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Does self-inflation mechanism with minimal cuff pressure reduce tracheal mucosal damage? A scanning electron microscopy study in piglets

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Background and goal of study: Recent studies have shown that sevoflurane is able to ameliorate lung damage caused by inflammation in vivo and in vitro. This lead to the question whether this might be a general effect of volatile anaesthetics. Desflurane is a widely used volatile anaesthetic in daily practice, but only limited data regarding lung protection are available at the moment. In this study, we investigated for the first time the potential protective and inflammatory effects of desflurane in an in vitro model of acute lung injury with sevoflurane as reference gas.

Material and methods: Monolayers of a cell line of alveolar epithelial cells (AEC, L2 cells) were stimulated for 2 hours with 20 μg/ml lipopolysaccharide (LPS), followed by a 2 h co-exposure to a CO2-air-mixture with or without 1 of MAC desflurane or sevoflurane, respectively. mRNA levels of monocyte chemoattractant protein-1 (MCP-1) and cytokine induced neutrophil chemoattractant protein-1 (CINC-1) were assessed at 4 h via qRT-PCR. Chemotactic activity of supernatants regarding neutrophil recruitment was assessed. Student’s t-test was performed. For all analyses, we considered p < 0.05 to be statistically significant.

Results and discussion: When treated with volatiles, mRNA-expression for MCP-1 was reduced by 33.1% ± 22.1 in the desflurane/LPS group and by 53.3% ± 13.8 in the sevoflurane/LPS group compared to untreated inflamed cells. The level of CINC-1 mRNA was also significantly lower in the desflurane/LPS (-46.9% ± 22.2) and sevoflurane/LPS group (-47.2% ± 23.2) compared to air/LPS.

Immunomodulating effect of desflurane in endotoxin-injured alveolar epithelial cells

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Conclusions: Desflurane seems to have a similar anti-inflammatory potential as previously shown with sevoflurane. Both volatile anaesthetics influence the inflammatory cascade by interfering with the same molecular pathway. This is a crucial step in acute lung injury for subsequent upregulation of inflammatory mediators. These data underline the hypothesis that the anti-inflammatory action of volatile agents is due to a group effect.

References
permeability were assessed by measuring the concentration of total protein in bronchoalveolar lavage fluid. Statistical analysis was performed using an analysis of variance and the Student-Newman-Keuls test.

Results: Compared to normal tidal volume ventilation, high tidal volume ventilation causes a remarked increase in SrC kinase activation, caveolin-1 phosphorylation and vascular permeability. Ropivacaine inhibited these effects (fig. 1).

Conclusion: We demonstrated the important role of Src-mediated caveolin-1 phosphorylation in the regulation of VILI. Importantly, ropivacaine attenuated VILI-induced vascular hyperpermeability via suppression of SrC kinase activation and caveolin-1 phosphorylation. These findings suggest that intratracheal instillation of local anesthetic ropivacaine may be a new direction for its potential therapeutic application in VILI.

Figure 1

In vitro exposure of human fibroblasts and human osteoblasts to the NSAIDs diclofenac and ketorolac is cytotoxic

José A. Aguirre1, Alain Borgeta, Melanie Haslerc, Caroline Fedderb, Beatrice Beck-Schimmera, 2
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Background: Diclofenac and Ketorolac are routinely used to control postoperative pain using infusion techniques. However, sparse data exist focusing on the possible interaction of these NSAIDs with nervous system and recurrently associated with a positive shift toward nervous system excitability. Peripheral nerve activity is mainly carried by voltage-gated sodium channel Nav1.7 expressing in the nervous system and recurrently associated with a positive shift toward nervous system excitability. Peripheral nerve activity is mainly carried by voltage-gated sodium channels (VGSC), with Nav1.7 isoform being an important candidate since loss of function mutations of its gene is associated with congenital inability to experience pain. Interestingly, ubiquitin ligases from the Nedd4-2 family are well known proteins that regulate the turnover of many membrane proteins such as VGSC and we showed Nedd2-2 is downregulated in experimental models of chronic pain. The aim of this study was to investigate the importance of Nedd2-2 in the modulation of Nav1.7 at the membrane.

Methods: In vitro: whole cell patch clamp on HEK293 cell line stably expressing Nav1.7. The peak current of INa was assessed by investigating the effect of its co-expression with Nedd4-2 on INa. Biotinylation of cell surface was used to isolate the currents was assessed by investigating the effect of its co-expression with Nedd4-2 on INa. Biotinylation of cell surface was used to isolate

Results of Nedd4-2 in the modulation of Nav1.7 at the membrane.

Regulation of the voltage-gated sodium channel Nav1.7 by ubiquitin ligase Nedd4-2

Cédric Laedermann1, Matthieu Cachemaillé, Hugues Abrié, Isabelle Decosterd
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Background and aim: Neuropathic pain (NP) is a frequent and disabling disorder occurring as a consequence of a direct lesion of the nervous system and recurrently associated with a positive shift toward nervous system excitability. Peripheral nerve activity is mainly carried by voltage-gated sodium channels (VGSC), with Nav1.7 isoform being an important candidate since loss of function mutations of its gene is associated with congenital inability to experience pain. Interestingly, ubiquitin ligases from the Nedd4-2 family are well known proteins that regulate the turnover of many membrane proteins such as VGSC and we showed Nedd2-2 is downregulated in experimental models of chronic pain. The aim of this study was to investigate the importance of Nedd2-2 in the modulation of Nav1.7 at the membrane.

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Figure 1: Effects of high tidal volume ventilation (HTV) and ropivacaine on pulmonary microvascular permeability. *P<0.05 vs. control. †P<0.05 vs. HTV

Figure 5

In vitro exposure of human fibroblasts and human osteoblasts to the NSAIDs diclofenac and ketorolac is cytotoxic

José A. Aguirre1, Alain Borgeta, Melanie Haslerc, Caroline Fedderb, Beatrice Beck-Schimmera
1Division of Anesthesiology, Balgrist University Hospital, Zürich, Switzerland; 2Institute of Physiology, Zurich Center for Integrative Human Physiology, University of Zurich, Switzerland; *Institute of Anesthesiology, University Hospital Zurich, Hof E 111, Rämistrasse 100, CH-8091 Zurich, Switzerland.

Background: Diclofenac and Ketorolac are routinely used to control postoperative pain using infusion techniques. However, sparse data exist focusing on the possible interaction of these NSAIDs with nervous system and recurrently associated with a positive shift toward nervous system excitability. Peripheral nerve activity is mainly carried by voltage-gated sodium channel Nav1.7 expressing in the nervous system and recurrently associated with a positive shift toward nervous system excitability. Peripheral nerve activity is mainly carried by voltage-gated sodium channels (VGSC), with Nav1.7 isoform being an important candidate since loss of function mutations of its gene is associated with congenital inability to experience pain. Interestingly, ubiquitin ligases from the Nedd4-2 family are well known proteins that regulate the turnover of many membrane proteins such as VGSC and we showed Nedd2-2 is downregulated in experimental models of chronic pain. The aim of this study was to investigate the importance of Nedd2-2 in the modulation of Nav1.7 at the membrane.

Methods: In vitro: whole cell patch clamp on HEK293 cell line stably expressing Nav1.7. The peak current of INa was assessed by investigating the effect of its co-expression with Nedd4-2 on INa. Biotinylation of cell surface was used to isolate
membrane-targeted Nav1.7. Furthermore, as the interaction between Nedd4-2 and Nav isoforms was previously reported to rely on an xPPxY sequence (PY-motif), we mutated this latter to study its impact in vivo these preliminary data.

Reference Values for Central Hyper- and Hyposensitivity of Mechanical and Thermal Pain Tests in a Pain-Free Population

Alban Y. Neziri, Pasquale Scaramozzino, Ole K. Andersen, Lars Arendt-Nielsen, Michele Curatolo

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Background: Quantitative sensory tests are widely used in human research to evaluate the effect of analgesics and explore altered pain mechanisms, such as central hypersensitivity and hypalgesia. In order to apply these tests in clinical practice, knowledge of reference values is essential. This study was designed to determine the reference values of pain thresholds for mechanical and thermal stimuli in a pain-free population.

Methods: 300 healthy subjects (152 males and 148 females, 18–80 years old) were tested. Pain detection and pain tolerance thresholds to pressure, heat and cold were determined at three body sites: 1) 2nd toe (for pressure) and lateral aspect of the leg (for heat and cold tests), 2) low back (LbA), and 3) supracapular region (SR). The influence of gender, age, height, weight, body mass index, body side of testing, depression, anxiety, catastrophizing and parameters of Short-Form 36 were analyzed by multiple regressions. Quantile regressions were performed to define the 5th, 10th, 25th and 75th, 90th and 100th percentiles as reference values for pain hypersensitivity and hypalgesia. Gender, age and/or the interaction of age with gender were the only variables that consistently affected the pain measures. Therefore, reference values were stratified by gender and age. Here we present a selection of the data, i.e. the 10th and 90th percentiles of pain detection thresholds (determination of central hypersensitivity) for pressure and heat stimulation. The 10th percentile of pressure pain detection threshold for 2nd toe, LbA and SR for age group 20–49 years were: for females 122, 143 and 123 kPa, respectively; for males 125, 227 and 168, respectively. Concerning heat pain detection thresholds, the 10th percentile for LbA and SR were: for females 39.6, 38.1 and 38.5 °C; for males 40.0, 38.3 and 39.0 °C, respectively.

Conclusions: Reference values of parameters related to pressure and thermal pain stimuli were defined. These reference values can be clinically applied for detecting abnormal pain reactions in individual patients. They may be utilized as a diagnostic tool for central sensory pathways and a prognostic tool to predict the course of the disease or screen patients for studies on mechanism-based treatment strategies.

Key words: Reference values; pain thresholds; pressure; heat; central hypersensitivity; hypalgesia

The Importance of Multi-Modal Pain Assessment: Factor Analysis of Responses to Electrical, Thermal, and Mechanical Painful Stimuli

Alban Y. Neziri, Michele Curatolo, Eveline Nunesch, Pasquale Scaramozzino, Ole K. Andersen, Lars Arendt-Nielsen, Peter Jun

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Background: During the last decade, a multi-modal approach has been established in human experimental pain research for assessing pain thresholds/responses to various experimental pain modalities. Studies have concluded that differences in responses to pain stimuli are mainly related to variation between individuals rather than variation in response to different stimulus modalities.

Methods: In a factor analysis of 300 consecutive volunteers (152 males, 148 females) who underwent tests with different experimental pain modalities, it was determined whether responses to different pain modalities represent different pathways in a pain-free population. Volunteers underwent single painful electrical stimulation, repeated painful electrical stimulation (temporal summation), test for reflex receptive field, pressure pain stimulation, heat pain stimulation, cold pain stimulation and a cold pressor test (ice water test).

Results: Five distinct factors were found representing responses to five distinct experimental pain modalities: pressure, heat, cold, electrical stimulation and reflex receptive fields. Each of the factors explained approximately 12 to 23% of the observed variance, and the factors cumulatively explained 89% of the variance. The correlation between the five factors was near null (median rho 0.00, range 0.04 to 0.05), with 95% confidence intervals for pair-wise correlations between two factors excluding any relevant correlation. Results were almost similar for analyses stratified according to gender and age. Conclusions: Responses to different experimental pain modalities represent different pathways and should be assessed separately in future clinical and pharmacological studies. This will further increase our understanding of the complexity of mechanisms leading to chronic or acute pain and its modification in experimental settings and clinical practice.

