Dissertation title:

Audit of peripheral neuromuscular stimulators at the hospitals staffed by the department of Anaesthesia and Perioperative Medicine at the University of Cape Town

by

Dr. Andries Thomas Joubert

Student no: **JBRAND009**

SUBMITTED TO THE UNIVERSITY OF CAPE TOWN

In partial fulfilment of the requirements for the degree

MMED in Anaesthesia

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

Date of submission: 18 November 2018

Supervisor: Dr. Owen Porrill

Specialist consultant

Department of Anaesthesia and Perioperative Medicine

University of Cape Town

University of Cape Town

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

University of Cape Town

Contents

Declaration

I herewith declare that this MMED minor dissertation is based on independent and original work (except where acknowledgements indicate otherwise) performed by myself with support from the named supervisor and co-investigators. Neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

The investigators have no conflicts of interest to declare.

Signed by candidate

Signature:_____ Date: 18 November 2018

Dr. Andries Thomas Joubert

Signed by candidate

Signature:_____ Date: 10 November 2018

Dr Owen Porrill (Supervisor)

Signed by candidate

Signature:_____ Date: 5th November 2018

Mr Justin Pead (Skin resistance circuit designer, Co-investigator)

Acknowledgements

The author would like to thank

- Dr. Owen Porrill for his input as supervisor
- Mr. Justin Pead for his help in designing and building the testing equipment.
- Emeritus Prof. Mike James for his insights provided regarding the audit design.
- Prof. Bruce Biccard for his contribution and insights regarding interpretation of the data.
- Prof. Ross Hofmeyr for his help with using the Endnote referencing software.
- Susan, Nicholas, Stefan and Benji for their sacrifice of much of our family time together while I was preparing this work.

Researchers' background:

Dr. Owen Porrill was a specialist anaesthetist who worked at Groote Schuur Hospital at the time of the audit data collection.

Dr. Andries Joubert worked as a registrar training in anaesthesia while conducting the research. He passed his fellowship in anaesthesiology exams (FCA) with the Colleges of Medicine of South Africa. The syllabus for the FCA includes a section on physics and measurement. An understanding of Ohm's Law also forms part of the syllabus.

Mr. Justin Pead is an electrical engineer at the Department of Electrical Engineering at the University of Cape Town.

Investigation site:

Department of Anaesthesia and Perioperative Medicine
Groote Schuur Hospital
Observatory
7925
Cape Town
South Africa

Abstract

Rationale: Inadequate monitoring of neuromuscular blockade (NMB) may result in worse patient outcomes, therefore NMB monitor availability is a minimum requirement for perioperative care according to the South African Society of Anaesthesiologists' (SASA) 2018 Practice Guidelines. The authors performed an audit of peripheral nerve stimulators (PNS) functionality and availability at their institution. In the researcher's experience the peripheral nerve stimulators (PNS) in use at his institution are not always easily available and some units malfunction at times. There are also not many units that can give a graphical display of a train of four ratio. This observation spurred the idea to do an audit on neuromuscular monitoring at this institution, by focusing on the availability and functionality of peripheral nerve stimulators.

Methods: After ethics approval was obtained, an audit was performed. In order to assess function, the PNS were attached to an electrical circuit with a skin equivalent resistance. The resultant current impulses generated using Train-of-Four (TOF) mode and Double Burst Stimulation modes (DBS) were recorded with a voltage scope meter and visually assessed that the TOF was present and appeared equal. PNS availability was assessed in theatre and recovery areas against the SASA guideline standard of nerve stimulator availability.

Results: Of the 65 PNS units assessed, 39 units were deemed to be dysfunctional and 26 units fully functional. The most frequent fault found (30 units) related to faulty or absent PNS electrode cables. Eight functional PNS units with TOF ratio display capability were found. The working PNS showed good inter-device peak voltage measurement correlation. Of the 59 areas identified where PNS should be easily available, only 37 areas met the PNS availability criteria suggested in the SASA guidelines.

Discussion: This audit revealed that overall there were not enough functional PNS available at the institution, when measured against the SASA standard. The clinical significance of these findings would vary depending on the actual usage rate of NMBs in the area concerned. The logistics of tracking a PNS unit's location also turns out to be paramount in situations where nerve stimulators have to be shared between areas. From a technical point of view, the working PNS were found to be very consistent in their delivered voltage bursts. Future use of the first generation PNS (without TOF ratio display) will continue to decline, because of their inability to monitor neuromuscular function by modern standards, and the poor availability of replacement parts for models no longer manufactured. The cost and availability of repairs and cable replacements should be factored into the decision when acquiring more PNS units.

Conclusion: This audit highlighted the need for more new generation PNS with TOF-ratio-display-ability to align the institution with the recommendations from SASA standards and the anaesthetic literature. It also highlighted the accuracy and consistency of delivered current bursts by the working PNS devices.

Glossary of terms used:

DBS - Double Burst Stimulation

NMB - Neuromuscular blockade

PACU – Post anaesthesia care unit

PNS - Peripheral nerve stimulators

PNS-zones – Areas where peripheral stimulator availability is needed according to South African Society of Anaesthesiologists' practice guidelines

PORC – Post-operative residual curarization

POPC - Post-operative pulmonary complications

RCWMCH – Red Cross War Memorial Children's Hospital

RNMB - Residual neuromuscular blockade

SASA - South African Society of Anaesthesiologists

TOF - Train-of-four peripheral nerve stimulator mode

PART A – STUDY PROTOCOL

Introduction (study protocol)

Monitoring of neuromuscular blockade (NMB) is considered to be a minimum requirement for providing an adequate standard of care in perioperative medicine and anaesthesia according to the South African Society of Anaesthesiologists' (SASA) guidelines.

The investigator previously found that some of the nerve stimulators in theatre did not seem to function reliably and that they were not always easily available in the theatres and recovery rooms. This observation sparked the idea to do an audit on neuromuscular monitoring at the hospitals staffed by the University of Cape Town's Department of Anaesthesia and Perioperative Medicine, by focusing on the availability and functionality of our peripheral nerve stimulators.

Background (study protocol)

History of NMB monitoring

The first muscle relaxant, d-tubocurarine, was introduced into anaesthetic practice in 1942 by Harold Griffith (Gillies & Wynands, 1985). As early as 1954, it was noted that patients who had received d-tubocurarine had a six fold higher mortality than patients who had not received the drug (Beecher & Todd, 1954). Use of a nerve stimulator to monitor the action of muscle relaxants was suggested in 1958. (Christie & Churchill-Davidson, 1958)

Post-operative residual curarization (PORC) refers to the situation where skeletal muscle paralysis has not been adequately reversed at the end of anaesthesia. This was first recognized in the 1960's in patients with renal function impairment where the clearance of NMB's was reduced (Khirwadkar & Hunter, 2012).

PORC was, in extreme cases, associated with mechanical respiratory failure due to respiratory muscle weakness. By 1971 it was suggested that the level of PORC could be assessed by using the train-of-four twitch technique (Ali, Utting & Gray, 1971). This involved the use of a peripheral nerve stimulator device to measure the ratio of the amplitudes of the fourth to the first twitch. A ratio of >0.7 was considered to indicate adequate recovery before endotracheal tube removal, given that it correlated well with the clinical parameters of head lift >5 seconds, hand grip strength, tongue protrusion and a vital capacity of >15ml/kg. This standard was used for many years thereafter.

In 1997 (Berg et al., 1997) a significant post-operative pulmonary complication rate was reported if the train of four value was <0.7 in the immediate post-operative period after pancuronium administration.

Around the same time it was demonstrated (Eriksson et al., 1997), using a small sample of volunteers, that pharyngeal tone approaches normal values when a concurrent train of four test (TOF), using the adductor pollicis muscle, demonstrates a ratio of more than 0.9. This cast doubt on the validity of the previously held threshold (a TOF ratio >0.7) being adequate for endotracheal tube removal. Subsequently a TOF ratio of >0.9 became the accepted standard to achieve before endotracheal tube removal (ETR).

In an editorial on PORC and evidence based medicine (Viby-Mogensen, 2000), it is stated that failure to antagonize vecuronium induced neuromuscular block will result in an unacceptably high incidence of patients with clinically significant PORC in the recovery room. It is also said that one cannot detect and confirm clinically significant PORC by tactile or visual assessment of peripheral nerve stimulation response. Even experienced observers cannot feel fade if the TOF ratio is above 0.4 (Viby-Mogensen et al., 1985) (Saddler et al., 1990). Mechanomyography, electromyography and acceleromyography provides more objective assessment of PORC. (Viby-Mogenson, 2000)

PORC has been associated with impaired respiratory physiology and an increase in post-operative complications, including:

- Critical respiratory events in the post anaesthetic care unit. (Murphy, G. S. et al., 2008)
    - In this study 0.8% of patients developed critical respiratory events (61 of 7459 patients). A subset (42) of the 61 patients were successfully matched with controls and analysed further. The most common complications found were hypoxaemia and upper airway obstruction. The TOF ratios, mean and (±standard deviation), in the critical respiratory event group were 0.62 (±0.2), and in the control patients the TOF ratios were 0.98 (±0.07).

- Impaired respiratory muscle function (Kumar et al., 2012)
    - This study demonstrated a 21% reduction in forced vital capacity and a 19% reduction in peak expiratory flow rate in the early post-operative period in patients with residual neuromuscular blockade (RNMB) when compared to the patients who had no RNMB. These patients with RNMB received vecuronium, atracurium or rocuronium intra-operatively, and had a train-of-four-ratio of less than 0.9 at the time of testing.

- Post-operative hypoxaemia (Sauer et al., 2011)
    - In this randomized prospective placebo controlled trial of 114 patients, patients received either neostigmine 20mcg/kg or placebo at the end of general anaesthesia that included rocuronium for neuromuscular blockade. Endotracheal tube removal was performed after no fade was detected on qualitative train-of-four stimulation and double-burst stimulation in the placebo group, and at a TOF ratio of 1.0 for the neostigmine group. Failure to reverse minimal PORC was associated with hypoxaemia in the post anaesthesia care unit (PACU), occurring about twice as often in the placebo group (29 occurrences) vs. the neostigmine group (16 occurrences)

- Increased risk of post-operative pulmonary complication.(McLean et al., 2015)

- Impaired clinical recovery (Murphy, G. S. et al., 2013)

In South Africa the following recommendations are made by the South African Society of Anaesthesiologists with regards to neuromuscular blockade monitoring and reversal (Kluyts et al., 2018)

- A peripheral nerve stimulator to monitor neuromuscular function is considered an essential item needed as a minimum requirement for the safe conduct of anaesthesia in any hospital.
- Peripheral nerve stimulators should be immediately available in theatre and in the recovery room.
- Patients should have recovered from neuromuscular blockade prior to handover to staff from the theatre recovery room, and thus also prior to discharge from the anaesthetist's care.

Methodology overview:

Methodology

- Study design
    - An audit of peripheral nerve stimulator (PNS) availability and function.
    - Comparison of our PNS equipment availability to the recommended standard.
- Characteristics of the study population
    - No human subjects will be used
- Recruitment and enrolment
    - No human subjects will be used
- Location of the research
    - This audit will be performed at the following locations: Groote Schuur Hospital, Mowbray Maternity Hospital, Red Cross War Memorial Hospital, New Somerset Hospital, Maitland Cottage Hospital and Valkenberg Hospital. It may also be performed in the operating theatres, Technical Services workshop or departments of anaesthesia. It may also be performed in the Electrical Engineering laboratory on UCT upper campus.
- Evaluator inclusion criteria
    - Evaluators need to be associated with the University of Cape Town or be current or past employees of the involved hospitals in one of the following roles:
        - Member of the Anaesthesia department, past or present as anaesthetists, or be
        - Employees of the Technical Support Services engineers at Groote Schuur Hospital or of the
        - Department of Electrical Engineering at the University of Cape Town

Research procedures and data collection methods

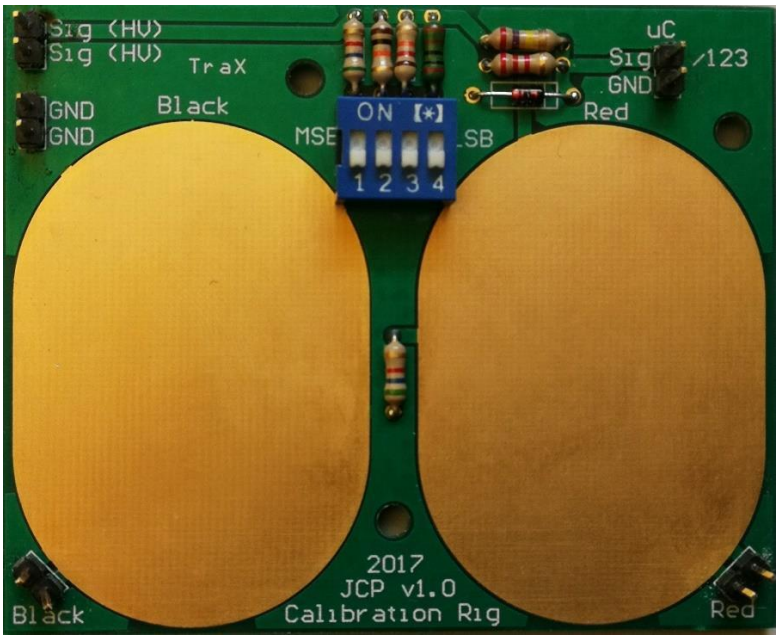

Figure 1, Latest version of resistance circuit for PNS testing

The study plan is to document the number of peripheral nerve stimulators that are available at the hospitals which are serviced by the Groote Schuur Hospital Department of Anaesthesia in the theatre and recovery areas. A unique identification number will be assigned to each nerve stimulator if they are not already labelled in such a way. Thereafter, the functionality of these PNS will be tested by confirming the presence of the electrical current bursts delivered during the TOF mode.

In order to perform this measurement, the PNS will be connected to a skin-equivalent-resistance circuit e.g. in figure 1, and the voltage produced by the electrical current bursts set at 60 mA will be measured over the resistor. A test circuit resistance of between 1 and 4.5 kOhm is described in testing manuals. It is planned to utilise a 2.47 kOhm resistance setting. Thereafter a graphic display of the voltage/time wave loop of the TOF current burst will be recorded in electronic / photographic format. The PNS's will be classified as either functional or faulty depending on the results of this test. The TOF peak voltage graph will be visually assessed for uniformness and deemed functional if the recorded voltage peaks appear equal in height. The voltage measurements will be recorded. A description of any faults found will also be documented. The type of faults found with specific brands of nerve stimulators may provide valuable information for the decision making process for future acquisitions of nerve stimulators. This procedure will then be repeated for each peripheral nerve stimulator tested.

