine 0.2% at 2 mL.h⁻¹ with mandatory 6 hourly (and PRN) boluses provides similar analgesia but with reduced side effects compared to 5 mL.h⁻¹ with PRN only boluses.

7. Anterolateral interscalene catheters perform more effectively and are procedurally more easily placed compared with catheters placed using the posterior approach.

8. Multi-orifice catheters do not provide any major advantage over end-hole interscalene catheters. No difference in efficacy is achieved by blindly advancing the catheter 2.5 cm versus 5 cm beyond the needle tip.
Appendix 2. Co-Authorship Forms

Co-Authorship Forms

The form is to accompany the submission of any PhD that contains research reported in published or unpublished co-authored work. Please include one copy of this form for each co-authored work. Completed forms should be included in all copies of your thesis submitted for examination and library deposit (including digital deposit), following your thesis abstract.

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Name of candidate: Kristine K Chen
Name of candidate: CT Chen
Name of contribution: Literature review and grading and manuscript preparation
Nature of contribution: Literature review and grading and manuscript preparation

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Certification by Co-Authors

The undersigned hereby certify that:

- the above statement correctly reflects the nature and extent of the PhD candidate’s contribution to this work, and the nature of the contribution of each of the co-authors, and
- in cases where the PhD candidate was the sole author of the work that the candidate wrote the text.

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The undersigned hereby certify that:
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Please indicate the chapter/section/pages of this thesis that are extracted from a co-authored work and give the title and publication details or details of submission of the co-authored work.

**Chapter v: Patient initiated mandatory boluses for ambulatory continuous interscalene analgesia: an effective strategy for optimising analgesia and minimising side effects.**


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The undersigned hereby certify that:
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- in cases where the PhD candidate was the lead author of the work, that the candidate wrote the text.

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Chapter vi: Posterior versus Anterolateral Approach Interscalene Catheter Placement

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The undersigned hereby certify that:

- the above statement correctly reflects the nature and extent of the PhD candidate’s contribution to this work, and the nature of the contribution of each of the co-authors; and
- in cases where the PhD candidate was the lead author of the work that the candidate wrote the text.

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Appendix 3. Block Description

As the primary focus of the current thesis concerns CISB, a detailed description of the technique is provided. This technique was developed during the studies conducted during this thesis, and was used for the described interventional studies. The technique is further described on the website: http://ultrasoundblock.com.

Surface landmarks: The following were first marked out:

1. Clavicle.

2. Posterior border of sternomastoid muscle from mastoid process to clavicle (accentuated by asking patient to lift their head off the pillow with the hand pressed against their forehead).

3. Level of the cricoid cartilage on line “(2)” (= approximately the C6 vertebral level).

4. Midpoint of line “(2)” distance between the mastoid process and the level of cricoid cartilage. The external jugular vein was often marked out to help avoid subsequent needle puncture, which can cause problematic bleeding.

Needle: 4-5 cm (depending on patient weight: usually 4 cm; > 100 kg = 5 cm) stimulating 18G Tuohy needle with multi-orifice catheter.

Setup

1. High resolution (10-15 MHz) linear probe e.g. Sonosite L38.

2. 4-5 cm Tuohy needle catheter kit with catheter cut using a surgical blade to approximately 20-25 cm (cutting the catheter makes catheter placement less technically challenging and improves patient acceptance).
3. Medical cyanoacrylate (e.g. dermabond 0.5 mL vial).

4. Catheter anchoring device (e.g. Lockit).

5. Tincture of benzoin (Friar’s balsam).

6. Surgical blade (to cut catheter).

7. Drapes.

Procedure
1. First a “modified” superficial cervical plexus block was performed. With a 22G blunt needle, bent to 30 degrees at its midpoint, 5 mL local anaesthetic was infiltrated 1 cm posterior to the posterior border of sternomastoid at the midpoint between the C6 level and mastoid process. Subcutaneously a further 2.5 mL was infiltrated along the posterior border of sternomastoid between the aforementioned point and the C6 level. A further 2.5 mL was infiltrated along a similar line 30 degrees posterior to the sternomastoid posterior border. This block anaesthetises the skin to be penetrated by the catheter needle and the skin of the shoulder (via the supraclavicular nerves).