Acknowledgments: This work was funded by the Swiss Science National Foundation, the Danish Research Council for Technology and Production and the Scientific Funds of the University Department of Anaesthesiology and Pain Therapy of the University of Bern. CTU Bern is supported by the Swiss National Science Foundation.

Key words: Factor analysis; Pain Threshold; Pain assessment; Experimental pain models

Impact of local anaesthetic injection speed on serum levels of bupivacaine and therapeutic safety in piglets

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Objectives: Systemic local anaesthetic (LA) toxicity due to inadvertent intravascular injection of LA is a rare but potentially catastrophic complication of regional anaesthesia. Strategies such as early recognition of intravascular injection and approaches to increase therapeutic safety are therefore required. This study aimed to investigate the impact of intravascular injection speed of bupivacaine on LA induced cardio-vascular morbidity and mortality in piglets.

Materials and methods: In 55 neonatal pigs, anaesthetised with sevoflurane, endotracheally intubated, and artificially ventilated, blood was drawn for the assessment of acid base state and plasma protein concentration. Then, bupivacaine was continuously infused through a central venous catheter at a rate of 1 mg/kg/min (group A) or 4 mg/kg/min (group B) and 16 mg/kg/min (group C) until mean arterial pressure (MAP, invasively measured) was 50% of initial value. Thereafter bupivacaine infusion was stopped and spontaneous course of haemodynamic observed. Time start-stop of bupivacaine infusion, amount of bupivacaine infused, bupivacaine plasma level at infusion stop, number of spontaneous survivors and time from bupivacaine stop to circulatory arrest was recorded. Data are compared using Kruskal-Wallis and Mann-Whitney tests. P < 0.05 data is median (range).

Results: There were no differences in weight, protein plasma level and pH among the three groups. MAP 50% was shortest in group C (63 s), longer in group B (119 s) and longest delayed in group A (297 s) (p < 0.001). Total amount of bupivacaine infused until MAP decreased to 50% of initial value was 4.95 (3.06–24.36) mg/kg in group A, 7.82 (5.45–12.91) mg/kg in group B and 17 (12–20) mg/kg in group C (p < 0.001). Bupivacaine plasma levels at MAP 50% were 53.8 (40.6–101.9) mg/L in group A, 155.9 (83.1–686.1) mg/L in group B and 438.9 (245–693) mg/L in group C (p < 0.001). Five of 15 piglets in group
A spontaneously recovered, while ingroup B and C all animals died from pulseless electric activity or asystole within 120 and 20.5 s respectively (p <0.001).

**Conclusion:** Higher infusion rates of bupivacaine coincide with much higher plasma bupivacaine levels when compared to absolute amount infused. This is most likely caused by reduced distribution time. Slow higher plasma bupivacaine levels when compared to absolute amount infused. This is most likely caused by reduced distribution time. Slow.

**Discussion:** Despite overwhelming results large numbers are often needed to detect rare complications or side effects. If all applications from any participating hospitals, even with small numbers, are registered via this website (www.soscisurvey.de/ultiva) a large datapool can be collected in a short time. This allows constant adjustment of the procedure as well a quick feedback in case adverse affects should appear.

**Conclusion:** The routine use of Remifentanil PCA in labour is a safe method with excellent acceptance of parturients, midwifes, obstetricians and anaesthetists. Furthermore it reduces costs, because less invasive analgesic methods are needed. The webbased data collection offers a quick nationwide launch together with excellent quality management.

**References**

**Patients’s satisfaction concerning postoperative analgesia after caesarean section: a comparison of 4 alternative analgesic regimen**

**Introduction:** Different routes of postoperative analgesia may be used after cesarean section: systemic, spinal or epidural [1]. Although the efficacy of these alternative analgesic regimen has already been studied [2, 3], very few studies have compared patients’ satisfaction between them.

**Methodology:** After ethical committee acceptation, 100 ASA 1 patients scheduled for an elective cesarean section were randomized in 4 groups. After a standardized spinal anesthesia (hyperbaric bupivacaine 10 mg and fentanyl 20 μg), each group had a different postoperative analgesic regimen:

- **Group 1:** oral paracetamol 4x1 g/24 h, oral ibuprofene 3x600 mg/24 h and subcutaneous morphine on need (0.1 mg/kg 6x24 h)
- **Group 2:** intrathecal morphine (100 μg) and then same as Group 1.
- **Group 3:** oral paracetamol 4x1 g/24 h, oral ibuprofene 3x600 mg/24 h and PCEA with fentanyl 5 μg/ml epidural solution
- **Group 4:** oral paracetamol 4x1 g/24 h, oral ibuprofene 3x600 mg/24 h and PCEA with bupivacaine 0.1% and fentanyl 2 μg/ml epidural solution.

After 48 hours, a specific satisfaction questionnaire was given to all patients which permitted to obtain 2 different scores concerning postoperative analgesia: a global satisfaction score (0–10) and a detailed satisfaction score (5 questions scored 0–10 with a summative score of 0–50). Both scores, expressed as mean ± SD, were compared between the 4 groups with a Kruskall-Wallis test and between each group with a Mann-Whitney test. A P-value <0.05 was considered significant.

**Results:**

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<th>Satisfaction scores</th>
<th>Gr. 1 (n = 25)</th>
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<td>global (0–10)</td>
<td>8.2 ± 1.2</td>
<td>9.0 ± 1.0</td>
<td>7.8 ± 2.1</td>
<td>6.5 ± 2.5</td>
</tr>
<tr>
<td>detailed (0–50)</td>
<td>40 ± 6</td>
<td>43 ± 5</td>
<td>38 ± 6</td>
<td>34 ± 8</td>
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| P-value          | 0.0006        | 0.0002        |

**Conclusion:** Satisfaction scores were significantly better in patients who received a systemic postoperative analgesia only (Groups 1 and 2) compared to patients who received systemic and epidural postoperative analgesia (Groups 3 and 4). The best scores were achieved with the combination of intrathecal morphine and multimodal systemic analgesia (Group 2) which allowed early ambulation without significant pain. Patients treated with postoperative epidural analgesia with combined local anesthetics and opioids (Group 4) obtained the worse scores (more restrictive nursing with less mobility, frequent asymmetrical block with insufficient analgesia on one side and motor block on the other).

**References**
ECG alterations in children during intravenous application of three different test solutions for regional anaesthesia

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Background: Animal studies have shown that ECG alterations caused by intravenous injection of a local anesthetic test dose are caused by epinephrine [1]. The aim of this study was to elucidate whether these ECG findings in small non-anesthetized pigs provoked by a test dose of epinephrine, bupivacaine and their combination are reproducible in paediatric patients.

Methods: With Hospital Ethics Committee approval and written parental/patient consent, paediatric patients from birth up to 16 years of age undergoing general anaesthesia were randomized into three groups. After induction of general anaesthesia using sevoflurane, muscle paralysis and tracheal intubation 0.2 ml/kg of the corresponding test solution was rapidly intravenously administered: group 1 received bupivacaine 0.125%, group 2 bupivacaine 0.125% plus epinephrine 1:200000, and group 3 plain epinephrine 1:200000. The ECG was recorded and analysed later on by a blinded assessor for alterations in heart rate and T-wave elevation. An increase of heart rate of ≥10 bpm and an increase in T-wave of ≥25% respectively above baseline value were considered as a positive result [2].

Results: So far 26 paediatric patients aged 0.2–14.8 yrs (median 5.5 yrs) weighing 4.1–58 kg (19 kg) were studied. After intravenous injection of 0.2 ml/kg test solution, an increase in heart rate of ≥10 bpm was found in 6 (36%) patient of group 1 (n = 7), in 6 (78%) of group 2 (n = 9) and in 6 (78%) of group 3 (n = 9). T-elevation was found in 0 patient of group 1 and in all patients of group 2 (n = 9) and 3 (n = 10).

Discussion and conclusion: The preliminary findings of this study demonstrate that in children ECG alterations caused by intravenous injection of a local anesthetic (LA) test dose are caused by epinephrine. The manifestation of elevated T-wave seems to be more sensitive than increase in heart rate to detect intravenous injection of a LA test dose with epinephrine. The intravenous injection of plain bupivacaine alone cannot be detected by ECG. Based on our study results, an epinephrine containing LA solution and ECG control must be used for the reliable detection of inadvertent LA injection in children.

References

The performance of the pediatric-sized i-gel™ compared with the Ambu Aura Once™ Laryngeal Mask in anesthetized and ventilated children

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Goal of study: The pediatric i-gel (Intersurgical Ltd, Wokingham, Berkshire, UK) is a downsized adult i-gel which features a gastric channel (except size 1). The aim of this prospective RCT was to compare the performance of the widely used Ambu Aura Once mask (Ambu A/S, Ballerup, Denmark) with the i-gel in children, assuming equal success and airway seal pressure.

Materials and methods: With IRB approval and informed consent we included 201 children of both genders, aged 0–17 years, 5–50 kg, ASA physical status I–II, scheduled at the University Hospital of Bern for elective surgery under general anaesthesia. Block randomization according to children’s weight was performed after induction of anaesthesia. Primary outcome variables were insertion success and airway leak pressure; secondary outcomes included time to sufficient ventilation, fiberoptic glottic view, success of gastric catheter insertion with the i-gel, and adverse events.

Results and discussion: Demographic data of the 201 children did not differ between groups (age 6.2 ± 3.8 years, p = 0.84; weight 24.5 ± 11.2 kg, p = 0.904; ASA physical status, p = 0.920). Male:female ratio was 147:54 and gender between the groups (p = 0.192); more boys were included due to the high number of circumcisions. The Ambu was inserted in 99 and the i-gel in 102 children. In 44 of the 95 successfully inserted i-gels (46%), the device had the tendency to slide out and needed to be taped down to maintain sufficient airway leak pressure while this was not necessary in the 97 successful Ambu masks (p <0.001). There were no major side effects with both devices.

Table 1
Supraglottic mask performance in 201 children.

<table>
<thead>
<tr>
<th>Mask Type</th>
<th>Ambu Aura Once (n = 99)</th>
<th>i-gel (n = 102)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success n (%)</td>
<td>97 (98)</td>
<td>95/102 (93)</td>
<td>0.187</td>
</tr>
<tr>
<td>Airway Leak Pressure (cm H2O)</td>
<td>19 ± 4</td>
<td>21 ± 5</td>
<td>0.001</td>
</tr>
<tr>
<td>Insertion time (sec)</td>
<td>23 ± 8</td>
<td>27 ± 11</td>
<td>0.045</td>
</tr>
<tr>
<td>Fiberoptic view grade 1/2/3/4/ missing n (%)</td>
<td>85/8/1/0/3 (88/8/1/0/3)</td>
<td>84/9/2/0/0 (89/9/2/0/0)</td>
<td>0.737</td>
</tr>
<tr>
<td>Gastric tube insertion successful n (%)</td>
<td>Not possible</td>
<td>92/95 (87)</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

* 1 full view of glottis, 2 = partial view, 3 = only epiglottis visible, 4 = no glottic structures visible; grade 3 and 4 matched for statistical analysis. n.a. = not applicable.