These findings will then be compared against the recommendation for PNS availability for neuromuscular monitoring from SASA to see if the recommended standard is met.

Defining "adequate availability" requires some interpretation. For the purpose of this study, value will be placed on having a "known specific location" for the device. If the device is kept in a specific labelled place just outside theatre, it will be defined as adequately available. On the other hand, if a unit is shared between multiple theatres and is not kept in a defined location within those theatres, it will be deemed "not easily available".

If availability of functional nerve stimulators falls short of the recommended standard, the number

of nerve stimulators needed and the areas of need will be identified and recorded.

The results of this audit will form the basis for future annual audits. The audit findings will be made available to the clinical engineering workshops and clinical managers.

In preliminary discussions with the technical team at Groote Schuur's Clinical Engineering department, the investigator realised that the department of Clinical Engineering at Groote Schuur Hospital does not have access to a modern scope meter. Modern scope meters can accurately record, store and display the TOF recordings in a format that is downloadable for future reference. This is already an important finding for this audit. The investigator subsequently arranged with engineers from the UCT department of electrical engineering to utilise their scope meters and expertise in performing these audit recordings.

Data safety and monitoring

- The data will be stored on the principal and co-investigators' computers and/or Dropbox accounts, which are password protected.

Data analysis

- Statistical analysis will be limited to analysis relevant to performing audits.
- The tested peripheral nerve stimulators will be classified as functional or not. These evaluations will be recorded on an excel spreadsheet.
- The data will be reported as proportions.

- Describe mechanisms to ensure the accuracy and reliability of the data collected.

  A high quality scope meter with graphical display will be used. An engineer from the department of Electrical Engineering at the University of Cape Town (UCT) will be involved with the design of the skin resistance circuit board for the measurements taken.

Description of risks and benefits

There will be no risks to patients from the performance of this audit. A replacement PNS monitor will be made available in the relevant clinical areas from which PNS are removed while the devices are being tested. This precaution is taken to ensure PNS availability for clinical work within the areas audited. PNS that are discovered to be faulty on evaluation will be given to the theatre clinical technicians, who will see to the further evaluation and repair or replacement of the affected units.

Potential benefits

Ensuring that functioning PNS are available in all the relevant areas will likely increase their usage. This will lead to closer monitoring of, prevention and better treatment of, PORC (post-operative residual curarization). Prevention and treatment of PORC should result in improved patient morbidity and mortality. It could also prevent the psychological trauma that a patient with PORC may experience.

The audit findings will be made available to the medical engineers and clinical managers. The data can then be used as the basis of an annual repetition of this audit. This will become a powerful tool, contributing to the process of keeping our fleet of PNS adequate in numbers and in a working

condition.

Informed consent process

Informed consent is not needed from patients.

Reimbursement for participation

No reimbursement given

Audit findings

In total 59 “areas where a peripheral stimulator should be easily available” (PNS-zones) were identified. These areas consisted of 48 operating theatre or procedural areas (e.g. Catheterisation Laboratory, ECT Suite) and 11 recovery areas.

Of these areas, 37 PNS-zones were deemed to meet the PNS availability criteria suggested in the SASA guidelines. When looking at the data in more detail, one would see that a PNS unit was found to be physically present in 21 areas, easily available in 19 areas and not easily available in 19 areas. The 3 areas that resulted in the discrepancy between the 40 PNS-zones one would expect to be deemed appropriate and the 37 PNS-zones actually deemed appropriate are as follows: At a PNS-zone at RCWMCH a unit was found to be present and available in the Catheterisation Laboratory, but the battery was flat. The unit was thus available but overall it did not meet the SASA standard. Along the same lines, the PNS-unit found at Maitland Cottage hospital for both their theatre area and recovery area was available but faulty with severely corroded battery contact points (Neuromuscular blocking drugs are rarely used at this location for paediatric orthopaedic surgery). Those 3 areas were thus also deemed not to have a PNS available to the SASA standard. The 16 areas remaining included the following: No PNS unit was available at Valkenberg Hospital where anaesthesia for electro-convulsive therapy is performed. In the event of encountering a suxemethonium apnoea, a nerve stimulator would have to be borrowed from Groote Schuur Hospital which is 1.7km away. At Groote Schuur Hospital in the C6 Radiation Oncology theatre there was no PNS unit found, with the closest PNS unit found in the C8 interventional radiology suite (although this was not known in C6), or alternatively in the main theatre unit a couple of hundred metres away on a different floor level. At Groote Schuur Hospital a further five theatre blocks had one nerve stimulator per block, shared between multiple theatres but with no standardised base location. At Red Cross Hospital the trauma unit theatre and day case theatres on ground floor level did not have a PNS present, with the closest units available upstairs in the main theatre complex.

As previously mentioned, defining “adequate availability” requires some interpretation. For the purpose of this study, value was placed on having a “known specific location” for the device and the perceived need for the device intra-operatively. If the device was kept in a specific labelled place just outside theatre, it would be defined as adequately available. On the other hand, if a unit was shared between 4 theatres and was kept in a random location somewhere in those theatres it was deemed “not easily available”. At RCWMCH 3 units were shared between 7 theatres, but with more units further away in the technicians’ office. The much lower usage of NDMR in the paediatric population compared to adult patients and the fact that the PNS-units were kept in well labelled locations, led us to believe that these PNS-zones were adequately covered. For argument sake, if the same ratio was found in a block of eye and neurosurgery theatres where most cases in each theatre would need PNMB

monitoring, we would have deemed those PNS-zones as “PNS not easily available.”

In terms of testing individual devices, the aim was to find all the PNS units in clinical use and in the facilities’ storage areas. 65 PNS units were thus found and assessed. This included the units in the clinical areas, (but also the units found in the equipment rooms or clinical technicians rooms of the theatres as directed by the relevant technicians.) The different makes and models are depicted in the pie chart below. Of these assessed units 39 were deemed to be dysfunctional and the remaining 26 units were deemed fully functional.