2. Next the patient was placed supine with the head turned to the contralateral side.

3. The catheter needle entry point was approximately 3 cm cephalad of the C6 level just posterior to the posterior border of the sternomastoid. Puncturing the external jugular vein was avoided.

4. The nerve stimulator was set to 0.8-1 mA with a pulse width of 0.1 ms and a frequency of 2 Hz.
5. The ultrasound probe was placed on neck at the C6/C7 vertebral level (=cricoid cartilage level) and the 1-2 most superficial elements of the brachial plexus were visualised. Probe orientation was in the axial plane and angled slightly towards the ipsilateral shoulder ("axial-oblique"). A picture in one's mind was made of the probable direction of the plexus. The roots appear hypoechoic between the surrounding hyperechoic scalene muscles. The medially located carotid artery and internal jugular vein represent a convenient initial landmark. Once visualised, the probe was moved 2-3 cm laterally: the roots are usually 2-3 cm lateral to the great vessels at approximately the same depth.

6. With a 10 mL dextrose filled syringe attached directly to the Tuohy needle, the needle was advanced until tissue displacement was observed just lateral to the most superficial brachial plexus root/trunk but superficial to the middle scalene muscle fascia.

7. The fascia overlying the middle scalene muscle was penetrated (always associated with a “pop” when using an 18G Tuohy needle – this requires a short, sharp deliberate needle movement once the needle tip is against the fascia).

8. The needle tip was angled medially until the appropriate root/trunk medial movement was observed and preferably also a deltoid (anterior shoulder movement), biceps or triceps motor response.

9. 10 mL dextrose 5% was injected aiming to observe hypoechoic injectate spread immediately lateral/under the most superficial root/trunk. With this needle alignment and an 18G Tuohy tip, intraneural needle placement is probably impossible, so the aim was to place the needle tip/injectate spread as close as possible to the target roots/trunks.
10. The probe was put down, and the needle stabilised in position by transferring the hand previously holding the probe to the needle hub. The syringe was disconnected and the catheter advanced at least 5 cm beyond the needle tip.

11. The needle was withdrawn over the catheter and the catheter immediately stabilised by pressing the catheter against skin with a finger at the skin entry point.

12. The catheter was withdrawn to 3 cm beyond the needle tip.

13. Medical cyanoacrylate was applied (e.g. dermabond®) to the skin entry site (aids secural and minimises local anaesthetic leakage).

14. Tincture of benzoin or "Skin-Prep®" was applied to a 2 cm radius of skin around catheter puncture site (improves dressing adhesion).

15. A Lockit® catheter fixation device was applied.

16. The catheter was protected from the surgical drapes using a small gauze and paper tape.

17. The catheter was dressed after surgery.

**Aseptic technique**

1. Sterile gloves.
2. Sterile catheter block tray.
3. Alcoholic chlorhexidine skin prep
4. Barrier drape
5. Probe wiped with disinfectant but no probe sheath.
6. “No touch technique” (non-dominant hand unsterile, dominant hand sterile).
**Modifications**

1. If sonographic visualisation of the appropriate roots/trunks proved difficult, scanning was distally/caudally to locate the supraclavicular brachial plexus (hyperechoic appearance superolateral to the subclavian artery), then retraced proximally to locate the diverging hypoechoic roots/trunks within the scalene muscles. If imaging was still difficult, ultrasound was used to approximate the needle tip position (approximately 2-3 cm lateral to carotid artery), the probe was dropped and then the aim was for a sustained deltoid/biceps/triceps/pectoralis motor response at between 0.2-0.5 mA.

2. If the catheter wouldn’t advance past the needle tip, the needle tip was slightly withdrawn (< 0.5 cm) while continuously attempting catheter advancement. If that failed, 10 mL was injectated through the needle prior to readvancing the catheter. In a small proportion of patients, the catheter simply wouldn’t advance despite the aforementioned manoeuvres. The needle was removed and another needle puncture point was used.

3. If inadvertent external jugular vein puncture occurred, 1-2 vials of medical cyanoacrylate were applied.

4. The long thoracic and dorsal scapular nerves lie approx. 1 cm deep to the skin and 0.7 cm lateral (posterior) to the plexus, directly in the path of a needle advanced from posterior. Contact with the nerves is unlikely when using the antrolateral approach.
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