Conclusion: The pediatric-sized i-gel is suitable for ventilation of anesthetized children and offers the additional advantage of gastric access. Compared to the Ambu Aura Once, it shows higher airway leak pressures, but longer insertion times. However, especially in small children, the i-gel has the tendency to slide out and often needs to be taped down.
Thoracic paravertebral puncture and placement of catheters in human cadavers: where do catheters go?

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Introduction: Paravertebral regional anaesthesia is used to treat pain after thoracic, cardiac, breast and upper abdominal surgery, avoids epidural space puncture and may therefore reduce possible injury of the thoracic spinal cord. The aim of this anatomical study was: 1. To develop an ultrasound-guided approach to the paravertebral space; 2. To investigate a possible discrepancy between needle tip and final catheter tip position.

Methods: 6 cadavers were studied with Institutional approval for the procedure. A total of 36 paravertebral punctures using an 18 G Tuohy needle were performed (three punctures on each side of the thoracic vertebral column). The needle tips were advanced under real-time ultrasound guidance slightly lateral and deeper to the lateral border of the inferior articular process of a vertebra (which is easily visualized using ultrasound) in an out-of-plane approach. The position of the needle tip was controlled by performing the first CT-scan. After placement of the catheters through the needles – the catheter insertion depth was randomly varied between 1 and 3 cm – the position of the catheter tips were again assessed by a second CT-scan and image reconstructions.

Results: The first CT-scan showed that all needle tips were correctly positioned into the paravertebral space, close to the intervertebral foramen by using ultrasound guidance. One catheter could not be advanced beyond the needle tip despite turning the axis of the needle and further injections of saline to dilate the space. All 35 other catheters could be advanced through the needles. The second CT-scan showed a discrepancy between needle tip position and final catheter tip position. 25 catheter tips were found subpleurally at the level of the vertebral body or prevertically; 5 catheters remained close to the intervertebral foramen. 2 catheters were completely misplaced into the pleural space.

Conclusion: We developed a novel ultrasound approach to precisely place the tip of the needle into the paravertebral space close to the emerging intercostal nerves under real-time ultrasound guidance. Next, the pigtail catheters were blindly introduced through the needles until the needles and the needles were left in place. 60 needles and catheters were placed, three on each side of the thoracic vertebral column. To detect the needle tip and the exact catheter location a CT-scan of the entire thorax was performed.

Results: Catheter placement was accomplished without difficulty in 58 cases. In 2 instances, the catheters could only be introduced after a new puncture. CT-evaluation revealed that only 3 catheters failed to form a coil after placement. 52 catheter tips were found to lie in the paravertebral space, either close to the intervertebral foramen, slightly lateral but subpleurally, or slightly anterior to the intervertebral foramen but also subpleurally. 8 catheters were in the paravertebral space but anteriorly, at the level of the sympathetic trunk. No catheter was misplaced into the epidural, pleural or the prevertebral spaces. The mean distance of the catheter tips to the needle tips was 0.8 cm (SD 0.5).

Novel Catheters For Regional Anesthesia – Pigtail Catheter for Continuous Sciatic Nerve Block

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Introduction: The use of continuous peripheral nerve blocks for pain therapy after orthopedic surgery provides sustained analgesia, while potentially minimizing the need for opioids. A major concern with the use of continuous peripheral nerve blocks is the difficulty to place the catheter tips close enough to the nerves to accomplish effective analgesia. The final position of the catheter tip is not predictable and can be inadequate in 10–50% of cases (Capdevila X, Aneseth Analg 2002). The use of ultrasound guidance to precisely place needles adjacent to nerves is undisputed. However, ultrasound is less effective regarding catheter positioning. The explanation for this unsatisfactory performance during placement may lie in the catheter construction material; currently used catheters are stiff and designed to avoid kinking and are often leaving the initial place of insertion. Therefore, we developed a soft pigtai catheter which coils as it is advanced beyond the needle tip, thus allowing the catheter tip to remain close to the initial needle tip position.

Methods: 10 cadavers in legal custody of the Institute of Anatomy of Bern, have been studied with institutional approval. First, Tuohy needles were placed into the thoracic paravertebral space close to the emerging intercostal nerves under real-time ultrasound guidance. Next, the pigtail catheters were blindly introduced through the needles and the needles were left in place. 60 needles and catheters were placed, three on each side of the thoracic vertebral column. To detect the needle tip and the exact catheter location a CT-scan of the entire thorax was performed.

Results: Catheter placement was accomplished without difficulty in 58 cases. In 2 instances, the catheters could only be introduced after a new puncture. CT-evaluation revealed that only 3 catheters failed to form a coil after placement. 52 catheter tips were found to lie in the paravertebral space, either close to the intervertebral foramen, slightly lateral but subpleurally, or slightly anterior to the intervertebral foramen but also subpleurally. 8 catheters were in the paravertebral space but anteriorly, at the level of the sympathetic trunk. No catheter was misplaced into the epidural, pleural or the prevertebral spaces. The mean distance of the catheter tips to the needle tips was 0.8 cm (SD 0.5).

Conclusion: The combination of an ultrasound guided approach together with a novel pigtai catheter might be the solution to provide an exact catheter placement into the paravertebral space. This is mandatory for an effective and long lasting postoperative analgesia during continuous infusion of local anesthetics.
Tropisetron blocks analgesic action of acetaminophen – a human pain model study

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Background: The mechanism underlying the analgesic action of acetaminophen is still unclear. Therefore we investigated a possible interaction of acetaminophen with central serotogenic pathways. The effects of acetaminophen, tropisetron, the combination of both drugs, and saline on pain perception and central sensitization in healthy volunteers were compared.

Methods: Sixteen healthy volunteers were included in this randomized, double-blind, placebo-controlled, cross-over study. Intracutaneous electrical stimulation (46.1 ± 19.1 mA) induced acute pain (numeric rating scale, 6 of 10) and stable areas of hyperalgesia and allodynia. Pain intensities and areas of hyperalgesia and allodynia were regularly assessed before, during, and after a 15 min infusion of acetaminophen, tropisetron, the combination of both drugs, and saline. Acetaminophen concentration measurements were performed to rule out any pharmacokinetic interaction.

Results: Both acetaminophen and tropisetron led to decreased pain ratings as compared to saline. However, when acetaminophen and tropisetron were administered simultaneously, the pain ratings were not affected. There was no significant difference in the evolution of the hyperalgesic and allodynic areas during the study period between the study groups. Acetaminophen serum levels were not significantly different when associated with tropisetron, although we observed a trend to lower acetaminophen concentrations when both drugs were concurrently administered.

Conclusion: While no combination of acetaminophen and tropisetron showed no analgesic action, either drug on its own led to decreased pain ratings as compared to saline.

Postoperative Cognitive Dysfunction (POCD) and Inflammatory Markers in Elderly Patients

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Introduction: Particularly in elderly patients, the brain responds to a systemic inflammatory response with an increased production of systemic inflammatory response with an increased production of anticholinergic drugs are associated with impaired cognitive functions [1]. In the perioperative phase many substances with anticholinergic effects are administered and disturbed cholinergic transmission is a hypothetical cause of postoperative cognitive dysfunction (POCD). Serum anticholinergic activity (SAA; pmol/ml) may be measured as a summary marker of anticholinergic activity in an individual patient's blood. We hypothesised that an increase in SAA from preoperatively to one week postoperatively is associated with POCD in elderly patients.

Methods: Thirty-two patients aged >65 years undergoing elective major surgery under standardized general anaesthesia (thiopental, sevoflurane, fentanyl) were investigated. Cognitive functions were measured preoperatively and 7 days postoperatively using the extended version of the Consortium to Establish a Registry for Alzheimer’s Disease – Neuropsychological Assessment Battery. POCD was defined as a postoperative decline >1 z-score in at least 2 cognitive domains. SAA was measured preoperatively and 7 days postoperatively at the time of cognitive testing.

Results: 50% of the investigated patients developed POCD. There were no statistically significant differences between patients with and without POCD regarding the duration of anaesthesia, SAA preoperatively (median (range) 1.0 (0.3 to 5.0) vs 1.5 (0.4 to 5.0), SAA 7 days postoperatively (median (range) 1.3 (0.1 to 7.0) vs 1.4 (0.6 to 5.5) or changes in SAA (median (range) 0.1 (−1.6 to 2.5) vs 0.2 (−1.4 to 2.8). The variability of SAA in individual patients was considerable and marked changes in SAA between the two examinations were observed in some patients. However, there was no significant relationship between changes in SAA and changes in cognitive function.

Conclusion: In this preliminary analysis of a small group of patients, changes in SAA in the perioperative phase were highly variable. SAA was not associated with POCD suggesting that POCD is not simply caused by anticholinergic drugs administered in the perioperative phase. A further analysis of a larger group of patients is in progress.

References
1 Ancelin ML, et al. BMJ. 2006;332:455.

Effects of von Willebrand syndrome type IIA on postoperative bleeding in patients undergoing aortic valve replacement

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Introduction: Acquired von Willebrand syndrome type IIA describes the loss of the largest von Willebrand factor multimers and is frequently found in patients with severe aortic stenosis [1]. We hypothesized that patients undergoing aortic valve replacement with von Willebrand syndrome type IIA will have increased postoperative bleeding due to impaired primary haemostasis.

Methods: With written informed consent we included 30 consecutive patients with severe aortic stenosis defined as valve orifice area <1.0 cm² in this preliminary analysis. We performed von Willebrand factor multimer analysis and measured plasma von Willebrand factor antigen and collagen binding activity by ELISA immediately before and on the first day after surgery. In all patients, postsurgical blood loss from mediastinal drainages was documented after 3, 6, 12 and 24 hours.

Interpretation: In this small group of patients, high IL-6 values postoperatively were associated with POCD supporting a role for systemic inflammation in the development of POCD. In patients with POCD, duration of anaesthesia was significantly longer, and intraoperative blood losses were larger. These risk factors will need to be confirmed in a larger group of patients. The difference in length of stay may be indicative of postoperative complications, which have been linked to POCD earlier.

Supported by SNF Grant 32003B-121956

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NO POCD (n = 14)</th>
<th>POCD (n = 17)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (mg/dl) preop.</td>
<td>4.0 [1.0–24.5]</td>
<td>4.2 [0.3–36.2]</td>
<td>0.6</td>
</tr>
<tr>
<td>2 days postop.</td>
<td>223 [20–318]</td>
<td>98 [4.5–384]</td>
<td>0.07</td>
</tr>
<tr>
<td>7 days postop.</td>
<td>58 [15–147]</td>
<td>44 [11–148]</td>
<td>0.2</td>
</tr>
<tr>
<td>IL-6 (U/ml) preop.</td>
<td>2 [2–28.1]</td>
<td>2 [2–73]</td>
<td>0.8</td>
</tr>
<tr>
<td>2 days postop.</td>
<td>56 [17–315]</td>
<td>20 [2–123]</td>
<td>0.009</td>
</tr>
<tr>
<td>7 days postop.</td>
<td>9 [2–77]</td>
<td>4 [2–16]</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Results: Mean age in the enrolled patients (15 male and 15 female) was 74 ± 9 years (range, 58–88 years). Based on the preoperative multimer analysis, von Willebrand syndrome type IIA was diagnosed in 25 (81%) patients. In the preoperative analysis, collagen binding and von Willebrand factor antigen activity were reduced in 15 patients (50%) and 3 (10%) patients, respectively. On the first day after surgery, multimer analysis, von Willebrand factor antigen activity, and collagen-binding activity were already normalized in all patients. Cumulative postoperative blood loss was 120 ± 150 ml (mean ± SD) after 3 hours, 210 ± 215 ml after 6 hours, 300 ± 285 ml after 12 hours, and 425 ± 315 ml after 24 hours. Blood loss of more than 1000 ml after the first 24 hours was found in two patients (6%), both of them had a loss of the largest von Willebrand factor multimers. No patient required re-exploration for massive bleeding.