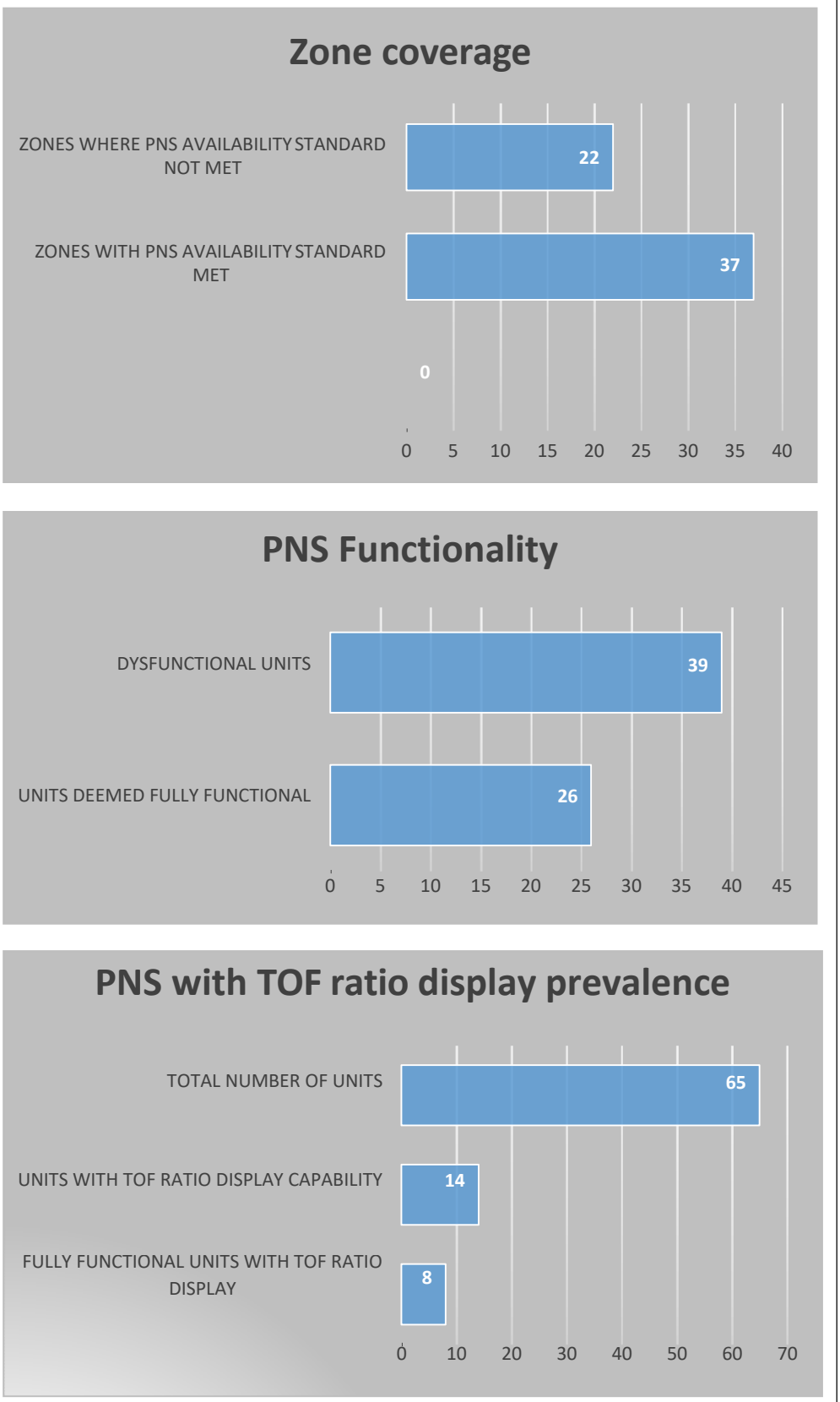

Figure 2: Summary of Audit results

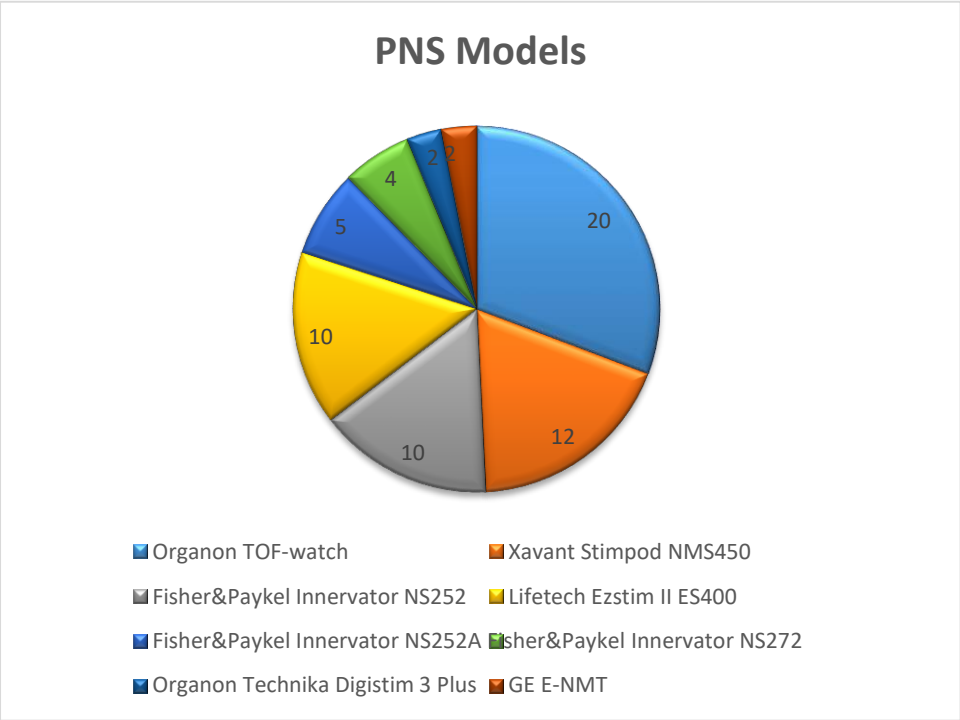

Figure 3: PNS makes and models encountered

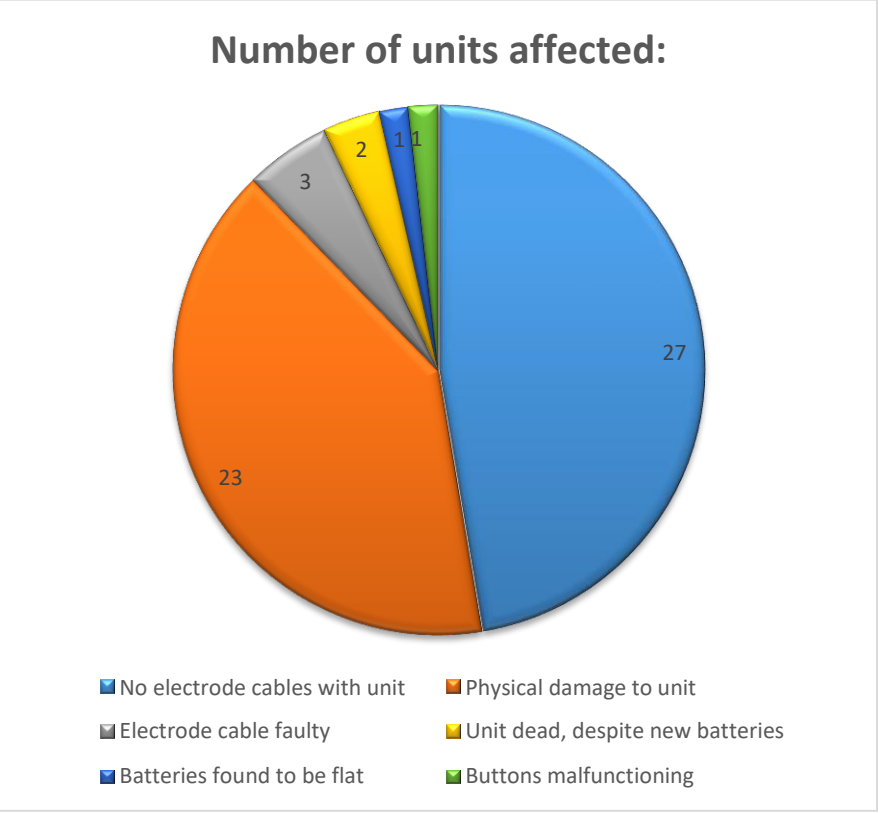

Figure 4: Faults found with PNS

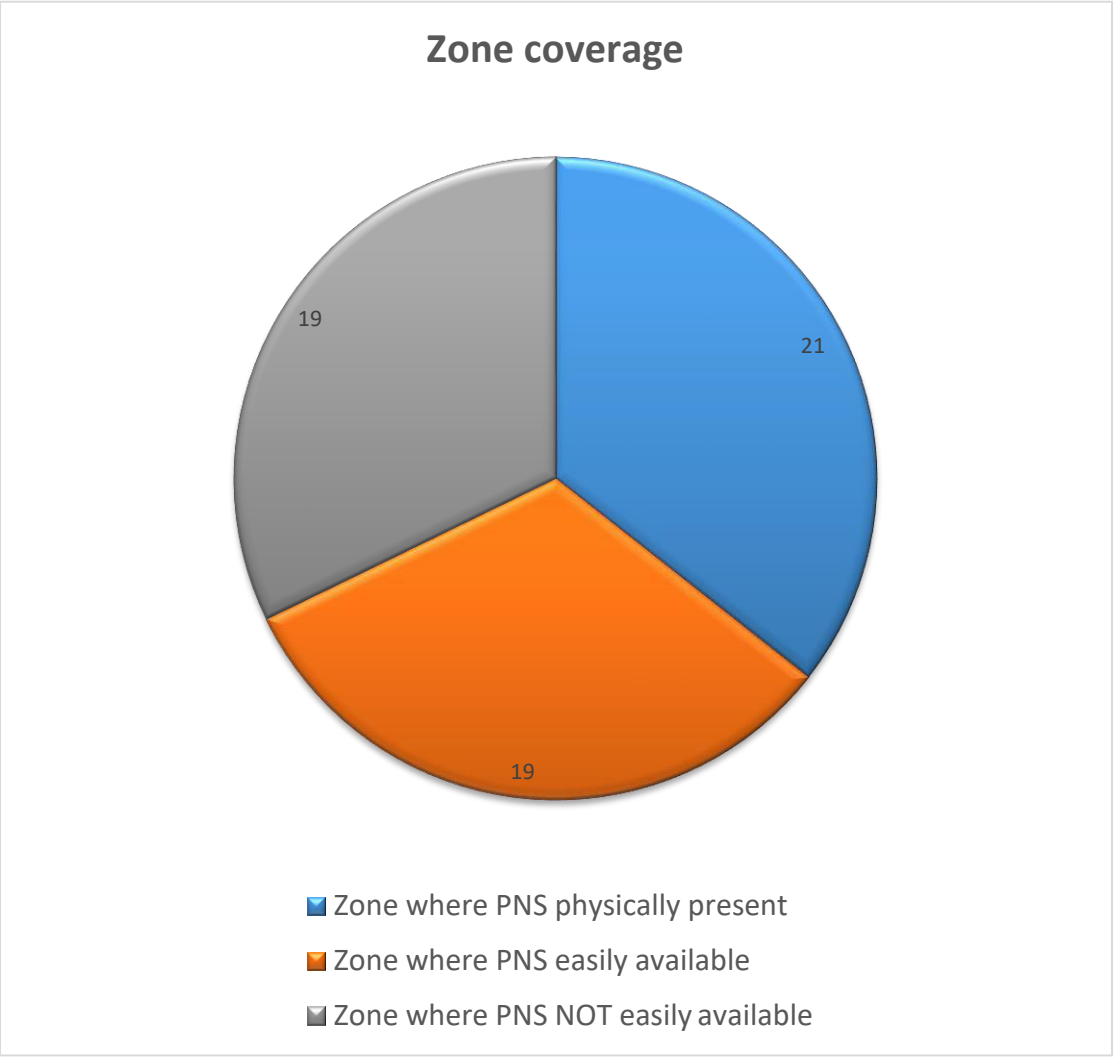

Figure 5: Zone coverage further detailed (PNS = Peripheral nerve stimulator)

The faults found with the units were as follows:

- Absence of electrode cables was found in 27 units. These cables were either lost during clinical use, or discarded by technicians when they found the cables to be malfunctioning. Given that many of the units were no longer manufactured or supported by their manufacturers, these cables could no longer be ordered from them.
  Only 3 units were found to have faulty cables, but it may well be the most frequent malfunction found on the peripheral nerve stimulators, if one takes into account that a large portion of the "missing" cables may have originated with cable malfunction.
- Physical damage was found in 23 of the units. The plastic housings of many units were fractured, presumably from dropping them on a hard surface during clinical use. The battery covers were missing from many units, which often resulted in unreliable contact between the batteries and electrodes. The batteries also tend to fall out easily in these scenarios, so many units were found with bits of sticky tape stuck on the unit in lieu of the battery cover to keep the batteries in place.
- Two units would not switch on despite a change of batteries.
- Batteries were found to be flat in 1 device in clinical use.
- In one device the DBS button would not trigger a response.

The overall consistency of the delivered voltage spikes is noteworthy. In total 61 units were able to give scope meter recordings, although this was often performed with a set of "loan cables" where the units' original cables were damaged or missing. This translated into 244 peak values for TOF voltage peak measurements. An assessment was made of the mean and standard deviation of the peak values measured with the scope meter. In terms of this assessment all 61 the peak burst voltages of the first voltage impulse recorded was grouped together (PBV1), and likewise the groups of data thus classified for impulse groups 2, 3 and 4. The skewness and kurtosis suggested normal distribution of the data and there was no sign change from baseline readings with paired t-tests.

Peak burst voltage	Skewness	Kurtosis	Mean	(Standard Deviation)
PBV1	-0,906	0,163	144,79	(3,647)
PBV2	-0,797	-0,29	144,66	(3,526)
PBV3	-0,613	-0,39	144,64	(3,665)
PBV4	-0,778	-0,138	144,59	(3,644)

Table 1: Assessment of Peak Voltage Data (PBV = Peak burst voltage group)

Data Pair	Mean	Standard deviation	*p*- value
Pair 1: PBV1 - PBV2	0,131	0,866	0,241
Pair 2: PBV1 - PBV3	0,148	0,98	0,244
Pair 3: PBV1 - PBV4	0,197	1,166	0,193

Table 2: Data from paired samples test (PBV = Peak burst voltage group)

In terms of the 7 units that did not deliver fully appropriate traces, the following is noted: Two Fisher and Paykel Innervator 252 units (labelled GSHPNS002 and GSHPNS003) gave "error 26" messages with no current bursts delivered. This error code was not listed with the units' instruction manual. One Lifetech EZ stim unit (NSHPNS007) was found to have a faulty cable. Units that could not be switched on could obviously not provide test readings (including the units labelled GSHPNS011, MCHPNS001). In one unit the DBS button was broken and no DBS recording could be made (labelled GSHPNS012). In one unit the DBS pulse conduction was not reliable (labelled GSHPNS035).

In a few units a current of 60mA could not be confirmed: One unit (labelled GSHPNS005) only had "level 1-8" on the current dial. At level 6&8 the voltages generated suggested currents in the ballpark of 60mA. In an older model Organon Technika Digistim 3 Plus (labelled GSHPNS038) the highest current setting was around 55 mA.

TOF-ratio display capability was only represented in 14 of the units. Of these 14 units only 8 were fully functional.

Discussion of results

This audit revealed that overall there were not enough functional PNS available at the institution, when measured against the SASA standard. If you apply the highest standard, there were 8 functioning TOF-R capable peripheral nerve stimulators available to cover 59 areas. If we add the handheld devices without TOF-Ratio capability, 37 areas out of the 59 (63%) are covered. These assessments were in keeping with the author's experience of PNS availability while working in clinical practice at this institution, where it was often difficult to locate a PNS at short notice.

The clinical significance of the shortage of PNS units varies depending on the actual need for PNMB monitoring in the area concerned. Despite this, the SASA practice guidelines do not make concessions for areas where PNS are less likely to be used and describe this as an essential monitor that needs to be immediately available. Thus, a lower likelihood of needing the device should not be used as an excuse for inadequate coverage. Despite the standard recommended by the SASA guidelines, for some hospitals the equipment budget may not lend itself to the purchasing of a PNS unit for each PNS-zone. In this real life financially constrained setting, it makes sense for theatre equipment managers to at least first ensure adequate PNS availability in the areas where it is most often needed while working towards adequate coverage.

The logistics of tracking a PNS unit's location is very important in situations where nerve stimulators have to be shared between locations. In areas where the nerve stimulator may be used in more than 2 locations, immediate availability of the device is lost once it is in use. In order to facilitate locating the device, the unit has to be stored in a specific named "base" location, and the whereabouts of the device must be documented once it is removed. This could be with the use of a simple notebook kept at the "base location", or by online systems such as a device location Whatsapp group shared between users of the device.

From a technical point of view the working PNS were found to be very consistent in their delivered current bursts. This novel information is important when troubleshooting a peripheral neuromuscular monitoring unit. Looking at our data set there would be a high likelihood of the electrode cable being the problem. Another possible relevant factor that was not explored in this study is the likelihood of skin resistance contributing to measurement variance, since skin resistance may vary with skin thickness, moisture content and temporal association with prior electrical stimulation. It has also been known for a long time that skin impedance decreases when exposed to higher intensity currents. (Stephens, 1963)

There are problems with the older PNS units, which comprise the majority of units in the institution:

- The inability of these devices to exclude incomplete return of neuromuscular function by modern standards make them all but obsolete. However, some value remains in the ability to demonstrate very deep NMB levels where fade is detectable clinically and to demonstrate where a TOF count less than 4 is present.

- The lack of manufacturer support for many of the first generation units in use at our institution shortens the foreseeable lifespan of the remaining functional units. Most of these units will become unusable at some point when they break down and need maintenance or repairs. Many of these PNS models are no longer manufactured.

It can be inferred that it is unlikely that NMB monitoring is performed to the current accepted standard of a "TOF-R of > 0.9" if we have only 8 such devices available to cover 59 PNS zones at our institution.

Implications for the institution from the audit findings

1. A modern scope meter with the ability to store and download test data in a downloadable format should be procured for the clinical engineering department, both to facilitate their day to day functioning, and also to assist future audit projects of electronic devices.

2. At the time of this write-up a further 8 E-NMT units have already been delivered to GSH hospital, and the plan is to continue acquiring more TOF-R capable units as the budget allows.

3. An awareness and educational campaign needs to be launched within the department of anaesthesia to educate and motivate anaesthetists to:

    a. Utilize appropriate NMB monitoring, and
    b. Advocate for the provision of adequate numbers of PNS-devices.

4. The cost and availability of repairs and cable replacements should be factored into the decision when acquiring more PNS units. The machine mounted PNS units retail for more than 3 times the price of the handheld devices. It is hypothesized that the machine mounted units may last longer due to:
    - Higher quality electrode cabling
    - Less handling of the machine mounted units, resulting in
        - A smaller chance of being dropped and broken
        - Less winding up / coiling of the electrode cables which may prolong cable life.

5. The cost-benefit ratio of these two current options (E-NMT vs. Xavant Stimpod NMS450) should be further audited while in use to help guide future acquisitions of these devices.

Audit conclusion:

This audit highlighted the need for more new generation PNS with TOF-ratio-display-ability at the hospitals staffed by the department of Anaesthesia and Perioperative Medicine at the University of Cape Town, to be aligned with the recommendations from the anaesthetic literature. It also highlighted the need for an improved sharing system in those areas were PNS: clinical area ratio is <1. This research also highlighted the accuracy and consistency of delivered current bursts by the working PNS devices. There are opportunities for further research in evaluating the contribution of skin related factors on the conduction of current bursts with PNS's.

PART B - STRUCTURED LITERATURE REVIEW:

Introduction and objectives (literature review)

Monitoring of neuromuscular blockade (NMB) is considered to be a minimum requirement for providing an adequate standard of care in perioperative medicine and anaesthesia according to the South African Society of Anaesthesiologists' (SASA) guidelines.

The investigator previously found that some of the nerve stimulators in theatre did not seem to function reliably and that they were not always easily available in the theatres and recovery rooms. This observation spurred the idea to do an audit on neuromuscular monitoring at the hospitals staffed by the University of Cape Town's department of anaesthesia, by focusing on the availability and functionality of our peripheral nerve stimulators.

This literature review aims to highlight the evidence base for the current guidelines on neuromuscular monitoring as published by SASA. The investigators did not come across any similar audits during their literature search.

Literature search strategy

The literature search was performed using 3 databases, namely PubMed, Scopus and Africawide. The search results were limited to English and Afrikaans studies and animal studies were also excluded. A number of further exclusion keywords were added to the search terms to limit the amount of irrelevant material generated, which was identified in trial runs of the search.

The particular terms used were as follows:

((((((((((((((Postoperative residual curarization[Title] OR postoperative neuromuscular blockade[Title]) OR postoperative neuromuscular function[Title]) OR Residual paralysis[Title]) OR Partial paralysis[Title]) OR Partial neuromuscular block[Title]) OR (Reversal[All Fields] AND neuromuscular blockade[Title])) OR (Peripheral[All Fields] AND neuromuscular monitor[Title])) OR Peripheral nerve stimulator[Title]) OR TOF ratio[Title]) OR Train of four[Title]) OR Double burst stimulation[Title]) NOT deep brain stimulation[Title/Abstract]) NOT Myasthenia[Title]) NOT Infection[Title]) NOT Blood[Title]) NOT Leucocyte[Title]) NOT Intoxication [Title]

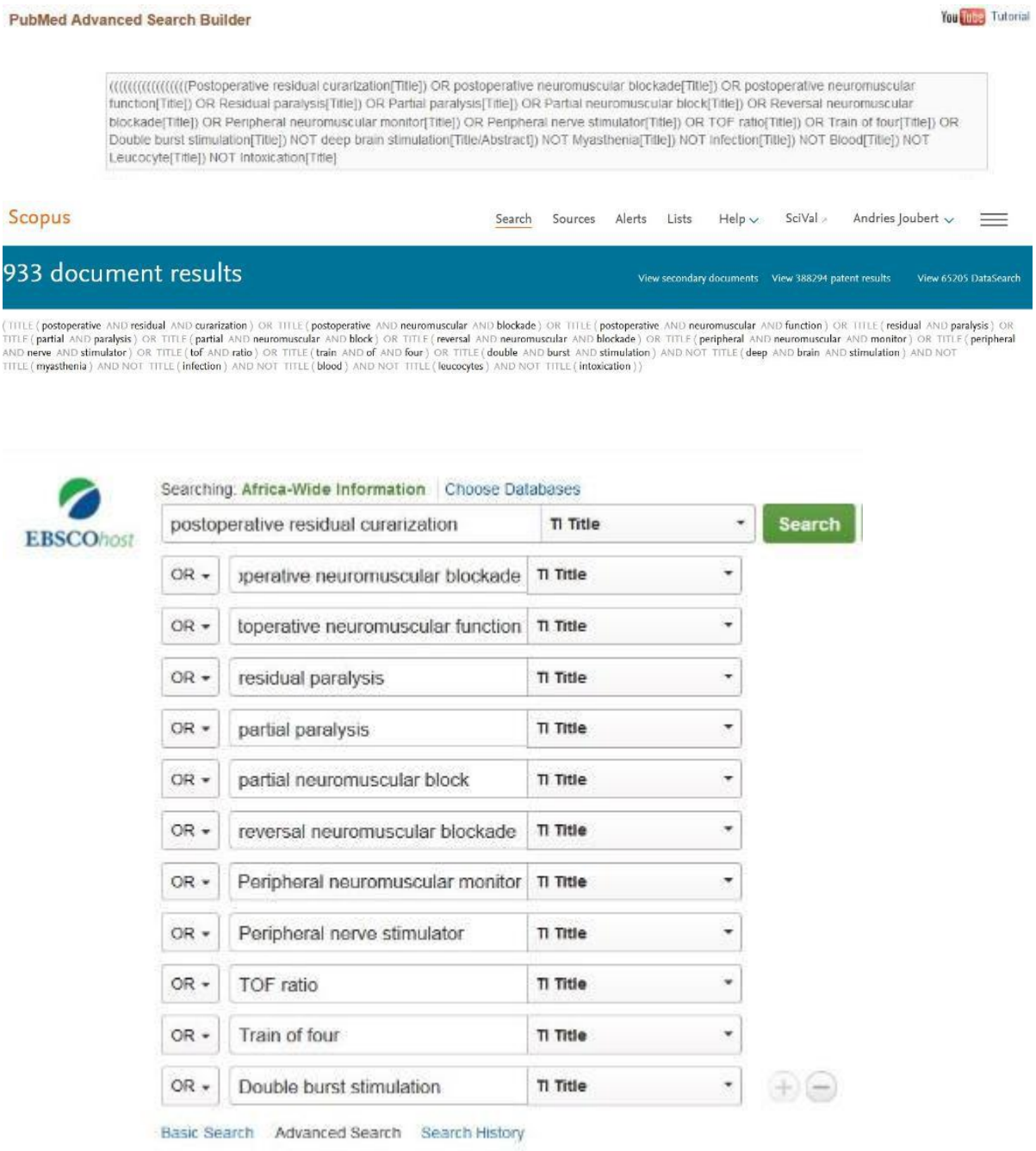

Figure 6: Screenshots demonstrating search terms on PubMed, Scopus and Africawide

From the initial search results, journal titles were screened and accepted or discarded depending on the perceived relevance from the journal title. The accepted/selected articles were further investigated for their relevance in contributing to the body of knowledge regarding Post-operative residual curarization (PORC) and peripheral nerve stimulator use. In the PubMed search the initial search produced more than 4600 hits. From these 152 articles were thought to have some relevance to the literature review topic and 26 review articles were found with some relevance to the research topic. From the Scopus database search 205 articles was identified with some relevance to the research topic. In the Africawide search 8 articles with some relevance to the research topic were found. Whilst reading through some of the journal articles found, further articles of relevance were identified from the article's reference lists and those were further evaluated as was deemed necessary. In the final publication-ready article produced, 30 of these sources found were used as references. Of note, the investigators did not come across any similar audits during their literatures search.

Background (literature review)

History and practice of NMB monitoring

The first muscle relaxant, d-tubocurarine, was introduced into anaesthetic practice in 1942 by Harold Griffith (Gillies & Wynands, 1985). As early as 1954, it was noted that patients who had received d-tubocurarine had a six fold higher mortality than patients who had not received the drug (Beecher & Todd, 1954).

The situation where skeletal muscle paralysis has not been adequately reversed at the end of anaesthesia has been described as post-operative residual curarization (PORC).
This was first recognized in the 1960's in patients with renal function impairment where the clearance of NMB's was reduced. (Khirwadkar & Hunter, 2012)

In 1958 the use of a nerve stimulator to monitor the action of muscle relaxants was suggested (Christie & Churchill-Davidson, 1958), but for many years thereafter only clinical parameters were used to infer the absence of clinically significant PORC in the recovery area, including:

- Head lift more than 5 seconds
- Tongue protrusion
- Vital capacity >15ml/kg (Brand et al., 1977)
- Hand grip strength (Russell & Serle, 1987);

PORC was, in extreme cases, associated with mechanical respiratory failure due to respiratory muscle weakness. By 1971 it was suggested that the level of PORC could be assessed by using the train-of-four twitch technique (TOF) (Ali, Utting & Gray, 1971). This involved the use of a peripheral nerve stimulator device (PNS) to measure the ratio of the amplitudes of the fourth to the first twitch. A ratio of >0.7 was considered to indicate adequate recovery before endotracheal tube removal, given that it correlated well with the clinical parameters of head lift for more than 5 seconds, hand grip strength, tongue protrusion and a vital capacity of more than 15ml/kg. This standard was used for many years thereafter. Years later (Berg et al., 1997) a significant post-operative pulmonary complication rate was reported if the train of four value was <0.7 in the immediate post-operative period after pancuronium administration.

Around the same time it was demonstrated (Eriksson et al., 1997), using a small sample of volunteers, that pharyngeal tone approaches normal values when a concurrent train of four test (TOF) of the adductor pollicis muscle demonstrates a ratio of more than 0.9. This cast doubt on the validity of the previously held threshold of a TOF ratio > 0.7 being adequate for endotracheal tube removal. Subsequently a TOF ratio of > 0.9 became the accepted standard to achieve before endotracheal tube removal (ETR).

Another concern is related to the inability to detect fade by clinical examination during TOF delivery. It is said that one cannot detect and confirm clinically significant PORC by tactile or visual assessment of the peripheral nerve stimulation response. Even experienced observers cannot feel fade if the TOF ratio is above 0.4 (Viby-Mogensen et al., 1985) (Saddler et al., 1990). Mechanomyography, electromyography and acceleromyography are alternative measurement techniques that provide more objective assessments of PORC. (Viby-Mogenson, 2000)

Recent studies have shown that the TOF ratio is slightly overestimated when it is determined using acceleromyography. Thus it is questioned whether a TOF ratio of 1.0 should rather be aimed for in order to infer an effective TOF ratio more than 0.9. (Capron et al., 2004, Kopman, A. F., Klewicka & Neuman, 2002)

Clinical significance

It is well described in the literature that PORC leads to increased post-operative complications, including:

- Airway and breathing compromise
- An unpleasant patient experience (Murphy, G. S. et al., 2013) (Murphy, Glenn S et al., 2003) and
- Decreased theatre efficiency

In the South African context two studies reported incidences of 29% and 43% respectively for PORC with TOF <0.9. (Invernizzi & Gopalan, 2016, Nell et al., 2004) Elsewhere a meta-analysis in 2007 inferred that PORC is common, with an estimated TOF < 0.9 incidence rate of about 41% in patients who received intermediate acting NMB's. (Naguib, Kopman & Ensor, 2007)

Airway and breathing compromise:

- Increased episodes of aspiration are described. A five times higher rate of laryngeal penetration was described in a study of healthy volunteers with partial neuromuscular paralysis given an infusion of atracurium with concomitant monitoring of the TOF ratio and video radiography of the larynx during swallowing. (Sundman et al., 2000)

- PORC is associated with an increased risk of post-operative pulmonary complications (POPC), defined as: respiratory failure, pulmonary oedema, tracheal re-intubation and pneumonia. Data from a retrospective analysis of hospital records of 48499 patients showed an association between higher doses of neuromuscular blocking drugs and POPC. (McLean et al., 2015)

- More episodes of upper airway obstruction during transport to the PACU were observed in patients managed with conventional qualitative TOF assessment compared to similar patients managed with acceleromyographic quantitative TOF monitoring. This data was from a study

of 179 patients, comparing the ability of qualitative and quantitative assessment of neuromuscular function to help detect (and indirectly reduce) the occurrence of PORC after endotracheal tube removal. In the conventional TOF group the mean TOF ratio was lower when checked in PACU for the study. It was found that 0% of patients in the acceleromyographic group needed manoeuvres to open their airway during transport to PACU, compared with 11% of patients in the conventional TOF group. (Murphy, Glenn S et al., 2008)

- Post-operative hypoxaemia (Sauer et al., 2011). In this randomized prospective placebo controlled trial of 114 patients, patients received either neostigmine 20 mcg/kg or placebo at the end of general anaesthesia that included rocuronium for neuromuscular blockade. Endotracheal tube removal was performed after no fade was detected on qualitative train-of-four stimulation and double-burst stimulation in the placebo group, and at a TOF ratio of 1.0 for the neostigmine group. Failure to reverse minimal PORC was associated with hypoxaemia in the post anaesthesia care unit (PACU), occurring about twice as often in the no-neostigmine placebo group (29 occurrences) vs. the neostigmine group (16 occurrences)

- Critical respiratory events in the post anaesthetic care unit (Murphy, G. S. et al., 2008). In this study 0.8% of patients developed critical respiratory events (61 of 7459 patients). A subset (42) of the 61 patients were successfully matched with controls and analysed further. The most common complications found were hypoxaemia and upper airway obstruction. The TOF ratios, mean and (±standard deviation), in the critical respiratory event group were 0.62 (±0.2), and in the control patients the TOF ratios were 0.98 (±0.07).

- Impaired respiratory muscle function (Kumar et al., 2012). This study demonstrated a 21% reduction in forced vital capacity and a 19% reduction in peak expiratory flow rate in the early post-operative period in patients with residual neuromuscular blockade (RNMB) when compared to the patients who had no RNMB. These patients with RNMB received vecuronium, atracurium or rocuronium intra-operatively, and had a train-of-four-ratio of less than 0.9 at the time of testing.

An unpleasant experience:

- In one study, 149 patients arriving in PACU were divided into two groups based on a measured TOF ratio of < 0.9 and ≥ 0.9 respectively. (Murphy, G. S. et al., 2013) The 48 patients who fell in the TOF ratio < 0.9 group were found to have, after arrival in PACU:
    - A feeling of general muscle weakness in 73% at 60 min
    - Inability to swallow in 29% at 20min
    - Inability to speak normally in 33% of patients at 40 min
    - Inability to cough normally in 27% at 40 min
    - Inability to breathe deeply in 15% of patients at 40 min
    - Blurry vision in 23% and diplopia in 10% at 60 min
    - Inability to perform a 5-second head lift in 58% at 20 min
    - Inability to perform a sustained 5 second hand grip in 21% at 20 min and in 6% at 40 min
    - Inability to perform a 5 second tongue protrusion in 5% of patients at 40min

It is no surprise that some of these symptoms associated with PORC are reported as unpleasant. (Kopman, Aaron F, Yee & Neuman, 1997)

Decreased perioperative efficiency

Longer time to discharge from the Post Anaesthetic Care Unit (PACU) has been described for patients with PORC (Butterly et al., 2010) In this study of 246 consecutive PACU patient admissions, the average time in PACU was 243min for patients with adequate recovery compared to 323 minutes for patients who had a TOF ratio of <0.9.

Slower postoperative weaning from ventilation and longer times to endotracheal tube removal have been associated with lower TOF ratios after cardiac surgery. (Murphy, Glenn S et al., 2003) This prospective randomized double blinded trial studied the recovery of neuromuscular function in two patient groups who received either rocuronium or pancuronium. An association was demonstrated between lower TOF ratios, slower ventilator support withdrawal and longer times to removal of endotracheal tubes.

Why do some anaesthetists monitor NMB inadequately?

At the authors' institution, the perceived lack of availability of PNS could contribute to inadequate monitoring and management of neuromuscular blockade. This encouraged the authors to perform an audit of PNS.

Worldwide it is described that many anaesthetists are still not monitoring the level of neuromuscular blockade with a quantitative modality such as the TOF ratio. Hypothesis as to why that may be, include:(Brull & Prielipp, 2015)

- Heuristics: Clinician behaviour may be affected by heuristics. Heuristics are educated mental guesses or shortcuts made based on pattern recognition from prior clinical experience e.g. "Vecuronium blockade can always be reversed an hour after intubation". This pattern of thinking may lead to:
- Confirmation bias, which involves accepting subjective data as supportive of a desired outcome e.g. "a strong hand grip" to confirm the anticipated lack of PORC after reversal with neostigmine. This confirmation bias often contributes to and compounds an existing "anchoring bias", e.g. "All my cases do well in PACU since I am a great anaesthetist with expertise and experience"
- Production pressure to optimize turnaround time between surgical operating time, in combination with
- Complacency bred from past "successes". These past "successes" (partially explained by the low incidence of attribution of significant post-op morbidity to inadequate neuromuscular reversal) breed a delusional complacency. This can be followed by disbelief and confusion when urgent endotracheal tube reinsertion is required shortly after arrival in PACU.

Summary of the literature:
What should anaesthetists be doing?

In South Africa the following recommendations are made with regards to neuromuscular blockade monitoring and reversal (Kluyts et al., 2018) (South African Society of Anaesthesiologists [SASA] 2018):

- A peripheral nerve stimulator to monitor neuromuscular function is considered an essential item needed as a minimum requirement for the safe conduct of anaesthesia in any hospital.
- Peripheral nerve stimulators should be immediately available in theatre and in the recovery room.
- Patients should have recovered from neuromuscular blockade prior to handover to staff from the theatre recovery room, and thus also prior to discharge from the anaesthetist's care.