Conclusion: Von Willebrand syndrome type IIA was common in patients with aortic stenosis but normalized within 24 hours of aortic valve replacement, and it did not cause increased postoperative bleeding due to impaired primary haemostasis. Despite these findings in our small patient population, von Willebrand syndrome type IIA has to be taken into consideration when massive postoperative bleeding occurs in patients with aortic stenosis in whom other reasons for impaired haemostasis have been excluded.

Reference

Do Patients with Postoperative Thoracic Epidural Analgesia Need an Indwelling Transurethral Catheter after Thoracic Surgery?


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Background: In contrast to our expectations, we found in a previous study that thoracic epidural analgesia (TEA) was effective in the segments T4-T11 for postoperative pain management after open renal surgery significantly impaired bladder function with decreased detrusor contractility and increased postvoid residuals under urodynamic assessment. These findings suggest that postvoid residual urine volumes should be monitored under TEA or a transurethral catheter left in place. Here we evaluated the effect of TEA on bladder emptying pre- and postoperatively using ultrasound in patients with T4/5 or T5/6 between the segments T4-T8 in patients undergoing thoracotomy.

Conclusion: The median postvoid residual did not change significantly pre- and postoperatively (0 ml (0–95) vs 0 ml (0–430), P = 0.09). However, a significant decrease in bladder capacity at strong desire to void and voided volumes was observed (P <0.01). Of the 3 male patients with an initial IPSS >3 and ≤7, all developed a postvoid residual >100 ml (140, 310 and 430 ml), which required an indwelling catheter.

Conclusions: As observed in our previous study, we found a decrease in the voided volume. However, the majority of patients under TEA after thoracotomy had normal postvoid residuals and did not need a transurethral catheter. Our findings further suggest that patients with an IPSS >3 should be closely monitored postoperatively as they may be at risk of developing a significant postvoid residual under TEA.

Nedd4-2 ubiquitin ligase: a contributor to experimental neuropathic pain?

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1Brain Mind Institute, EPFL, Lausanne; 2Department of Clinical Research, University of Bern, Bern, Switzerland

Background: Neuropathic pain is associated with altered expression of voltage-gated sodium channels (VGSCs) leading to peripheral nerve hyperexcitability. Interestingly, in cell expression systems, the ubiquitin ligase Nedd4-2 regulates the cell membrane density of the most abundant peripheral and pain-related VGSC, namely Nav1.7, and decreases its sodium current. Yet nothing is known about the involvement of Nedd4-2 in nociception and chronic pain. Therefore, the goal of this study is (i) to characterize Nedd4-2 and Nav1.7 expression in an experimental model of neuropathic pain (ii) to design by viral vector-mediated gene therapy an approach to depic the implication of Nedd4-2 in chronic pain.

Methods: Western Blot and immunohistochemistry experiments detecting Nav1.7 and Nedd4-2 were performed in rodent DRGs 3 days after spared nerve injury (SNI). For the viral vector-mediated gene therapy, a recombinant Adeno-Associated Virus (rAAV2/6) was followed 2 weeks after SNI surgery. Data are generated expressing the Nedd4-2 gene. Intrathecal injection of rAAV was able to counteract the colocalizing with markers of small nociceptive neurons. Furthermore, Nav1.7 are largely expressed in overlapping cell populations, chiefly colocalizing of small nociceptive neurons. Furthermore, we report that intrathecal injection of rAAV can be used to evaluate the reversal of Nedd4-2 expression in SN animals.

Results: Intrathecal injection of rAAV is able to counteract the colocalizing with markers of small nociceptive neurons. Furthermore, are largely expressed in overlapping cell populations, chiefly western-blot analysis. In addition, we show that Nedd4-2 and Nav1.7 are largely expressed in overlapping cell populations, chiefly colocalizing of small nociceptive neurons. Furthermore, we report that intrathecal injection of rAAV can be used to evaluate the reduction of Nedd4-2 expression in SN animals.

Conclusions: As observed in our previous study, we found a decrease in the voided volume. However, the majority of patients under TEA after thoracotomy had normal postvoid residuals and did not need a transurethral catheter. Our findings further suggest that patients with an IPSS >3 should be closely monitored postoperatively as they may be at risk of developing a significant postvoid residual under TEA.

Conclusion: Our results indicate that Nedd4-2 is mainly expressed in nociceptors and downregulated after nerve injury. Moreover, our data suggest that the reduction of Nedd4-2, after nerve injury, may modulate Nav1.7 activity and contribute to hyperexcitability in neuropathic pain. A normal level of Nedd4-2 can be restored using a viral vector and we will further assess its functional effect on pain sensitivity.

Effect of rufinamide on gating properties of voltage-gated sodium channel Na,1.7

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Background: Voltage-gated sodium channels (Nav1.x) are important players in chronic pain. A particular interest has grown in Nav1.7, expressed in nociceptors, since mutations in its gene are associated to two inherited pain syndromes or insensitivity to pain. Rufinamide, a drug used to treat refractory epilepsy such as the Lennox-Gastaut syndrome, has been shown to reduce the number of action potentials in cortical neurons without completely blocking Na channels.

Aim: The goal of this study was to investigate the effect of rufinamide on Nav1.7 current.

Methods and results: Whole-cell patch clamp experiments were performed using HEK293 cells stably expressing Nav1.7. Rufinamide significantly decreased peak sodium current by 28.3, 212 and 12.5% at concentrations of 500, 100 and 50µM respectively (precise EC50 could not be calculated since higher rufinamide concentrations could not be achieved in physiologic solution). No significant difference on the V1/2 of voltage-dependence of activation was seen; however a shift in the steady-state inactivation curve was observed.
Methods: slow depolarization. Inactivation to increase excitability thresholds of C fibers. Recent afferents. DC depolarization can cause sufficient sodium channel initiation and propagation of action potentials in primary sensory channels has been shown to be essential for signalling pain. We Voltage gated sodium (Na+) channels are essential for the N. Vastani, D.R. Spahn, K. Maurer of local anesthetics nerve conduction in the presence of low concentrations treated for epilepsy, 15 μM, rufinamide only minimally blocks Nav1.7. However, it stabilizes the inactivated state and exerts frequency-dependent inhibition of Nav1.7. These pharmacological properties may be of use in reducing ectopic discharges as a causal and symptom-related contributor to neuropathic pain syndrome.

Small depolarizing ramp currents can be used to block nerve conduction in the presence of low concentrations of local anesthetics N. Vastani, D.R. Spahn, K. Maurer Institute of Anesthesiology, University Hospital of Zurich, Switzerland Aims: Voltage gated sodium (Na+) channels are essential for the initiation and propagation of action potentials in primary sensory afferents. DC depolarization can cause sufficient sodium channel inactivation to increase excitability thresholds of C fibers. Recent investigations suggest that a slow membrane depolarization is a specific stimulus for activation of Nav1.7. This subtype of sodium channels has been shown to be essential for signalling pain. We investigated the effects of different sodium channel blockers on unmethylated C fibers stimulated with and without a pre-conditioning slow depolarization. Methods: C fibre compound action potentials (C-CAP) were recorded extracellularly in vitro using a skin nerve preparation from adult rats. A computerized threshold tracking program (Otrac®) was used to determine the membrane threshold, peak amplitude and latency. Parameters were tracked continuously over time. Nerve fibres were stimulated with a supramaximal 1 ms current pulse either alone or after a small, slow 300 ms conditioning polarizing ramp current, in the presence and absence of various sodium channel blockers (TTX, Lidocaine, Rolipram). Different depolarizing ramps (between −10 and +100% of the original threshold current) were investigated. Results: The membrane threshold at the end of the 20% depolarizing ramp is strongly raised in the presence of both 60 nM TTX (108 ± 4%) and 80 μM Lidocaine (147 ± 15%; n = 10), in comparison to control threshold. The effect is significantly larger using a 20 % conditioning ramp, compared to 10%. In separate experiments the same effect is shown to be concentration dependent with thresholds in pain (80 μM: 157 ± 13%, n = 10). A weaker effect is seen with lidocaine. Conclusions: The level of preconditioning ramp stimuli determines the inactivation of sodium current. In the presence of sodium channel blockers the same conditioning stimulus causes a much larger effect than expected by the sodium channel blocker alone. Therefore, we conclude that small depolarizing ramp currents can be used to block nerve conduction in the presence of low concentrations of local anesthetics. The effect of a conditioning threshold ramp (between −10 and +100% of the original threshold current) on sodium channel blockers may be exerting their effect on sodium channel subtypes.

Peripheral Nerve Neuropathy is Associated with a Giall Reaction in the Gracile Nucleus Associated with a regulation on GABA transporters GAT-1 Romain-Daniel Gosselin, Damien Bieber, Isabelle Decosterd Pain Research Unit, Department of Anesthesiology and DBCM, CHUV/UNIL, Lausanne Allodynia (pain in response to normally painless stimulation) and paresthesia (erroneous sensory experience) are two debilitating symptoms of neuropathic pain. These stem, at least partly, from profound changes in the non-nociceptive sensory pathway that comprises large myelinated neuronal afferents terminating in the gracile and cuneate nuclei. Further than neuronal changes, well advanced evidence indicates that glial cells (especially in the spinal cord) are key actors in neuropathic pain, in particular the possible alteration in astrocytic capacity to reuptake neurotransmitters (glutamate and GABA). Yet, the possibility of such a changed astrocytic scavenging capacity remains unexplored in the dorsal column pathway. The present study was therefore undertaken to assess whether peripheral nerve injury (spared nerve injury model, SNI) could trigger a glial reaction, and especially changes in glutamate and GABA transporters, in the gracile nucleus. SNI surgery was performed on male Sprague-Dawley rats. Seven days after surgery, rats were used for immunofluorescence (fixation and brain slicing), western-blots (fresh brain freezing and protein extraction) or GABA reuptake on synaptosomes. We found that SNI results in a profound glial reaction in the ipsilateral gracile nucleus. This reaction was characterized by an enhanced immunolabelling for microglial marker Iba1 as well as astrocytic protein GFAP (further confirmed by western-blot, p <0.05, n = 7). These changes were not observed in sham animals. Immunofluorescence and western-blot analysis shows that the GABA transporters were not significantly upregulated in the ipsilateral gracile nucleus (p <0.001; n = 7), with no detectable change in GAT-3 or glutamate transporters EAAT-1 and EAAT-2. Double immunofluorescence shows that GAT-1 and GFAP colocalize within the same cells. Furthermore, the upregulation of GAT-1 was shown to occur all along the rostrocaudal axis of the gracile nucleus. Finally, synaptosomes from ipsilateral gracile nucleus show an increased capacity to reuptake GABA. Together, the data presented here show that glial cells in the gracile nucleus may contribute to neuropathic pain, in particular through an upregulation of the GABA transporter GAT-1. Hence, this study points to role of an increased GABA transport in the dorsal column nuclei in neuropathic pain, calling attention to GAT-1 as a putative future pharmacological target to treat allodynia and paresthesia.