It is well described in the literature that PORC leads to increased post-operative complications, including:

- Airway and breathing compromise
- An unpleasant patient experience (Murphy, G. S. et al., 2013) (Murphy, Glenn S et al., 2003) and
- Decreased theatre efficiency

It is now widely accepted that patients should have their neuromuscular function monitored peri-operatively during and after the administration of neuromuscular blocking agents until full return of neuromuscular function, and that failure to antagonize neuromuscular block may result in an unacceptably high incidence of patients with clinically significant PORC in the recovery room.(Viby-Mogensen, 2000)

It is also described in the literature that PORC cannot be assessed adequately without an objective measure of neuromuscular function (Saddler et al., 1990, Viby-Mogensen et al., 1985). Taken in conjunction with the SASA recommendations above, it is the author's opinion that neuromuscular function should be assessed using a PNS device with TOF ratio display capabilities whenever possible. Older style PNS devices without TOF ratio display capabilities should thus only be used if no better devices are available.

Reversal agents should be administered appropriately, using quantitative TOF ratio evidence to guide the need for its administration, i.e. reversal agents to be administered if the TOF ratio is <0.9.

When TOF ratio capable devices are not available

In the situation where TOF ratio capable devices are not available and older generation PNS are used, the following is recommended (Thilen & Bhananker, 2016):

- Start monitoring early, before administration of NMB drugs. This way technical errors such as faulty cables are excluded, and a baseline reference TOF twitch is obtained.

- Reduce follow up doses of PNMB drugs for outliers who are found to take longer to recover after their initial dose of PNMB
- Be conscious of the variation between different sites of PNMB monitoring
    - The Ulnar nerve/adductor pollicis site is the preferred site for monitoring,
    - Posterior tibial nerve/ great toe function recovers quicker after NMB, thus assessment here underestimates residual NMB.
    - Facial nerve/eye muscle site monitoring has been shown to be unreliable with a heightened incidence of PORC if it is used to guide neostigmine therapy.
- Avoid unnecessarily deep NMB. For many procedures, e.g. lower abdominal surgeries, a block depth with TOF count 1 to 2 is usually appropriate.
- Confirm an adequate level of spontaneous recovery prior to giving neostigmine.
    - Ideally a TOF count of 4 should be present before neostigmine administration, rather than the TOF count of >1 mentioned in older guidelines.
    - If spontaneous recovery has occurred to the point where no fade on TOF stimulation can be palpated, then the neostigmine dose given should not exceed 20 – 25 mcg/kg
- One should err on giving rather than not giving neostigmine reversal, given that the complications of PORC outweighs the theoretical risks of short-lived paradoxical weakness with reversal of NMB agents in patients with high TOF ratios. (Murphy, G S & Kopman, 2016)

The elderly patient

Slower clearance and altered pharmacokinetics of neuromuscular blockers play a significant role in the higher observed incidence of PORC in patients older than 65 years. This effect is more pronounced with the aminosteroids, but is also described to a lesser extent with the benzylisoquinoline class of neuromuscular blockers. Pharmacodynamics are much less affected but some dose reductions may still be needed. Therefore, the monitoring of neuromuscular blockade in the elderly should be routinely performed with TOF ratio display capable monitoring to ensure that a TOF ratio > 0.9 is achieved at the end of anaesthesia. (Stankiewicz-Rudnicki, 2016)

Looking to the future

Novel drugs may influence the long term management of neuromuscular blockade perioperatively. Sugammadex can rapidly reverse even deep neuromuscular blockade by encapsulating aminosteroids i.e. rocuronium and also vecuronium (Paton et al., 2010). However, its high cost prohibits routine use for reversal in South Africa.

Cysteine may become a PNMB reversal drug if/when gantacurium is released for routine use in anaesthetic practice (de Boer & Carlos, 2018). Gantacurium is an isoquinolinium diester derivative of chlorofumaric acid which closely mimics the onset and offset of patterns of succinylcholine. The quick offset of gantacurium stems from cysteine adduction induced chemical degradation. Degradation by

pH-sensitive hydrolysis also contributes to the metabolism as a slower process. Reversal of PNMB induced by gantacurium can also be performed with edrophonium administration.

Calabadion is a novel reversal agent that can encapsulate both aminosteroid and benzylisoquinolinium NMBD's with a greater affinity for these drugs than sugammadex. (De Boer & Carlos, 2018)

While these novel agents that rapidly reverse neuromuscular blockade will likely decrease the incidence of PORC, the requirement to monitor intra-operative neuro-muscular function will remain, especially for operations such as retinal eye surgery and brain surgery, where prevention of sudden movement or coughing will remain crucial.

Further research opportunities:

There are opportunities for further research in evaluating the contribution and effect of skin related factors on the measurement of residual paralysis with peripheral nerve stimulators. TOF measurements may theoretically be influenced by the properties of the skin itself, since skin resistance may vary with skin thickness, moisture content and temporal association with prior electrical stimulation. It has also been known for a long time that skin impedance decreases when exposed to higher intensity currents. (Stephens, 1963)

Research opportunities exist to identify the most important barriers to appropriate neuromuscular blockade monitoring in South Africa. If anaesthetists in well-resourced settings are not monitoring PNMB adequately, one can assume that monitoring is inadequate in more resource-constrained settings. Investigating these factors would provide insight on how to direct our limited resources in South Africa to best address the problems encountered.

References:

Ali, H.H., Utting, J.E. & Gray, T.C. 1971. Quantitative assessment of residual antidepolarizing block (Part II). *BJA: British Journal of Anaesthesia.* 43(5):478-485.

Beecher, H.K. & Todd, D.P. 1954. A study of the deaths associated with anesthesia and surgery : Based on a study of 599,548 anesthesias in ten institutions 1948-1952, inclusive. *Annals of Surgery.* 140(1):2-34.

Berg, H., Viby-Mogensen, J., Roed, J., Mortensen, C.R., EngbÆK, J., Skovgaard, L.T. & Krintel, J.J. 1997. Residual neuromuscular block is a risk factor for postoperative pulmonary complications. *Acta Anaesthesiologica Scandinavica.* 41(9):1095-1103.

Brand, J.B., Cullen, D.J., Wilson, N.E. & Ali, H.H. 1977. Spontaneous recovery from nondepolarizing neuromuscular blockade: Correlation between clinical and evoked responses. *Anesthesia and Analgesia.* 56(1):55-58.

Brull, S.J. & Prielipp, R.C. 2015. Reversal of neuromuscular blockade: "Identification friend or foe". *Anesthesiology.* 122(6):1183-1185.

Butterly, A., Bittner, E.A., George, E., Sandberg, W.S., Eikermann, M. & Schmidt, U. 2010. Postoperative residual curarization from intermediate-acting neuromuscular blocking agents delays recovery room discharge. *British Journal of Anaesthesia.* 105(3):304-309.

Capron, F., Alla, F., Hottier, C., Meistelman, C. & Fuchs-Buder, T. 2004. Can acceleromyography detect low levels of residual paralysis? A probability approach to detect a mechanomyographic train-of-four ratio of 0.9. *Anesthesiology.* 100(5):1119-1124.

Christie, T.H. & Churchill-Davidson, H.C. 1958. The St. Thomas's Hospital nerve stimulator in the diagnosis of prolonged apnoea. *Lancet.* 271(7024):776.

De Boer, H.D. & Carlos, R.V. 2018. New drug developments for neuromuscular blockade and reversal: Gantacurium, CW002, CW011, and Calabadion. *Current Anesthesiology Reports.* 8: 119-124

Eriksson, L.I., Sundman, E., Olsson, R., Nilsson, L., Witt, H., Ekberg, O. & Kuylenstierna, R. 1997. Functional assessment of the pharynx at rest and during swallowing in partially paralyzed humans: Simultaneous videomanometry and mechanomyography of awake human volunteers. *Anesthesiology.* 87(5):1035-1043.

Gillies, D.M.M. & Wynands, J.E. 1985. Obituary Dr. Harold Griffith 1894–1985. *Canadian Anaesthetists' Society Journal.* 32(5):570-574.

Invernizzi, J.R.R. & Gopalan, P.D. 2016. Postoperative neuromuscular function following non-depolarising muscle blockade in patients at Inkosi Albert Luthuli central hospital, Durban. *Southern African Journal of Anaesthesia and Analgesia.* 22(4):121-124.

Khirwadkar, R. & Hunter, J.M. 2012. Neuromuscular physiology and pharmacology: an update. *Continuing Education in Anaesthesia, Critical Care & Pain.* 12(5):237-244.

South African Society of Anaesthesiologists. 2018. *South African society of anaesthesiologists practice guidelines 2018 revision*. Available: https://www.sasaweb.com/ContentDetails/ContentDetails#?ContentId=38&SubMenuType=1 [2018, September 08].

Kopman, A.F., Yee, P.S. & Neuman, G.G. 1997. Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. *Anesthesiology.* 86(4):765-771.

Kopman, A.F., Klewicka, M.M. & Neuman, G.G. 2002. The relationship between acceleromyographic train-of-four fade and single twitch depression. *Anesthesiology.* 96(3):583-587.

Kumar, G.V., Nair, A.P., Murthy, H.S., Jalaja, K.R., Ramachandra, K. & Parameshwara, G. 2012. Residual neuromuscular blockade affects postoperative pulmonary function. *Anesthesiology.* 117(6):1234-1244.

McLean, D.J., Diaz-Gil, D., Farhan, H.N., Ladha, K.S., Kurth, T. & Eikermann, M. 2015. Dose-dependent association between intermediate-acting neuromuscular-blocking agents and postoperative respiratory complications. *Anesthesiology.* 122(6):1201-1213.

Murphy, G.S. & Kopman, A.F. 2016. "To reverse or not to reverse?" The answer is clear! *Anesthesiology.* 125(4):611-614.

Murphy, G.S., Szokol, J.W., Marymont, J.H., Greenberg, S.B., Avram, M.J. & Vender, J.S. 2008. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. *Anesthesia & Analgesia.* 107(1):130-137.

Murphy, G.S., Szokol, J.W., Marymont, J.H., Vender, J.S., Avram, M.J., Rosengart, T.K. & Alwawi, E.A. 2003. Recovery of neuromuscular function after cardiac surgery: pancuronium versus rocuronium. *Anesthesia & Analgesia.* 96(5):1301-1307.

Murphy, G.S., Szokol, J.W., Marymont, J.H., Greenberg, S.B., Avram, M.J., Vender, J.S. & Nisman, M. 2008. Intraoperative acceleromyographic monitoring reduces the risk of residual blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology.* 109(3):389-398.

Murphy, G.S., Szokol, J.W., Avram, M.J., Greenberg, S.B., Shear, T., Vender, J.S., Gray, J. & Landry, E. 2013. Postoperative residual neuromuscular blockade is associated with impaired clinical recovery. *Anesthesia & Analgesia.* 117(1):133-141.

Naguib, M., Kopman, A.F. & Ensor, J.E. 2007. Neuromuscular monitoring and postoperative residual curarisation: a meta-analysis. *British Journal of Anaesthesia.* 98(3):302-316.

Nell, W.T., Stevenson, N., Ridgard, T., Van der Westhuizen, F.W., Diedericks, J. & Joubert, G. 2004. Post-operative neuromuscular function of patients receiving non-depolarising muscle relaxants at Universitas hospital, Bloemfontein, South Africa. *Southern African Journal of Anaesthesia and Analgesia.* 10(1):6-8.

Paton, F., Paulden, M., Chambers, D., Heirs, M., Duffy, S., Hunter, J., Sculpher, M. & Woolacott, N. 2010. Sugammadex compared with neostigmine/glycopyrrolate for routine reversal of neuromuscular block: A systematic review and economic evaluation. *British Journal of Anaesthesia.* 105(5):558-567.

Russell, W.J. & Serle, D.G. 1987. Hand grip force as an assessment of recovery from neuromuscular block. *Journal of Clinical Monitoring.* 3(2):87-89.

Saddler, J.M., Bevan, J.C., Donati, F., Bevan, D.R. & Pinto, S.R. 1990. Comparison of double-burst and train-of-four stimulation to assess neuromuscular blockade in children. *Anesthesiology.* 73(3):401-403.

Sauer, M., Stahn, A., Soltesz, S., Noeldge-Schomburg, G. & Mencke, T. 2011. The influence of residual neuromuscular block on the incidence of critical respiratory events. *European Journal of Anaesthesiology.* 28(12):842-848.

Stankiewicz-Rudnicki, M. 2016. Neuromuscular blockade in the elderly. *Anaesthesiology Intensive Therapy.* 48(4):257-260.

Stephens, W. 1963. The current-voltage relationship in human skin. *Medical Electronics and Biological Engineering.* 1(3):389-399.

Sundman, E., Witt, H., Olsson, R., Ekberg, O., Kuylenstierna, R. & Eriksson, L.I. 2000. The incidence and mechanisms of pharyngeal and upper esophageal dysfunction in partially paralyzed humans: Pharyngeal videoradiography and simultaneous manometry after atracurium. *Anesthesiology.* 92(4):977-984.

Thilen, S.R. & Bhananker, S.M. 2016. Qualitative neuromuscular monitoring: How to optimize the use of a peripheral nerve stimulator to reduce the risk of residual neuromuscular blockade. *Current Anesthesiology Reports.* 6:164-169.

Viby-Mogensen, J. 2000. Postoperative residual curarization and evidence-based anaesthesia. *British Journal of Anaesthesia.* 84(3):301-303.

Viby-Mogensen, J., Jensen, N.H., Engbaek, J., Ording, H., Skovgaard, L.T. & Chraemmer-Jørgensen, B. 1985. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology.* 63(4):440-443.

Viby-Mogenson, J. 2000. Postoperative residual curarization and evidence-based medicine. *British Journal of Anaesthesia.* 84(3):301 - 303.

PART C – PUBLICATION READY MANUSCRIPT

(Reference styling and font changed as per Southern African Journal of Anaesthesia and Analgesia's "Instructions to author's")

Article title:

Audit of peripheral neuromuscular stimulators at the hospitals staffed by the department of Anaesthesia and Perioperative Medicine at the University of Cape Town

Authors:

1. Joubert AT, MBChB, FCA(SA), Department of Anaesthesia, University of Cape Town, South Africa
2. Porrill O, MB BCh, FCA, Department of Anaesthesia, University of Cape Town, South Africa
3. Pead JC, BSc Hon Eng Mechatronics, MSc Electro-Mechanical Engineering, Department of electrical engineering, University of Cape Town, South Africa

Corresponding author:

Dr. Andries T. Joubert

PO Box 8064

Nahoon

East London, South Africa

5210

Mobile phone no. +27 72 864 1233

e-mail: andries.thomas.joubert@gmail.com

Keywords:

Peripheral nerve stimulator, Peripheral neuromuscular monitor, Postoperative residual curarization, Postoperative neuromuscular blockade, Residual paralysis, Post-operative neuromuscular function.

Abstract

Background: Inadequate monitoring of neuromuscular blockade (NMB) may result in worse patient outcomes, therefore NMB monitor availability is a minimum requirement for perioperative care according to the South African Society of Anaesthesiologists' (SASA) 2018 guidelines. The authors performed an audit of peripheral nerve stimulators (PNS) functionality and availability at their institution.

Methods: The PNS were attached to an electrical circuit with a skin equivalent resistance. The resultant current impulses generated using Train-of-Four (TOF) mode and Double Burst Stimulation modes were recorded with a voltage scope meter. PNS availability was assessed in theatre and recovery areas.

Results: Of the 65 PNS units assessed, 39 units were deemed to be dysfunctional and 26 units fully functional. The most frequent fault found (30 units) related to faulty or absent PNS electrode cables. Eight functional PNS units with TOF ratio display capability was found. The working PNS showed good inter-device peak voltage measurement correlation. Of the 59 areas identified where PNS should be easily available, only 37 areas met the PNS availability criteria suggested in the SASA guidelines.

Conclusion: This audit highlighted the need for more new generation PNS with TOF-ratio-display-ability to align the institution with the recommendations from SASA standards and the anaesthetic literature. It also highlighted the accuracy and consistency of delivered current bursts by the working PNS devices.

Introduction

History and practice of NMB monitoring

The first muscle relaxant, d-tubocurarine, was introduced into anaesthetic practice in 1942 by Harold Griffith[1]. As early as 1954, it was noted that patients who had received d-tubocurarine had a six fold higher mortality than patients who had not received the drug[2]. The situation where skeletal muscle paralysis has not been adequately reversed at the end of anaesthesia has been described as post-operative residual curarization (PORC). This was first recognized in the 1960's in patients with renal function impairment where the clearance of NMB's was reduced.[3] In 1958 the use of a nerve stimulator to monitor the action of muscle relaxants was suggested[4], but for many years thereafter only clinical parameters were used to infer the absence of clinically significant PORC in the recovery area, including:

- Head lift more than 5 seconds
- Tongue protrusion
- Vital capacity >15ml/kg [5]
- Hand grip strength [6];

PORC was, in extreme cases, associated with respiratory failure due to respiratory muscle weakness. By 1971 it was suggested that the level of PORC could be assessed by using the train-of-four twitch technique (TOF).[7] This involved the use of a peripheral nerve stimulator (PNS) to measure the ratio of the amplitudes of the fourth to the first twitch. A ratio of > 0.7 was considered to indicate adequate recovery before endotracheal tube removal, given that it correlated well with the clinical parameters mentioned above. This standard was used for many years thereafter. In 1997 [8] a significant post-operative pulmonary complication rate was reported if the train of four value was <0.7 in the immediate post-operative period after pancuronium administration.

Around the same time it was demonstrated [9] (by TOF-testing the adductor pollicis muscles of a small sample of volunteers) that pharyngeal tone approaches normal values when the concurrent TOF demonstrates a ratio of more than 0.9. This cast doubt on the validity of the previously held threshold being adequate for endotracheal tube removal. Subsequently a TOF ratio of >0.9 became the accepted standard to achieve before endotracheal tube removal.

Another concern is related to the inability to detect fade by clinical examination during TOF delivery. It is said that one cannot detect and confirm clinically significant PORC by tactile or visual assessment of the peripheral nerve stimulation response. Even experienced observers cannot feel fade if the TOF ratio is above 0.4 [10, 11]. Mechanomyography, electromyography and acceleromyography are alternative measurement techniques that provide more objective assessments of PORC. [12]

Recent studies have shown that the TOF ratio is slightly overestimated when it is determined using acceleromyography. Thus it is questioned whether a TOF ratio of 1.0 should rather be aimed for when acceleromyography is used, in order to ensure a TOF ratio above 0.9. [13, 14]

Clinical significance

It is well described in the literature that PORC leads to increased post-operative complications, including:

- Airway and breathing compromise

- An unpleasant patient experience [15] [16] and
- Decreased theatre efficiency

In the South African context two studies reported incidences of 29% and 43% respectively for PORC with TOF <0.9. [17, 18] Elsewhere a meta-analysis in 2007 infer that PORC is common, with an estimated TOF < 0.9 incidence rate of about 41%, in patients who received intermediate acting NMB's. [19]

Airway and breathing compromise:

- A five times higher rate of aspiration (laryngeal penetration) was described in a study of partially paralysed healthy volunteers given an infusion of atracurium with concomitant monitoring of the TOF ratio and video radiography of the larynx. [20]

- PORC is associated with an increased risk of post-operative pulmonary complications (POPC), defined as: respiratory failure, pulmonary oedema, tracheal reintubation and pneumonia. Data from a retrospective analysis of hospital records of 48499 patients showed an association between higher doses of neuromuscular blocking drugs and POPC. [21]

- More episodes of upper airway obstruction during transport to the PACU were observed in patients managed with conventional qualitative TOF assessment compared to similar patients managed with acceleromyographic quantitative TOF monitoring. [22]

- Post-operative hypoxaemia [23]
    - In this randomized prospective placebo controlled trial of 114 patients, patients received either neostigmine 20mcg/kg or placebo at the end of general anaesthesia that included Rocuronium for neuromuscular blockade. Failure to reverse minimal PORC was associated with hypoxaemia in the post anaesthesia care unit (PACU), occurring about twice as often in the no-neostigmine placebo group (29 occurrences) vs. the neostigmine group (16 occurrences)

- Critical respiratory events in the post anaesthetic care unit. [24]
    - In this study 0.8% of patients developed critical respiratory events (61 of 7459 patients). The most common complications found were hypoxaemia and upper airway obstruction. The TOF ratios, mean and (±standard deviation), in the critical respiratory event group were 0.62 (±0.2).

An unpleasant experience:

- In one study, 149 patients arriving in PACU were divided into two groups based on a measured TOF ratio of < 0.9 and ≥ 0.9 respectively. The 48 patients who fell in the TOF ratio < 0.9 group were found to have, after arrival in PACU:
    - A feeling of general muscle weakness in 73% at 60min
    - Inability to swallow in 29% at 20min
    - Inability to speak normally in 33% of patients at 40min
    - Inability to cough normally in 27% at 40min
    - Inability to breathe deeply in 15% of patients at 40min
    - Blurry vision in 23% and diplopia in 10% at 60min

It is no surprise that some of these symptoms associated with PORC are reported as unpleasant. [25]

Decreased perioperative efficiency

Longer times to discharge from the Post Anaesthetic Care Unit (PACU) has been described for patients with PORC [26] In this study of 246 consecutive PACU patient admissions, the average time in PACU was 243min for patients with adequate recovery compared to 323 minutes for patients who had a TOF ratio of <0.9.

Slower postoperative weaning from ventilation and longer times to endotracheal tube removal has been associated with lower TOF ratios after cardiac surgery. [16]

Why do some anaesthetists monitor NMB inadequately?

At the authors' institution, the perceived lack of availability of PNS could contribute to inadequate monitoring and management of neuromuscular blockade. This encouraged the authors to perform an audit of PNS.

Worldwide it is described that many anaesthetists are still not monitoring the level of neuromuscular blockade with a quantitative modality such as the TOF ratio. Hypothesis as to why that may be, include:[27]

- Heuristics,
- Confirmation bias,
- Production pressure to optimise turnaround time and
- Complacency bred from past "successes".

What should anaesthetists be doing?

In South Africa the following recommendations are made with regards to neuromuscular blockade monitoring and reversal [28] (South African Society of Anaesthesiologists [SASA] 2018):

- A peripheral nerve stimulator to monitor neuromuscular function is considered an essential item needed as a minimum requirement for the safe conduct of anaesthesia in any hospital.
- Peripheral nerve stimulators should be immediately available in theatre and in the recovery room.
- Patients should have recovered from neuromuscular blockade prior to handover to staff from the theatre recovery room, and thus also prior to discharge from the anaesthetists care.

It is described in the literature that PORC cannot be assessed adequately without an objective measure of neuromuscular function [10, 11]. Taken in conjunction with the SASA recommendations above, it is the author's opinion that neuromuscular function should be assessed using a PNS device with TOF ratio display capabilities.

Methodology

Overview

- The study was designed as an audit of PNS availability and function with the aim to compare our PNS equipment availability to the recommended standard. More than 90% of data collection was done between 2 January 2018 and 2 February 2018, and the last area was assessed on 15 May 2018. Ethics approval was obtained from the University of Cape Town, Faculty of Health Sciences Human Research Ethics Committee, HREC REF: 771/2017

- Study location
    - This audit was performed at the hospitals staffed by the department of Anaesthesia and Perioperative Medicine at the University of Cape Town, which included the following locations: Groote Schuur Hospital, Mowbray Maternity Hospital, Red Cross War Memorial Children's Hospital, New Somerset Hospital, Maitland Cottage Hospital and Valkenberg Hospital (hereafter referred to as "the authors' institution".)

- Research procedures and data collection methods

  The number of PNS available in the theatre and recovery areas of the institution were documented. These findings were judged against the 2012 SASA practice guidelines. A unique identification number was assigned to each PNS unit. Thereafter, the functionality of these units was tested by confirming the presence of the electrical current bursts delivered during the TOF and double burst stimulation (DBS) modes. In order to perform these measurements, the PNS were connected to a skin-equivalent-resistance circuit built by the co-author Mr Pead. (See Figure 1)

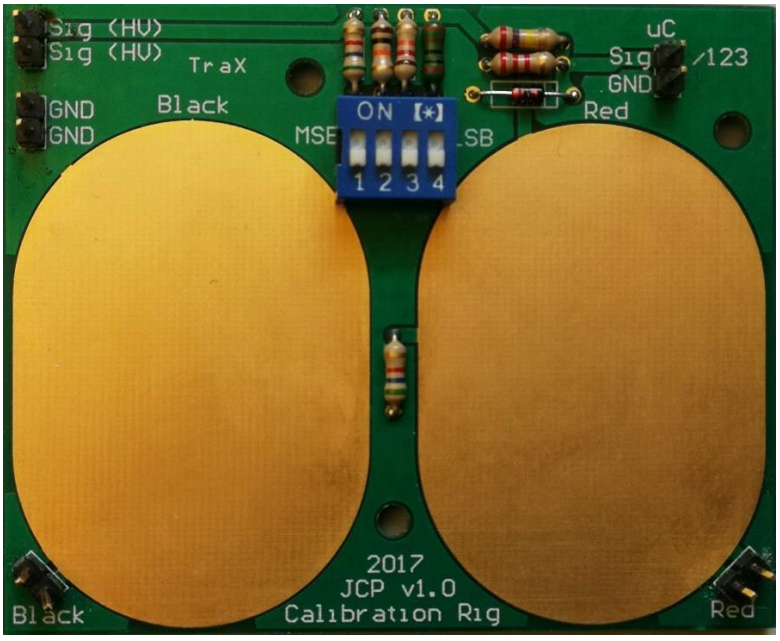

Figure 1: Latest version of resistance circuit for PNS testing

It was opted to use a 2.47kOhm resistor for this, given that between 1 and 4.5 kOhm is described in test manuals. The voltage produced by the electrical current bursts set at 60mA were measured over the resistor. Thereafter a graphic display of the voltage/time wave loop of the TOF and DBS current bursts were recorded in numerical (Excel®) and digital photographic (PNG file) format using a Keysight InfiniiVision EDUX1002G Digital Storage Oscilloscope. The PNS were classified as either functional or faulty depending on the results of this test, applying Ohm's law. Data were recorded by Dr. Joubert and stored on a password-protected Excel spreadsheet.

Statistics

Complex statistical analysis was not needed. The nerve stimulators were classified as functional or not, and the nature of the faults described. The areas assessed for PNS availability were classified into three groups with PNS either "physically present", "easily available" or "not easily available."

Given the striking repeatability of the PNS recordings between devices, it was opted to use descriptive statistical analysis of this data to demonstrate and emphasize this finding using the mean and standard deviation, once it was confirmed that the data was normally distributed.

Results:

In total 59 areas where a peripheral stimulator should be easily available (PNS-zones) were identified. These areas consisted of 48 operating theatre or procedural areas (e.g. Catheterisation laboratory, Electroconvulsive therapy suite) and 11 recovery areas.

Of these areas, 37 PNS-zones were deemed to meet the PNS availability criteria suggested in the SASA guidelines. When looking at the data in more detail, one would see that a PNS unit was found to be physically present in 21 areas, easily available in 19 areas and not easily available in 19 areas. Three areas were found with dysfunctional PNS, resulting in them being classified as available but not meeting the overall availability standard.

PNS units are often shared between operating theatres to save costs. Therefore it is important to define adequate availability. For the purpose of this study, importance was placed on having a "designated specific location" for the device. If the device was kept in a specifically labelled location just outside theatre, it would be labelled as adequately available. On the other hand, if a unit was shared between theatres but was not kept in a designated location it was deemed "not easily available".