Induction of general anesthesia with propofol and sevoflurane change axonal excitability of primary sensory afferents K. Maurer, J. Wacker, D.R. Spahn Institute of Anesthesiology, University Hospital of Zurich, Switzerland Aim: To evaluate the effect of propofol (di-isopropyl-phenol) and sevoflurane on axonal excitability of peripheral sensory nerves after induction of anesthesia. Methods: After obtaining institutional ethics committee approval (University Hospital Zurich, Stv. 5-2008) and written informed consent, we randomized 40 patients who underwent surgery under general anesthesia into a propofol or sevoflurane group. Before induction of anesthesia we measured nerve excitability parameters of sensory afferents on the median nerve (strength-duration time constant, the recovery cycle after a supramaximal stimulus and threshold electrotetons) using a different conditioning stimulus (Otrac®). No opioids, benzodiazepines or muscle relaxants were used during the measurement period. 15 minutes after the induction the same electrophysiological parameters were measured. Values are presented as mean ± standard deviation. We performed a paired t-test to compare changes within the two groups and an unpaired t-test to compare changes between the two groups. A p-value <0.01 was considered significant. Results: Both, propofol and sevoflurane induced a significant increase in skin temperature (propofol: +1.2 °C; sevo: +1.7 ± °C) and a significant decrease in mean arterial pressure (propofol: –20.4 ± 2.5 mm Hg; sevo: –33.1 ± 3.5 mm Hg). Certain electrophysiological parameters significantly changed: peak response decreased (propofol: –0.10 ± 0.02 mV, sevo: –0.16 ± 0.03 mV), relative refractory period shortened (propofol: –0.58 ± 0.16 ms, sevo: –0.54 ± 0.11 ms) and overshoot after a hyperpolarizing conditioning stimulus decreased (propofol: 3.6 ± 0.58% for C fibre, 3.5 ± 0.8% for A delta fibre). Finally, synaptosomes from ipsilateral gracile nucleus show an upregulation of the GABA transporter GAT-1. Hence, this study points to role of an increased GABA transport in the dorsal column nuclei in neuropathic pain, calling attention to GAT-1 as a putative future pharmacological target to treat allodynia and paresthesia.

Conclusion: Propofol and sevoflurane evoked similar changes in nerve excitability of sensory afferents during anesthesia induction. An increase of the skin temperature at the recording site caused a faster kinetic of voltage-gated ion channels and therefore accounts partially for the observed changes (e.g., relative refractory period). At the same time, propofol and sevoflurane caused a partial block of the same ion channels (e.g. peak response). Our results demonstrate that both propofol and sevoflurane, modulate excitability of primary sensory afferents in concentrations used in clinical practice.

Evidence for Expansion of Spinal Reflex Receptive Fields in Chronic Pain Patients with Endometriosis Albain Y. Nazir*, S. Haessler, Steen Petersen-Felix*, Michael Müller*, Lars Arendt-Nielsen*, Jose Biurrun Manresa, Ole K. Andersen*, Michele Curatolo* *University Department of Anesthesiology and Pain Therapy, University Hospital of Bern, Inselspital, Bern, Switzerland; University Department of Obstetrics and Gynecology, University Hospital of Bern, Inselspital, Bern, Switzerland; Center for Sensory-Motor Interaction, Department of Health Science and Technology, Aalborg University, Denmark Background: Widespread central hypersensitivity is present in many chronic pain conditions and contributes to pain and disability. Expansion of receptive fields of spinal cord nociceptive neurons may...
be one of the mechanisms underlying central hypersensitivity, but so far no method to assess receptive fields in humans has been available. Using a novel method to quantify nociceptive receptive fields by means of spinal withdrawal reflexes, we tested the hypothesis that patients with chronic endometriosis pelvic pain display an expansion of receptive fields, compared with pain-free subjects. Secondary endpoints were the subjective pain thresholds and the thresholds to evoke a nociceptive reflex after single and repeated (temporal summation) electrical sural nerve stimulation.

**Methods:** 20 patients and 25 pain-free female subjects were tested. Electrical stimuli were applied to 10 sites on the foot sole to evoke reflexes in the tibialis anterior muscle. The reflex receptive field (RRF) was defined as the area of the foot (expressed as fraction of the foot sole) from which a nociceptive reflex could be evoked by the electrical stimulus. For the secondary endpoints, the electrical stimuli were applied at the cutaneous innervation area of the sural nerve. Pain and reflex thresholds after single and repeated stimulation (5 stimuli at 2 Hz) were recorded.

**Results:** Endometriosis patients displayed a larger RRF area compared with pain-free subjects. Median (25–75 percentiles) of the two groups were 0.48 (0.38–0.54) and 0.33 (0.27–0.39), respectively (p = 0.008). Pain and reflex thresholds after sural nerve stimulation (secondary endpoints) were significantly lower in patients than in controls (p <0.001 for all measurements).

**Conclusions:** This study provides for the first time evidence for widespread expansion of receptive fields in chronic pain patients. It thereby identifies a mechanism that may underlie central hypersensitivity in human chronic pain conditions. This phenomenon may become target for the development of future therapeutic interventions.

**Acknowledgments:** This work was funded by the Swiss Science National Foundation, the Danish Research Council for Technology and Production and the Scientific Funds of the University Department of Anesthesiology and Pain Therapy of the University of Bern.

**Key words:** Receptive fields, Central Sensitization, Nociceptive Reflex, Endometriosis, Pelvic pain.

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**Intrathecal drug delivery systems for cancer pain**

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1Department of Anesthesiology and Pain Management, Center for Neuromodulation; 2Department of Anesthesiology, University Hospital Center and University of Lausanne (CHUV)

**Introduction:** A substantial number of patients with cancer suffer considerable pain at some point during their disease, and approximately 25% of cancer patients die in pain. In cases of uncontrolled pain or intolerable side effects, intrathecal drug delivery system (IDDS) is a recognised management option. Indeed, IDDS offers rapid and effective pain relief with less drug side effects compared to oral or parenteral administration. The aim of this study is to retrospectively review our series of cancer patients treated with IDDS.

**Method:** Data was extracted from the institutional neuromodulation registry. Patients with cancer pain treated with IDDS from 01.01.1997 to 30.12.2009 were analysed for subjective improvement, changes in pain intensity (VAS) and survival time after implantation. Measurements were available for a decreasing number of patients as time since baseline increased.

**Results:** During the studied period, 78 patients were implanted with IDDS for cancer pain. The mean survival time was 11.1 months (median: 3.8 months) and 14 patients (18%) were still alive at the end of the studied period. Subjective improvement was graded between 55 and 85% during the first year. Mean VAS during the first year remained lower than VAS at baseline.

**Discussion:** IDDS has been shown to be cost-effective in several studies. Although initial costs of implantation are high, the cost benefits favour analgesia with implanted intrathecal pumps over epidural external systems after 3 to 6 months in cancer patients. Improved survival has been associated with IDDS and in this series both the mean and median survival times were above the cut-off value of three months. The mean subjective improvement was above 50% during the first year, suggesting a good efficacy of the treatment, a finding that is consistent with the results from other groups. Changes in pain intensity are difficult to interpret in the context of rapidly progressive disease such as in terminal cancer. However, mean VAS from 1 thru12 months were lower than baseline, suggesting improved pain control with IDDS, or at least a stabilisation of the pain symptoms.

**Conclusion:** Our retrospective series suggests IDDS is effective in intractable cancer pain and we believe it should be considered even in terminally ill patients with limited life expectancies.

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**Intrathecal administration of Ziconotide: does single-shot injection predict efficacy?**

C. Perruchoud1,2, M. Boyli1,2, A. Smit1, B. Rutschmann1,2, A. Durrell, E. Buchser1,2

1Department of Anesthesiology and Pain Management, Center for Neuromodulation; 2Department of Anesthesiology, University Hospital Center and University of Lausanne (CHUV)

**Introduction:** Though a trial of intrathecal (IT) therapy should always be performed before implantation of a definitive intrathecal pump, there is no agreement as to how this test should be performed. Ziconotide is trialed in most of cases with continuous IT administration using implanted catheters. Unlike other intrathecal drugs, there is little experience with single bolus IT injections of ziconotide. The aim of the study is to assess the feasibility of single-shot IT trialing with ziconotide.

**Patients and methods:** Eleven consecutive patients with chronic neuropathic intractable pain were trialed with a single IT bolus of 2.5 mcg of ziconotide. Pain and side effects are monitored for at least 72 hours after the injection. Depending on the response, a second injection is given a week later, with either the same dose (if VAS decreased ≤50% with side effects), a higher dose of 3.75 mcg (if VAS decreased ≥50% without side effects) or a lower dose of 1.25 mcg (if VAS decreased ≤50% but with side effects). If VAS decreased less than 50% and side effects occurred, no further injection was performed. When VAS decreased >50% without side effects after the first or the second dose, the result is confirmed by one more injection of the same dose one week later. The trial is considered positive if two successive injections provide a VAS decreased more than 50% without side effects.

**Results:** Eleven patients (6 females and 5 males) were included. Nine patients experienced modest or no pain relief. Four of these had significant side effects (dizziness, nausea, vomiting or abdominal pain) and had no further injection. In the others 5, one patient retired from study and four received a second injection of 3.75 mcg. The trial was negative in all 5 cases because of side effects (dizziness, drowsiness, weakness, muscle cramps), the pain decreased in only 2 patients. Two patients experienced profound pain relief with an IT injection of 2.5 mcg. One patient had no side effects and the other had dizziness and drowsiness that disappeared with an injection of 1.25 mcg. Pain relief without adverse effects was confirmed with the second injection. The trial was considered positive for those two patients.

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**Evaluation of pain caused by locoregional anesthesia procedures**

D. Walther, N. Gilliard, MD, P. Frascarolo, PhD, E. Albrecht, MD

CHUV

**Introduction:** Locoregional anesthesia can be a painful procedure and may therefore decrease patient’s acceptance. The purpose of the present study was to evaluate the pain caused by different locoregional anesthesia techniques in comparison to pain induced by peripheral intravenous (IV) cannulation.

**Methods:** This prospective observational study used a visual analogue scale (VAS), consisting of a 100 mm line, in order to quantify the levels of pain perceived during single-shot peripheral nerve blocks, continuous peripheral nerve blocks, spinal anesthesia and peripheral IV cannulation. Peripheral nerve blocks were performed with both neurostimulation and ultrasound guidance.
**Obstetric analgesia and anesthesia in Switzerland in 2007**

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(CHUV), 1011 Lausanne

**Introduction:** The last twenty years has witnessed important changes in the field of obstetric analgesia and anesthesia. In 2007, we conducted a survey to obtain information regarding the clinical practice of obstetric anesthesia in our country. The main objective was to ascertain whether recent developments in obstetric anesthesia had been adequately implemented in our current clinical practice.

**Methodology:** A confidential questionnaire was sent to 391 identified Swiss obstetric anesthetists. The questionnaire included 58 questions on 5 main topics: activity and organization of the obstetric unit, practice of labor analgesia, practice of anesthesia for cesarean section, prevention of aspiration syndrome, and pain treatment after cesarean section.

**Results:** The response rate was 80% (311/391). 66% of the surveyed anesthetists worked in intermediate size obstetric units (500–1500 deliveries per year). An anesthetist was on site 24/24 hours in only 53% of the obstetric units. Epidural labor analgesia with low dose local anesthetics combined with opioids was used by 87% but only 30% used patient controlled epidural analgesia (PCEA). Spinal analgesia was the first choice for elective and urgent cesarean section for 95% of the responders. Adequate prevention of aspiration syndrome was prescribed by 78%. After cesarean section, a multimodal analgesic regimen was prescribed by 74%.

**Conclusion:** When comparing these results with those of the two previous Swiss surveys [1, 2], it clearly appears that Swiss obstetric anesthetists have progressively adapted their practice to current clinical recommendations. But this survey also revealed some insufficiencies:

1. Of the public health system:
   a. Insufficient number of obstetric anesthetists on site 24 hours/24.
   b. Lack of budget in some hospitals to purchase PCEA pumps.

2. Of individual medical practice:
   a. Frequent excessive dosage of hyperbaric bupivacaine during spinal anesthesia for cesarean section.
   b. Frequent use of crystalloid preload before spinal anesthesia for cesarean section.
   c. Frequent systematic use of opioids when inducing general anesthesia for cesarean section.
   d. Fentanyl as the first choice opioid during induction of general anesthesia for severe preeclampsia.

In the future, wider and more systematic information campaigns by the Swiss Association of Obstetric Anesthesia (SAOA) should be able to correct these points.

**References**


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**Effects of Local Anesthetics on Fibroblasts**

Andreas Schlicker1, Caroline Fedder2, José Aguirre3, Alain Borgeat4, Beatrice Beck-Schimmer5

1 Institute of Anesthesiology, University Hospital Zurich, Switzerland
2 Institute of Anesthesiology, Balgrist University Hospital Zurich, Switzerland

**Background:** Regional anesthesia with lidocaine, bupivacaine or ropivacaine is routinely used to manage perioperative pain. Sparse data exist focusing on the effects of local anesthetics (LA) on human fibroblasts, which are actively involved in wound healing. Therefore, we investigated the effect of the three LA on growing human fibroblasts in an in vitro model focusing on cell viability, survival and proliferation rate.

**Methods:** Human fibroblasts were exposed to 0.3 mg/ml and 0.6 mg/ml of each LA for 2 days, followed by an incubation with normal growth medium for another 1, 4 or 7 days (group 1). Alternatively, cells were permanently incubated with LA for 3, 6 or 9 days (group 2). At each time point live cells were counted using trypan blue staining, cell viability was measured by the tetrazolium bromide assay and proliferation tests were performed with the colorimetric bromodeoxyuridine assay. Production of reactive oxygen species (ROS) was determined, measuring the oxidation of non-fluorescent-2,7'-dichlorofluorescein to the fluorescent form of the dye.

Three-way analysis of variance and Spearman's correlation was used to analyze data.

**Results:** Treatment of cells with the three LA showed a concentration-dependent cytotoxic effect of lidocaine, bupivacaine or ropivacaine on fibroblasts, which are actively involved in wound healing. Therefore, we investigated the effect of the three LA on growing human fibroblasts in an in vitro model focusing on cell viability, survival and proliferation rate.

**Conclusions:** The safety and effectiveness of acute pain management is insufficient, because the anesthetic techniques are complex and require specific expertise. The implementation of an anesthesiologist-acute pain unit is essential. Moreover, this unit contributes to decrease patient's morbidity and mortality [2] and can participate to control of health care costs. This project has been deposited to the hospital's authority.

**References**

Potential influence of the anesthetic technique used during open radical prostatectomy on prostate cancer-related outcome

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Background: Recently published studies suggest that the anesthetic technique used during oncological surgery impacts cancer recurrence. To evaluate the effect of anesthetic technique on disease progression and long-term survival, we compared patients receiving general anesthesia plus thoracic epidural analgesia and perioperative pain control after conventional stellate ganglion block with patients receiving general anesthesia alone undergoing open retropubic radical prostatectomy with extended pelvic lymph node dissection.

Methods: Two sequential series were studied. Patients receiving general anesthesia combined with epidural analgesia (January 1994 – June 1997, n = 103) were retrospectively compared with a group given general anesthesia combined with ketorolac-morphine analgesia (July 1997 – December 2000, n = 158). Biochemical recurrence-free, clinical progression-free, cancer-specific and overall survival were assessed using the Kaplan-Meier technique and compared using a log rank test.

Results: Significant differences were found between the two groups for biochemical recurrence-free, cancer-specific or overall survival. Patients receiving general anesthesia combined with epidural analgesia had a significantly longer biochemical recurrence-free and clinical progression-free survival than patients receiving general anesthesia plus thoracic epidural analgesia and perioperative pain control after conventional stellate ganglion block.

Conclusions: General anesthesia with epidural analgesia was associated with a reduced risk of clinical cancer progression. But no significant differences in the survival could be observed between general anesthesia alone plus postoperative thoracic epidural analgesia and general anesthesia plus intra- and postoperative thoracic epidural analgesia after prostatectomy.

Ultrasound imaging to estimate the risk of conventional stellate ganglion block

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Department of Anaesthesiology and Pain Therapy, Inselspital, University Hospital of Bern, University of Bern, Switzerland

Background: Stellate ganglion block is a frequently performed intervention for diagnosis and management of various vascular disorders and chronic pain states in the upper extremity, head, and neck. The most common technique is the blind approach at the C6 transverse process (Chassagnac’s tubercle) after manual lateral dislocation of the carotid artery and the jugular vein. Severe complications have been reported, due to accidental puncture of relevant brain supplying arteries (e.g., vertebral artery, ascending cervical artery), or the oesophagus.

Objectives: To describe the sonographic anatomy of the anterior cervical region C6 focusing on hazardous structures.

Methods: The anterior cervical region of 55 healthy volunteers was scanned bilaterally. The presence of the oesophagus or relevant arteries (located within a 1 cm wide band between the thyroid and the carotid artery anterior to the transverse process of C6) were noted before and after manual lateral dislocation of the large vessels. Dislocation was performed with an 11 mm narrow curved array transducer, simulating the dislocating finger.

Results: On the right side, the oesophagus never was located in front of the target point. On the left side, the oesophagus was present in front of the target point in 10/35 cases. After the dislocation manoeuvre, the oesophagus disappeared in 14/35 cases but remained in front of the target point in 5/35 cases and appeared in front of the target point from a previously safe location in 3/35 cases. Relevant arteries in front of the target point could be visualized bilaterally alone and 16/35 cases on the right and left side, respectively. After the dislocation manoeuvre they still were present in 8/35 and 13/35 cases on the right and left side, respectively.

Conclusion: In this descriptive study, both the oesophagus as well as relevant arteries could be located in front of the classic target point of conventional blind stellate ganglion block in a significant number of the 35 examined healthy volunteers. The simulated dislocation manoeuvre had little impact on moving these structures away from the target point and might actually increase the risk of oesophageal puncture in certain individuals. Ultrasound imaging is expected to improve safety of stellate ganglion blocks, as compared to the classic blind approach.
into the trachea and tracheal midline puncture as described by the dial of a clock between 11:00 and 13:00.

**Results:** Tracheal puncture and wire insertion was successful in eight of nine cadavers at the first attempt and in one at the second attempt (total of ten attempts, nine successful). In eight of nine successfully inserted wires the wire was placed at the defined midline.

**Tracheal Puncture of Nine Cadavers**

<table>
<thead>
<tr>
<th>First/ second attempt success</th>
<th>n (%) or mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical puncture level (tracheal ring)</td>
<td>1 (11) / 4 (44%) / 2 (22%)</td>
</tr>
<tr>
<td>Tracheal puncture technique</td>
<td>2 (22)</td>
</tr>
<tr>
<td>Lesion of tracheal structures (yes/ no)</td>
<td>1 (11) / 7 (78%) / 1 (11)</td>
</tr>
<tr>
<td>Lesion of thyroidal structures (no lesion/ isthmus/ lobe)</td>
<td>1 (11) / 7 (78%) / 1 (11)</td>
</tr>
</tbody>
</table>

**Conclusions:** Ultrasound guidance can facilitate successful tracheal puncture. However, an in-plane approach with a longitudinal ultrasound visualization of the trachea neither guarantees an exact midline puncture, nor allows detection of a misplaced guide-wire.

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**Highlights of Airway Management:**

A Multi-National Survey among Anaesthesiologists

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1University Department of Anaesthesiology, University Hospital and University, Bern, Switzerland; Department of Anaesthesiology, Perioperative Medicine and Pain Management, University of Miami Miller School of Medicine, Coral Gables, Miami, Florida, United States; Department of Anaesthesia, General Intensive Care and Pain Control, Division of Cardiothoracic and Vascular Anesthesia and Intensive Care, Medical University Vienna, Austria

**Background:** Highly controversial debates in airway management are: 1. Is Sellick’s manoeuvre advisable and how many anaesthesiologists still use it regularly? 2. Should we mask ventilate before applying muscle relaxants (MR)? 3. Do anaesthesiologists check for predictors of difficult mask ventilation (DMV)? We compared the approach to airway management among anaesthesiologists from Austria, Switzerland and the United Kingdom using anonymous questionnaires.

**Material and methods:** We distributed the same questionnaire during the main session of three anaesthesia meetings in Vienna, Austria (Hands-on Workshop Vienna 2009); Perth, UK (Difficult Airway Society Meeting); and Interlaken, CH (SGAr) in 2009. We checked for participants’ awareness concerning predictors for DMV, whether they mask ventilated before applying MR, asked about the use of cricoid pressure (Sellick’s manoeuvre), and recorded demographics.

**Results:** Mean age was 45 ± 9 ys, mean experience 15 ± 9 ys, equally distributed among questionnaires. There were less females in the UK (32%) compared to A (50%) and CH (41%, p = 0.066). Answers were similar in A and CH, but different to the UK. A minority routinely checked all five predictors for DMV preoperatively (A 8%, CH 9%, UK 15%).

**Discussion and conclusion:** Anaesthesiologists in the UK more consistently check predictors for DMV and take that into consideration when deciding whether or not to mask ventilate before applying MR. Almost half of anaesthesiologists from Austria and Switzerland never use Sellick’s manoeuvre because it is still often applied in the UK. It seems that non-English speaking anaesthesiologists tend to abandon Sellick’s manoeuvre because it might add to patients’ risks with no evident of any gained benefit whereas UK anaesthesiologists strongly believe in its effectiveness and apply the technique.