TOF-ratio display capability was only represented in 14 of the units. Of these 14 units only 8 were fully functional. (See Figure 2)

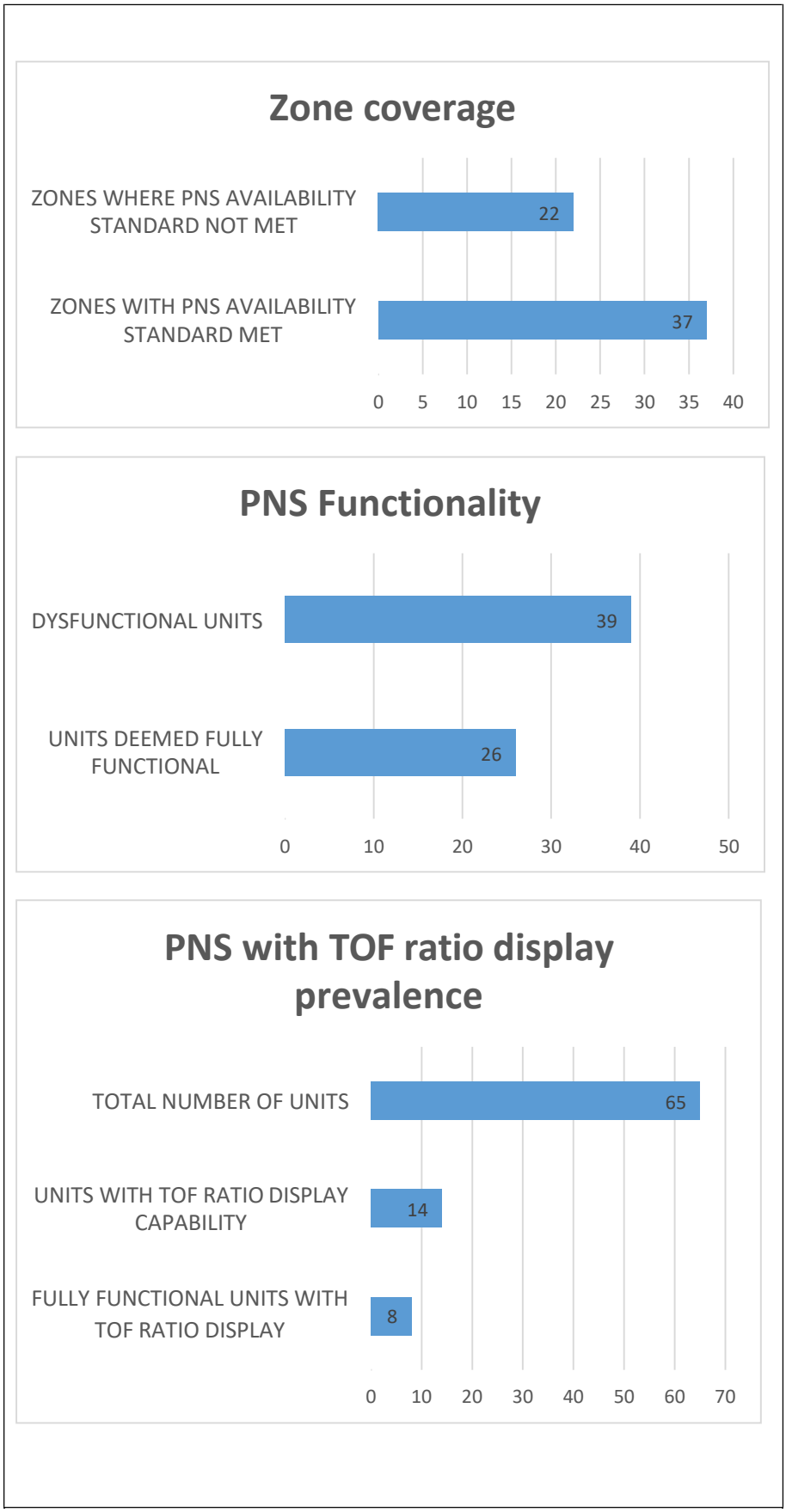

Figure 2: Summary of Audit results

65 PNS units were tested for functionality. The different makes and models are depicted in the chart below (figure 3). Of these units, 39 were deemed to be dysfunctional and the remaining 26 units were deemed fully functional.

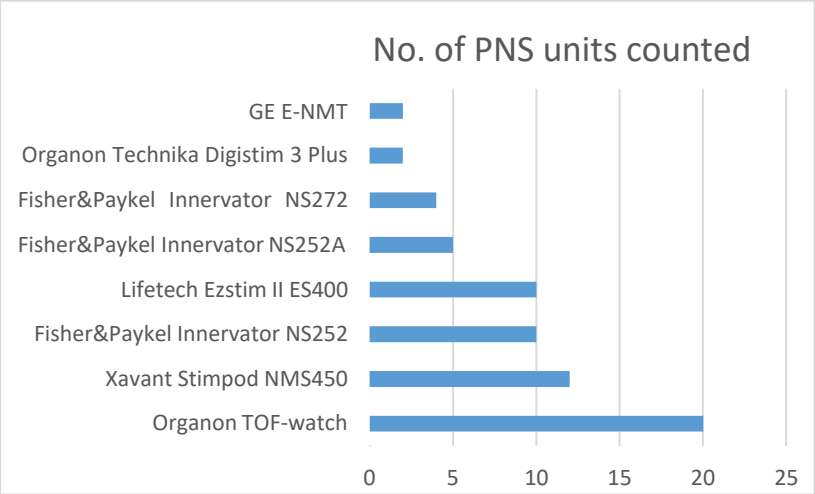

Figure 3: PNS makes and models encountered

The faults found with the units were as follow:

- Absence of electrode cables was found in 27 units. These cables were either lost during clinical use or discarded by technicians when found to be malfunctioning. Given that many of the units were no longer manufactured or supported by their manufacturers, replacement cables could not be acquired. Only 3 units were found to have faulty cables, but it may well be the most frequent malfunction found on the PNS, given that a large number of the "missing" cables may reflect original cable malfunction.
- The other malfunctions found are indicated in figure 4 below.

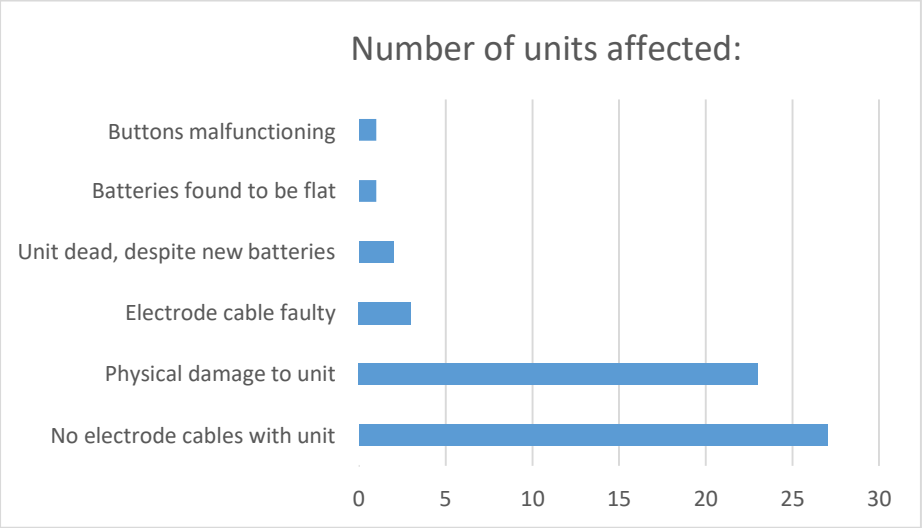

Figure 4: Faults found with PNS units

The overall consistency of the delivered voltage spikes is noteworthy. In total 61 units were able to give scope meter recordings, although this was often performed with a set of "loan cables" where the units' original cables were damaged or missing. This translated into 244 peak values for TOF voltage peak measurements. An assessment was made of the mean and standard deviation of the peak values measured with the scope meter. The skewness and kurtosis suggested normal distribution of the data and there was no sign change from baseline readings with paired t-tests.

Discussion:

The ability to monitor neuromuscular blockade is considered essential and is a minimum requirement for providing anaesthesia and perioperative care according to the 2012 SASA guidelines.

This audit revealed that there were not enough functional PNS available at the institution. There were 8 functioning TOF-R capable peripheral nerve stimulators available to cover 59 areas. If we add the handheld devices without TOF-Ratio capability, 37 areas out of the 59 (63%) are covered. This were in keeping with the author's experience of PNS availability while working in clinical practice at this institution, where it was often difficult to locate a PNS at short notice.

It can be inferred that it is unlikely that peripheral neuromuscular blockade monitoring is performed to the current accepted standard of a "TOF-Ratio of >0.9" if we have only 8 such devices available to cover 59 PNS zones at our institution.

The clinical significance of the shortage of PNS units vary depending on the actual need for PNMB monitoring in the area concerned. Despite this, the SASA practice guidelines do not make concessions for areas where PNS are less likely to be used and describe this as an essential monitor that needs to be immediately available. Thus, a lower likelihood of needing the device should not be used as an excuse for inadequate coverage.

The logistics of tracking a PNS unit's location is very important in situations where nerve stimulators have to be shared between locations. In areas where the nerve stimulator may be used in more than 2 locations, immediate availability of the device is lost once it is in use. In order to facilitate locating the device the unit has to be stored in a specific named "base" location, and the whereabouts of the device must be documented once it is removed. This could be done with the use of a simple notebook kept at the "base location", or by online systems such as a "device-location-Whatsapp-group" shared between users of the device.

From a technical point of view the working PNS were found to be very consistent in their delivered current bursts. This information is useful when troubleshooting a PNS unit. Looking at our data set there would be a high likelihood of the electrode cable being the problem rather that the rest of the electronic hardware.

Another possible relevant factor that was not explored in this study is the likelihood of skin resistance contributing to measurement variance. Skin resistance may vary with skin thickness, moisture content and temporal association with prior electrical stimulation. It has also been known for a long time that skin impedance decreases when exposed to higher intensity currents. [29]

There are problems with the older PNS units, which comprise the majority of units in the institution:

- The inability of these devices to exclude incomplete return of neuromuscular function by modern standards make them all but obsolete. However, some value remains in the ability to demonstrate very deep NMB levels were fade is detectable clinically and to demonstrate where TOF counts less than 4 are present.

- The lack of manufacturer support for many of the older PNS units in use at our institution shortens the foreseeable lifespan of the remaining functional PNS fleet. Some of these PNS models are no longer manufactured. Most of these units will thus become unusable at some point when they break down and need maintenance or repairs.

Implications for our region from the audit findings

- The performance of this audit helped catalyse the acquisition of further modern PNS units at our institution. At the time of this write-up a further 8 E-NMT units have already been delivered to GSH hospital and the plan is to continue building our fleet for the future.

- Procurement of a modern scope meter with the ability to store and download test data in a downloadable format should be considered for the clinical engineering departments of the hospitals where PNS are used. This equipment will facilitate routine maintenance and enable future audit projects of electronic devices.

- Hospitals needs to continue acquiring more TOF-R capable units to align themselves with measurement standards described in the literature.

- An awareness and educational campaign needs to be launched within the departments of anaesthesia to educate and motivate anaesthetists to:

    - Utilise appropriate PNMB monitoring, and
    - Advocate for the provision of adequate numbers of PNS devices.

- The cost and availability of repairs and cable replacements should be factored into the decision when acquiring more PNS units. The anaesthetic machine mounted PNS unit retail for about 3 times the price of the handheld device. It is hypothesized that the machine mounted units may last longer due to:
    - Higher quality electrode cabling
    - Less handling of the machine mounted units, resulting in
        - A smaller chance of being dropped and broken
        - Less winding up / coiling of the electrode cables which may prolong cable life.

- The cost-benefit ratio of the current options (E-NMT vs. Xavant Stimpod NMS450) should be further audited prospectively while in use to help guide future acquisitions of these devices.

- There may be a potential market for small cost-effective skin-equivalent resistance test-circuit devices that can give a binary confirmation of functionality for a PNS unit delivering TOF and DBS.

Summary

- Patients should have their neuromuscular function monitored perioperatively during and after the administration of neuromuscular blocking agents until full return of neuromuscular function.
- The practical "standard of care" for neuromuscular function monitoring is the use of acceleromyography in conjunction with device software that will express a Train-of-four ratio. [30]
- This audit highlighted the need at the author's institution for more new generation PNS with TOF-ratio-display-ability to align ourselves with the recommendations from the anaesthetic literature.
- It also highlighted the need for an improved sharing system in those areas were PNS: clinical area ratio is <1.
- This research also highlighted the accuracy and consistency of delivered current bursts by the working PNS devices.
- There are opportunities for further research in evaluating the contribution of skin related factors on the conduction of current bursts with PNS.

References:

1. Gillies DMM, Wynands JE. Obituary Dr. Harold Griffith 1894–1985. Can Anaesth Soc J 1985; 32: 570-4.

2. Beecher HK, Todd DP. A study of the deaths associated with anesthesia and surgery: based on a study of 599,548 anesthesias in ten institutions 1948-1952, inclusive. Ann Surg 1954; 140: 2-34.

3. Khirwadkar R, Hunter JM. Neuromuscular physiology and pharmacology: An update. Continuing Education in Anaesthesia, Critical Care & Pain 2012; 12: 237-44.

4. Christie TH, Churchill-Davidson HC. The St. Thomas's hospital nerve stimulator in the diagnosis of prolonged apnoea. Lancet 1958; 1: 776.

5. Brand JB, Cullen DJ, Wilson NE, Ali HH. Spontaneous recovery from nondepolarizing neuromuscular blockade: Correlation between clinical and evoked responses. Anesth Analg 1977; 56: 55-8.

6. Russell WJ, Serle DG. Hand grip force as an assessment of recovery from neuromuscular block. J Clin Monit 1987; 3: 87-9.

7. Ali HH, Utting JE, Gray TC. Quantitative assessment of residual antidepolarizing block (Part II). Br J Anaesth 1971; 43: 478-85.

8. Berg H, Viby-Mogensen J, Roed J, et al. Residual neuromuscular block is a risk factor for postoperative pulmonary complications. Acta Anaesthesiol Scand 1997; 41: 1095-103.

9. Eriksson LI, Sundman E, Olsson R, et al. Functional assessment of the pharynx at rest and during swallowing in partially paralyzed humans. Anesthesiology 1997; 87: 1035-43.

10. Viby-Mogensen J, Jensen NH, Engbaek J, Ørding H, Skovgaard LT, Chraemmer-Jørgensen B. Tactile and visual evaluation of the response to train-of-four nerve stimulation. Anesthesiology 1985; 63: 440-2.

11. Saddler JM, Bevan JC, Donati F, Bevan DR, Pinto SR. Comparison of double-burst and train-of-four stimulation to assess neuromuscular blockade in children. Anesthesiology 1990; 73: 401-3.

12. Viby-Mogenson J. Postoperative residual curarization and evidence-based medicine. Br J Anaesth 2000; 84: 301 - 3.

13. Capron F, Alla F, Hottier C, Meistelman C, Fuchs-Buder T. Can acceleromyography detect low levels of residual paralysis? Anesthesiology 2004; 100: 1119-24.

14. Kopman AF, Klewicka MM, Neuman GG. The relationship between acceleromyographic train-of-four fade and single twitch depression. Anesthesiology 2002; 96: 583-7.

15. Murphy GS, Szokol JW, Avram MJ, et al. Postoperative residual neuromuscular blockade is associated with impaired clinical recovery. Anesth Analg 2013; 117: 133-41.

16. Murphy GS, Szokol JW, Marymont JH, et al. Recovery of neuromuscular function after cardiac surgery: Pancuronium versus Rocuronium. Anesth Analg 2003; 96: 1301-7.

17. Invernizzi JRR, Gopalan PD. Postoperative neuromuscular function following non-depolarising muscle blockade in patients at Inkosi Albert Luthuli central hospital, Durban.

South *Afr J Anaesth Analg* 2016; 22: 121-4.

18. Nell WT, Stevenson N, Ridgard T, Van der Westhuizen FW, Diedericks J, Joubert G. Post-operative neuromuscular function of patients receiving non-depolarising muscle relaxants at Universitas Hospital, Bloemfontein, South Africa. South *Afr J Anaesth Analg* 2004; 10: 6-8.

19. Naguib M, Kopman AF, Ensor JE. Neuromuscular monitoring and postoperative residual curarisation: a meta-analysis. Br J Anaesth 2007; 98: 302-16.

20. Sundman E, Witt H, Olsson R, Ekberg O, Kuylenstierna R, Eriksson LI. The incidence and mechanisms of pharyngeal and upper esophageal dysfunction in partially paralyzed humans. Anesthesiology 2000; 92: 977-84.

21. McLean DJ, Diaz-Gil D, Farhan HN, Ladha KS, Kurth T, Eikermann M. Dose-dependent association between intermediate-acting neuromuscular-blocking agents and postoperative respiratory complications. Anesthesiology 2015; 122: 1201-13.

22. Murphy GS, Szokol JW, Marymont JH, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual blockade and adverse respiratory events in the postanesthesia care unit. Anesthesiology 2008; 109: 389-98.

23. Sauer M, Stahn A, Soltesz S, Noeldge-Schomburg G, Mencke T. The influence of residual neuromuscular block on the incidence of critical respiratory events. Eur J Anaesthesiol 2011; 28: 842-8.

24. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. Anesth Analg 2008; 107: 130-7.

25. Kopman AF, Yee PS, Neuman GG. Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. Anesthesiology 1997; 86: 765-71.

26. Butterly A, Bittner EA, George E, Sandberg WS, Eikermann M, Schmidt U. Postoperative residual curarization from intermediate-acting neuromuscular blocking agents delays recovery room discharge. Br J Anaesth 2010; 105: 304-9.

27. Brull SJ, Prielipp RC. Reversal of neuromuscular blockade: "Identification friend or foe". Anesthesiology 2015; 122: 1183-5.

28. Kluyts H, Sing U, Farina Z, et al. South African Society of Anaesthesiologists Practice Guidelines 2018 Revision. 2018. https://www.sasaweb.com/ContentDetails/ContentDetails#?ContentId=38&SubMenuType=1 (accessed 09 08 2018)

29. Stephens W. The current-voltage relationship in human skin. Medical electronics and biological engineering 1963; 1: 389-99.

30. Capron F, Fortier LP, Racine S, Donati F. Tactile fade detection with hand or wrist stimulation using train-of-four, double-burst stimulation, 50-hertz tetanus, 100-hertz tetanus, and acceleromyography. Anesth Analg 2006; 102: 1578-84.

PART D - APPENDICES

Glossary of terms used (article):

DBS - Double Burst Stimulation

NMB - Neuromuscular blockade

PACU – Post anaesthesia care unit

PNS -Peripheral nerve stimulators

PNS-zones – Areas where Peripheral stimulator availability is needed according to South African Society for Anaesthesiologists' practice guidelines.

PNM – Peripheral neuromuscular monitors (a synonym for PNS)

PORC – Post-operative residual curarization.

POPC - Post-operative pulmonary complications

RCWMCH – Red Cross War Memorial Children's Hospital

RNMB - Residual neuromuscular blockade, a synonym for PORC

SASA - South African Society of Anaesthesiologists

TOF - Train-of-Four peripheral nerve stimulator mode.

Human Ethics research Council approval form

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shurette.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

15 November 2017

HREC REF: 771/2017

Dr O Porrill
Anaesthesia
D23, NGSH

Dear Dr Porrill

PROJECT TITLE: AUDIT OF PERIPHERAL NEUROMUSCULAR MONITORS AT OUR INSTITUTION (THE HOSPITALS STAFFED BY THE DEPARTMENT OF ANAESTHESIA AND PERIOPERATIVE MEDICINE AT THE UNIVERSITY OF CAPE TOWN) MMed candidate-Dr A Joubert

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 November 2018.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

The HREC acknowledge that the student, Dr Andries Joubert will also be involved in this study.

Yours sincerely

signature removed to avoid exposure online

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 771/2017

Instructions to authors:

https://medpharm.tandfonline.com/action/authorSubmission?journalCode=ojaa20&page=instructions

https://medpharm.tandfonline.com/action/authorSubmission?show=instructions&journalCode=ojaa20

[Accessed 28 October 2018]

Instructions for authors

Thank you for choosing to submit your paper to us. These instructions will ensure we have everything required so your paper can move through peer review, production and publication smoothly. Please take the time to read and follow them as closely as possible, as doing so will ensure your paper matches the journal's requirements. For general guidance on the publication process at Taylor & Francis please visit our Author Services website.

AUTHORSERVICES
Supporting Taylor & Francis authors

This journal uses Editorial Manager to peer review manuscript submissions. Please read the guide for Editorial Manager authors before making a submission. Complete guidelines for preparing and submitting your manuscript to this journal are provided below.

Preparing your paper

All authors submitting to medicine, biomedicine, health sciences, allied and public health journals should conform to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, prepared by the International Committee of Medical Journal Editors (ICMJE).

[…]

Disclosure statement

Please include a disclosure of interest statement, using the subheading "Disclosure of interest." If you have no interests to declare, please state this (suggested wording: *The authors report no conflicts of interest*). For all NIH/Wellcome-funded papers, the grant number(s) must be included in the disclosure of interest statement. Read more on declaring conflicts of interest.

Clinical Trials Registry

In order to be published in a Taylor & Francis journal, all clinical trials must have been registered in a public repository at the beginning of the research process (prior to patient enrolment). Trial registration numbers should be included in the abstract, with full details in the methods section. The registry should be publicly accessible (at no charge), open to all prospective registrants, and managed by a not-for-profit organization. For a list of registries that meet these requirements, please visit the WHO International Clinical Trials Registry Platform (ICTRP). The registration of all clinical trials facilitates the sharing of information among clinicians,

researchers, and patients, enhances public confidence in research, and is in accordance with the ICMJE guidelines.

Complying with ethics of experimentation

Please ensure that all research reported in submitted papers has been conducted in an ethical and responsible manner, and is in full compliance with all relevant codes of experimentation and legislation. All papers which report *in vivo* experiments or clinical trials on humans or animals must include a written statement in the Methods section. This should explain that all work was conducted with the formal approval of the local human subject or animal care committees (institutional and national), and that clinical trials have been registered as legislation requires. Authors who do not have formal ethics review committees should include a statement that their study follows the principles of the Declaration of Helsinki.

Consent

All authors are required to follow the ICMJE requirements on privacy and informed consent from patients and study participants. Please confirm that any patient, service user, or participant (or that person's parent or legal guardian) in any research, experiment, or clinical trial described in your paper has given written consent to the inclusion of material pertaining to themselves, that they acknowledge that they cannot be identified via the paper; and that you have fully anonymised them. Where someone is deceased, please ensure you have written consent from the family or estate. Authors may use this Patient Consent Form, which should be completed, saved, and sent to the journal if requested.

Health and safety

Please confirm that all mandatory laboratory health and safety procedures have been complied with in the course of conducting any experimental work reported in your paper. Please ensure your paper contains all appropriate warnings on any hazards that may be involved in carrying out the experiments or procedures you have described, or that may be involved in instructions, materials, or formulae.

Please include all relevant safety precautions; and cite any accepted standard or code of practice. Authors working in animal science may find it useful to consult the International Association of Veterinary Editors' Consensus Author Guidelines on Animal Ethics and Welfare and Guidelines for the Treatment of Animals in Behavioural Research and Teaching. When a product has not yet been approved by an appropriate regulatory body for the use described in your paper, please specify this, or that the product is still investigational.

*** Original research (2800 – 3200 words/ 4-5 pages)**
*** Clinical Reviews (2400 words/ 3-4 pages)**
*** Drug Reviews (2400 words/ 3-4 pages)**
*** Case Studies (1800 words/ 3 pages)**
*** Scientific Letters (2400 words/ 3-4 pages)**
*** Letters to the Editor (400-800words]**

Title page
All articles must have a title page with the following information and in this particular order: Title of

the article; surname, initials, qualifications and affiliation of each author; The e-mail address of the corresponding author and at least 5 keywords.

Abstract
All articles should include an abstract. The structured abstract for an Original Research article should be between 200 and 230 words and should consist of four paragraphs labelled Background, Methods, Results, and Conclusions. It should briefly describe the problem or issue being addressed in the study, how the study was performed, the major results, and what the authors conclude from these results. The abstracts for other types of articles should be no longer than 230 words and need not follow the structured abstract format.

Keywords
All articles should include keywords. Up to five words or short phrases should be used. Use terms from the Medical Subject Headings (MeSH) of Index Medicus when available and appropriate. Key words are used to index the article and may be published with the abstract.

Acknowledgements
In a separate section, acknowledge any financial support received or possible conflict of interest. This section may also be used to acknowledge substantial contributions to the research or preparation of the manuscript made by persons other than the authors.

References
Cite references in numerical order in the text, in superscript format (Format> Font> Click superscript). Please do not use brackets or do not use the foot note function of MS Word.

In the References section, references must be typed double-spaced and numbered consecutively in the order in which they are cited, not alphabetically.

The style for references should follow the format set forth in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org) prepared by the International Committee of Medical Journal Editors. Abbreviations for journal titles should follow "Index *Medicus* format. Authors are responsible for the accuracy of all references. Personal communications and unpublished data should not be referenced. If essential, such material should be incorporated in the appropriate place in the text.

List all authors when there are six or fewer; when there are seven or more, list the first three, then ";et al."; When citing URLs to web documents, place in the reference list, and use the following format: Authors of document (if available). Title of document (if available). URL. (Accessed [date]).

The following are sample references:

1. Jun BC, Song SW, Park CS, Lee DH, Cho KJ, Cho JH. The analysis of maxillary sinus aeration according to aging process: volume assessment by 3-dimensional reconstruction by high-resolutional CT scanning. Otolaryngol Head Neck Surg. 2005 Mar; 132(3):429-34.
2. 2. Polgreen PM, Diekema DJ, Vandeberg J, Wiblin RT, Chen YY, David S, et al. Risk factors for groin wound infection after femoral artery catheterization: a case-control study. Infect Control Hosp Epidemiol [Internet]. 2006 Jan [cited 2007 Jan 5];27(1):34-7. Available from: http://www.journals.uchicago.edu/ICHE/journal/issues/v27n1/2004069/2004069.web.pdf.

More sample references can be found at: http://www.nlm.nih.gov/bsd/uniform_requirements.html

Tables
Tables should be self-explanatory, clearly organised, and supplemental to the text of the manuscript. Each table should include a clear descriptive title on top and numbered in Roman numerals (I, II, etc) in order of its appearance as called out in text. Tables must me inserted in the correct position in the text. Authors should place explanatory matter in footnotes, not in the heading. Explain in footnotes all non-standard abbreviations.

For footnotes use the following symbols, in sequence:*,†,‡,§,||,**,††,‡‡

Figures
All figures must be inserted in the appropriate position of the electronic document. Symbols, lettering, and numbering (in Arabic numerals e.g. 1, 2, etc. in order of appearance in the text) should be placed below the figure, clear and large enough to remain legible after the figure has been reduced. Figures must have clear descriptive titles.

Photographs and images
If photographs of patients are used, either the subject should not be identifiable or use of the picture should be authorised by an enclosed written permission from the subject. The position of photographs and images should be clearly indicated in the text. Electronic images should be saved as either jpeg or gif files. All photographs should be scanned at a high resolution (300dpi, print optimised). Please number the images appropriately.

Permission
Permission should be obtained from the author and publisher for the use of quotes, illustrations, tables, and other materials taken from previously published works, which are not in the public domain. The author is responsible for the payment of any copyright fee(s) if these have not been waived. The letters of permission should accompany the manuscript. The original source(s) should be mentioned in the figure legend or as a footnote to a table.

Review and action

Manuscripts are initially examined by the editorial staff and are usually sent to independent reviewers who are not informed of the identity of the author(s). When publication in its original form is not recommended, the reviewers' comments (without the identity of the reviewer being disclosed) may be passed to the first author and may include suggested revisions. Manuscripts not approved for publication will not be returned.

Ethical considerations
Papers based on original research must adhere to the Declaration of Helsinki on "Ethical Principles for Medical Research Involving Human Subjects"; and must specify from which recognised ethics committee approval for the research was obtained.

Conflict of interest

Authors must declare all financial contributions to their work or other forms of conflict of interest, which may prevent them from executing and publishing unbiased research. [Conflict of interest exists when an author (or the author's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her opinions or actions.]* *Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability. (Editorial) JAMA 2001: 286(10) The following declaration may be used if appropriate: "I declare that I have no financial or personal relationship(s) which may have inappropriately influenced me in writing this paper."

Submissions and correspondence
All submissions must be made online at http://www.editorialmanager.com/sajaa and correspondence regarding manuscripts should be addressed to:

The Editor, SAJAA, E-mail: toc@sajaa.co.za

Note: Ensure that the article ID [reference] number is included in the subject of your email correspondence.

Electronic submissions by post or via email
Authors with no e-mail or internet connection can mail their submissions on a CD to: SAJAA, PO Box 14804, Lyttelton Manor, 0140, Gauteng, South Africa.

All manuscripts will be processed online.

Article Publishing Charges
The South African Society of Anaesthesiologists is currently covering all APCs and authors will not be charged.