---

**Table 1**

<table>
<thead>
<tr>
<th>A (n = 109)</th>
<th>CH (n = 116)</th>
<th>UK (n = 60)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routinely checking predictors for DMV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, n (%)</td>
<td>15 (14)</td>
<td>12 (10)</td>
<td>16 (27)</td>
</tr>
<tr>
<td>Always checks if mask ventilation is possible, n (%)</td>
<td>80 (73)</td>
<td>78 (67)</td>
<td>19 (32)</td>
</tr>
<tr>
<td>Never checks if mask ventilation is possible, n (%)</td>
<td>9 (8)</td>
<td>8 (7)</td>
<td>11 (18)</td>
</tr>
<tr>
<td>Checks when predictors for DMV are present, n (%)</td>
<td>14 (13)</td>
<td>23 (20)</td>
<td>25 (41)</td>
</tr>
<tr>
<td>Never applying cricoid pressure, n (%)</td>
<td>45 (42)</td>
<td>55 (47)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Applying cricoid pressure during RSI, n (%)</td>
<td>53 (49)</td>
<td>36 (31)</td>
<td>58 (97)</td>
</tr>
</tbody>
</table>
Posters

Prediction of difficult intubation with advanced face recognition techniques: a preliminary study
C. Perruchoud1, J.P. Thirani2, A. Yuce3, P. Schoettler4
1Department of Anesthesiology, CHUV, Lausanne; 2Signal Processing Laboratory, EPFL, Lausanne

Introduction: Difficult tracheal intubation remains a constant and significant source of morbidity and mortality in anaesthetic practice. Insufficient airway assessment in the preoperative period continues to be a major cause of unanticipated difficult intubation. Although many risk factors have already been identified, preoperative airway evaluation is not always regarded as a standard procedure and the respective weight of each risk factor remains unclear. Moreover the predictive scores available are not sensitive, moderately specific and often operator-dependant. In order to improve the preoperative detection of patients at risk for difficult intubation, we developed a system for automated and objective evaluation of morphologic criteria of the face and neck using video recordings and advanced techniques borrowed from face recognition.

Method and results: Frontal video sequences were recorded in 5 healthy volunteers. During the video recording, subjects were requested to perform maximal flexion-extension of the neck and to open wide the mouth with tongue pulled out. A robust and real-time face tracking system was then applied, allowing to automatically identify and map a grid of 55 control points on the face, which were tracked during head motion. These points located important features of the face, such as the eyebrows, the nose, the contours of the eyes and mouth, and the external contours, including the chin. Moreover, based on this face tracking, the orientation of the head could also be estimated at each frame of the video sequence. Thus, we could infer for each frame the pitch angle of the head pose (related to the vertical rotation of the head) and obtain the degree of head extension.

Discussion and conclusion: Preliminary results suggest the high feasibility of the technique. The next step will be the application of the same automated and objective evaluation to patients who will undergo tracheal intubation. The difficulties related to intubation will be then correlated to the biometric characteristics of the patients. The objective in mind is to analyze the biometric data with artificial intelligence algorithms to build a highly sensitive and specific predictive test.

Flexible nasopharyngoscopy to assess the dislocation rate of postoperative airway exchange catheters in the post-operative care unit (PACU): Preliminary data from a prospective observational study
M. Wipfli, L. Theiler, C. Luyet, L. Lehmann, V. Krejci, R. Greif
University Department of Anesthesiology and Pain Therapy, University Hospital Bern, Switzerland

Background and aims: The Cook Airway Exchange Catheter (CAEC) is designed to secure the patient’s airway in case there is a need to change the endotracheal tube. It is also used as a post-intubation aid to facilitate quick tracheal access in case of re-intubation. Therefore the correct location of the CAEC in the trachea is of utmost importance. Only retrospective data on its use is available and very little is known about the monitoring of the correct placement postoperatively. The aim of this prospective, observational study was to gather information about the correct tracheal position of a CAEC in the post-anesthesia care unit (PACU).

Methods: With ethics committee approval and informed consent we consecutively included all patients entering the PACU with an oral or nasal CAEC after the extubation of the trachea over the CAEC in the consecutively included all patients entering the PACU with an oral or nasal CAEC after the extubation of the trachea. With ethics committee approval and informed consent we gathered information about the correct tracheal position of a CAEC in the post-anesthesia care unit (PACU).

Results:

<table>
<thead>
<tr>
<th>Dislocation rate</th>
<th>ORAL CAEC</th>
<th>NASAL CAEC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 20</td>
<td>n = 61</td>
</tr>
<tr>
<td>Dislocation rate %</td>
<td>15 (3)</td>
<td>3.3 (2)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>

Discussion and conclusion: Preliminary results suggest the high feasibility of the technique. The next step will be the application of the same automated and objective evaluation to patients who will undergo tracheal intubation. The difficulties related to intubation will be then correlated to the biometric characteristics of the patients. The objective in mind is to analyze the biometric data with artificial intelligence algorithms to build a highly sensitive and specific predictive test.

Ultrasonographic gastric antral area to assess gastric contents in children: comparison with total gastric fluid volume determined by magnetic resonance imaging
Achim Schmitz1, Christian Kellenberger2, Markus Weiss3, Thomas Schraner4
1Anästhesieabteilung; 2Abteilung Bildagnostik

Background: Ultrasonography (US) has recently been proposed for preoperative assessment of gastric contents in adults, using a single, anatomic landmark guided plane for calculation of gastric antral area (GAA) [1]. Supine (SUP), elevated 45° degree supine (E45) and right decubital (RDC) position have been described [1–3]. In children, GAA has not yet been validated.

Methods: Healthy volunteers aged from 6 to 12 years fasted overnight. Gastric content was examined before and at various instants up to 120 min after ingestion of 7 ml/kg diluted raspberry syrup. At each instant, gastric fluid volume (GFV) was determined by magnetic resonance imaging (MRI) and GAA was measured 3 times in each of the SUP, E45 and RDC position. Correlation coefficients (Pearson) between GAA and GFV were calculated for each US position. Demographic data are presented as range (median), values for GAA and GFV as mean ± standard deviation.

Results: 16 healthy children aged from 6.4 to 12.8 (9.2) years, weighing 21.6 to 40.7 (31.8) kg, were examined 1 to 3 times. Overall 23 examinations were conducted: 6 after overnight fasting, 3 directly after and 14 with a delay of 17 ± 36 min after ingestion of syrup. GFV was 56 ± 27 ml. Mean GAA was 221 ± 116 mm², 218 ± 112 mm² and 341 ± 188 mm² for SUP, E45 and RDC position, respectively. Variation coefficients for GAA measurements were 20.1 ± 11.6 %, 20.1 ± 12.3 % and 18.9 ±11.8 % for SUP, E45 and RDC position. Correlation between GFV and mean GAA was R = 0.62 (p < 0.01), R = 0.49 (p <0.05) and R = 0.73 (p <0.01) for SUP, E45 and RDC position, respectively.

Conclusion: Overall correlation between GAA and GFV was poor to moderate in children, with the RDC position producing the most reliable results. Interpretation of isolated GAA values could be misleading.

References

A novel puncture sled for ultrasound guided vascular access: Effect on success rates for novices
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University Department of Anesthesiology and Pain Therapy, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

Introduction: Most anesthesiologists are familiar with patients who have notoriously difficult intravenous catheter placements. There is growing evidence that the use of ultrasound to visualize and successfully place catheters into peripheral veins is of undisputable value in those patients. However the expertise required in using ultrasound guidance for intravenous catheter placement may be limited. The development of a puncture-aid which allows a single, short and effective puncture also in the hand of untrained personnel could be of great value. The aim of this study was to study whether a novel puncture sled would represent an advantage, especially in untrained operators.

Methods: Fifty medical students, novices for ultrasound guided procedures, were randomly assigned (closed envelope) to use

Table 2

<table>
<thead>
<tr>
<th>Relation between ETCO2-measurement and flexible nasopharyngoscopic verification: Figures are (n).</th>
<th>ENDIDTAL-CO2 curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAEC extra-tracheal</td>
<td>CAEC tracheal</td>
</tr>
<tr>
<td>Absent</td>
<td>2</td>
</tr>
<tr>
<td>Present</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
</tr>
</tbody>
</table>

Discussion of dislocated CAEC by ETCO2-measuring revealed a sensitivity of 40% a specificity of 85% a positive predictive value (PPV) of 15% and a negative predictive value (NPV) of 95%.

Conclusions: Inexistent or disappearing ETCO2 curve with the postoperative use of CAEC does not sufficiently predict its incorrect position (PPV = 15%) but the presence of a ETO2 curve indicates endo-tracheal placement of the CAEC with high probability (NPV = 95%). Fiberoptical visualization revealed a higher dislocation rate in orally placed catheters. Therefore, we recommend endoscopic control of possible CAEC dislocations before its removal to improve patient safety in the case that expected re-intubation problems are probable.
ultrasound combined with the puncture sled (sledgroup) or ultrasound without the puncture sled (control group). All participants had to perform a sequence of fifteen ultrasound guided phantom vessel (Branched 4 Vessel Vascular Access Phantom, Blue Phantom Products) punctures. The sled consists of a movable mounting for 20 G-catheters allowing only longitudinal axis movements as needed for punctures. Lateral movement will be prevented. The depth of the puncture can be adjusted by moving the position of the calibrated sled along the depth regulator as visualized in figure 1. The movement of the mounting is restricted to limit advancing of the needle tip to any further than exactly under the transducer and thus prevents a puncture beyond the structures visualized by the ultrasound. After the puncture, the sled can be withdrawn and the catheter left in place without further manipulations of the latter. For each of 15 attempts success was rated = 1 and failure = 0. Data are presented as mean ± SD.

Results: Figure 2 shows overall success count for fifteen attempts in the sled (14.1 ± 1.2) and the control group (11.1 ± 2.7). Box-whisker plots: box: 25 percentile, median, 75 percentile; whiskers: upper and lower fence. Open circle: extreme. \( \text{P} < 0.001 \), Mann-Whitney U). Figure 3 illustrates success rate in percent for each attempt in both groups \( \text{P} < 0.050 \), compared to control, Fisher’s exact test).

Conclusions: Ultrasound guided punctures can be learnt quickly. However, a sled as puncture-aid significantly improves the success rate of ultrasound guided vessel punctures in a phantom. It prevents a learning phase with failures and unnecessary needling.

Figures 1 and 2 show the setup of the ultrasound guided puncture with and without the sled. Figure 3 illustrates the success rate at each attempt, showing a significant improvement in the sled group compared to the control group.

Is a preanaesthetic information form really useful?

R. Straessle, N. Gilliard, MD, Ph. Frascarolo, PhD, Julien Rossat, MD, Eric Albrecht, MD

CHUV

Background: All patients should be fully informed about risks and benefits of anaesthetic procedures before giving a written consent. Moreover, satisfaction level may vary in proportion to given information. We aimed to determine, in a single-blind randomized controlled study, if an information form given before the preanaesthetic consultation could improve perceived information, information gain and satisfaction level.

Methods: Two hundred patients ASA I–III scheduled for elective orthopaedic surgery were randomized in two groups: a group which received an information form before the preanaesthetic consultation (IF group) and a control group (no information form). A standardized questionnaire was submitted after the preanaesthetic consultation, and after the operation. This 17-item questionnaire explored perceived information (5 items), information gain (3 items), and satisfaction level (9 items). The items of each topic were pooled and compared between groups.

Results: One hundred and eighty-five patients (92.5%) completed the study. IF group had a better perceived information (IF group 73% vs. control group 63%, \( \text{p} = 0.002 \)), a higher information gain (IF group 75% vs. control group 62%, \( \text{p} = 0.001 \)), and a higher satisfaction level (IF group 95% vs. control group 92%, \( \text{p} = 0.048 \)).

Conclusions: Our study suggests that an information form given before the preanaesthetic consultation enhances perceived information, information gain, and satisfaction level.

Quality control in anaesthesia: a retrospective survey

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Introduction: In Switzerland, the SGAR-SSAR encourages the participation with a national project of quality control (ADS) based on anaesthesia data. This data represents a medical point of view, regarding the technical and medical complications. We were interested in a quality inquiry, based on the patient’s point of view.

Methods: A questionnaire was created, evaluating the five following anaesthesiological allowances: a) out-patient preoperative consultation b) in-patient preoperative visit c) care in the operating room d) care in the recovery room and e) postoperative medical visit. For 1 month, all surgery patients were included in the protocol. Patients were either contacted at home by phone or interviewed at the hospital.

Results: 733 patients answered the questionnaire.

a) Out-patient preoperative consultation

Out of 381 patients seen, 321 estimated that this consultation was not necessary. Ten patients considered it useless. When asked about the fact that the consultant was not necessarily their anaesthetist for the procedure, 281 patients answered that they didn’t care, convinced that the record had been transmitted and that the other anaesthetist was competent as well. Thirty-four patients were disappointed not to have been informed of this fact.

b) In-patient preoperative visit

From the 450 patients visited, 437 were satisfied, 9 had no recollection and 4 complained of bad explanations about the anaesthetic technique.
Oxidative Stress and Apoptosis in Alveolar Epithelial Cells upon Exposure to Metal Oxide Nanoparticles

Ramon Frick1, Andreas Schlicker2, Wendelin J. Stark3, Beatrice Beck-Schimmer2
1Institute of Anesthesiology, University Hospital Zurich, Switzerland; 2Institute for Chemical and Bioengineering, ETH Zurich, Switzerland

Introduction: Metal oxide nanoparticles (NP) represent an industrially most relevant class of nanomaterials. The wide use, concerns over the impact of such materials on human health — especially on airway structures — has become a topic of great interest.

Aims and objectives: We investigated the level of intracellular oxidations and the apoptosis rate in alveolar epithelial cells (AEC) after exposure to manganese(III) oxide-NP (MnO2-NP), titanium dioxide-NP (TiO2-NP) and cerium dioxide-NP (CeO2-NP). We hypothesized that the presence of a high catalytic activity could strongly alter the damaging action of a nanomaterial. Sources of exposure to humans are e.g. occupational environment in metalworking (MnO2-NP), glass/ceramic applications (CeO2-NP) and cosmetic products (TiO2-NP). NP are comparable in their physical characteristics (size, surface area), but different in their catalytic potential were therefore investigated.

Methods: AEC were incubated with MnO2-NP, TiO2-NP and CeO2-NP at concentrations of 5 µg/ml, 10 µg/ml and 20 µg/ml. To quantify their halogenations, is still unclear. We now demonstrate in an in vitro model for the future treatment of patients suffering from severe lung inflammation or ischemia/reperfusion events. The protective effects can be provided in a hydrophilic, injectable formulation for the future treatment of patients suffering from severe lung inflammation or ischemia/reperfusion events.

Results: Upon exposure to the different particles no significant changes in mediator levels were found on healthy AEC. In inflamed AEC, however, a significant increase of CINC-1 levels was observed: incubation with LPS and 20 µg/ml of manganese (III) oxide nanoparticles caused an increase of 25% after 6h (p value <0.001) and 61% after 24h (p value = 0.001) compared to CINC-1 levels in endotoxin-injured cells. Production of MCP-1 was only moderately enhanced after 6h of exposure to manganese(III) oxide particles compared to LPS alone. The increase in lung inflammation could not be shown for titanium oxide and cerium oxide particles. No cytotoxicity could be detected for all three nanomaterials.

Conclusions: These data provide evidence that although belonging to the same group of nanoparticles, manganese(III) oxide has a different impact on AEC than titanium and cerium oxide. Acute exposure to manganese(III) oxide particles might be harmful in patients with inflammatory diseases.

Fluorinated carbon groups mediate the protective effect of volatile anesthetics in inflammatory tissue injury

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Volatile anesthetics not only provide protection against ischemia-reperfusion events but also modulate inflammatory response upon tissue injury. Whether these protective effects are mediated by the ether basic structure of volatile anesthetics or due to characteristics in their halogenations, is still unclear. We now demonstrate in an inflammation / injury model using lipopolysaccharides, that the fluorinated carbon groups are responsible for the immunomodulatory effects. Conditioning experiments in pulmonary endothelial and epithelial cells with ether basic structures of sevoflurane, diethyl-ether and various molecules of different chemical nature (including the sevoflurane metabolite hexafluorooisopropanol), carrying either a trifluorinated carbon group (CF3) or methyl group (CH3) were performed. Both, inflammatory response and the chemotactic activity in either cell line were dose-dependently decreased upon exposure to molecules with CF3 groups. This was not observed for the corresponding non-fluorinated molecules or diethyl-ether. Cytotoxicity could be excluded. These findings reveal that the beneficial effects are not limited to volatile anesthetics, but associated with a much broader class of molecules containing at least one CF3 group. Overcoming limitations of volatile anesthetics (requirement of close patient surveillance), the protective effects could be provided in a hydrophilic, injectable formulation for the future treatment of patients suffering from severe inflammation or ischemia/reperfusion events.

Ventilatory dependent PaO2 oscillations and their distribution in the systemic circulation

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1University Department of Anesthesiology and Pain Therapy, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; 2Department of Anesthesiology, Johannes Gutenberg-University, Medical Center Mainz, Mainz, Germany; 3Oscillox, LLC, Folsom, Pennsylvania, USA

Background: PaO2 oscillations at the brachiocephalic artery have been shown in a rabbit model of lung injury. However, exact relationship with the respiratory cycle and propagation velocity downstream the arterial circulation is unknown. A new pulmonary laveage model (i) we evaluated the temporal behavior of PaO2 oscillations compared to electrical impedance tomography (EIT) based assessment of ventilation processes and (ii) determined the propagation velocity of aortic PaO2 oscillations depending on cardiac output.

Method: With IRB approval fast intravascular PaO2 measurement was performed in 7 anesthetized pigs (25 ± 1.2 kg) by fiber optic, fluorescence-quenching oxygen probes (FOXY-AL300, Ocean Optics, Folsom, Pennsylvania, USA).
Dynamic changes of regional pulmonary aeration within the induction of lavage ARDS, measurements were taken at the ascending intravascular PaO₂ (AA) and at the aortic bifurcation (AB). Synchronized fast [7.4 (6.3–7.5)] and for EIT 7.0 ± 0.8 sec [7.5 (5.6–7.5)], Amplitude of [0.9–2.4], for AA 7.2 ± 0.5 sec [7.4 (6.2–7.5), for AB 7.2 ± 0.5 sec [7.5 (6.2–7.5)]. Amplitude of PaO₂ oscillations for AA was 64.1 ± 16.4 mm Hg [55.8 (50.1–90.4)] and for AB 49.2 ± 18.3 mm Hg [49.2 (26.7–71.8)]. Heart rate was 174 ± 29 beats per minute [172(140–221)] and cardiac output 5.2 ± 1.4 L/min [5.6 (3.1–7.1)].

Conclusions: PaO₂ oscillations are highly correlated with the respiratory circuit supporting the hypothesis of tidal change of shunt fraction due to recruitment and derecruitment of atelectasis. The impact of heart rate and cardiac output on blood flow velocity and the resulting aortic oxygen partial pressure oscillation distribution seems to be low.

Acknowledgements: All experiments were performed at the Department of Anesthesiology, Johannes Gutenberg-University; funding by DFG Ma2398/7 and SNF POIB–117065/1.

Results: Figure 1 illustrates a typical example of the tracings of lifetime sampled at AA and at AB with the corresponding EIT in one animal. Peak to peak time for AA vs. AB was 1.5 ± 0.6 sec [1.2 (0.9–2.4)], for AA 7.2 ± 0.5 sec [7.4 (6.2–7.5)], for AB 7.2 ± 0.5 sec [7.5 (6.2–7.5)]. Amplitude of PaO₂ oscillations for AA was 64.1 ± 16.4 mm Hg [55.8 (50.1–90.4)] and for AB 49.2 ± 18.3 mm Hg [49.2 (26.7–71.8)]. Heart rate was 174 ± 29 beats per minute [172(140–221)] and cardiac output 5.2 ± 1.4 L/min [5.6 (3.1–7.1)].

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transfemorally (n = 86), transsubclavian (n = 2), and transapical (n = 24). TAVI was performed in general anaesthesia (GA; n = 52) or local anaesthesia with sedation (LA-MAC; n = 60).

**Results:** Device success was 95% (107/112). Mean pre- and post-dilatation aortic valve gradients were 5.5 ± 1.2 and 7 ± 4 mm Hg, respectively. Major bleeding occurred in 3.7% periprocedurally and in 10% within 30 days. Permanent pacemaker implantation was necessary in 34%. Mortality: periprocedural 2.7%; in-hospital 3.6%; 30-day 8.9%. Anesthetic characteristics see table:

<table>
<thead>
<tr>
<th>n (%)</th>
<th>vasopressor converted to GA</th>
<th>CPR (intra-procedural)</th>
<th>extub. p.p.</th>
<th>fit for IMC</th>
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<tr>
<td>LA-MAC 60 (54%)</td>
<td>23 (38%)</td>
<td>4 (6.7%)</td>
<td>4 (6.7%)</td>
<td>56 (93%)</td>
</tr>
<tr>
<td>PAVI</td>
<td>GA 52 (46%)</td>
<td>51 (98%)</td>
<td>n/a</td>
<td>1 (19%)</td>
</tr>
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<td>28 (21%)</td>
<td>24 (100%)</td>
<td>0 (0%)</td>
<td>12 (50%)</td>
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<tr>
<td>Total 112 (100%)</td>
<td>74 (66%)</td>
<td>3 (2.7%)</td>
<td>5 (4.5%)</td>
<td>59 (80%)</td>
</tr>
</tbody>
</table>

**Conclusion:** TAVI has good haemodynamic results and a risk-adjusted mortality similar to that of surgical AVR. Transfemoral TAVI can be done in LA-MAC in up to 90% of cases; conversion to GA and/or CPR may be necessary in ≤10%. Elective GA is required for transapical TAVI and selected indications; it was associated with more vasopressor and resource use, but no different mortality.

**References**

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**Survey of neuromonitoring and neuroprotective strategies used by German cardiac anaesthesia groups**

**Objective:** The primary objective of this survey was to identify current practice in cardiovascular anaesthesia with regard to neuromonitoring and neuroprotection.

**Methodology:** The dataset is based on a questionnaire sent out to all German cardiac anaesthesia departments between October 2007 and January 2008. The survey enquired about preoperative evaluation of the cerebral vasculature, intraoperative use of neuromonitoring, use during cardiopulmonary bypass [CPB], postoperative monitoring, medication and transfusion is planned preoperatively.

**Results:** Of 80 mailed questionnaires 55% were answered. Methods used for intraoperative neuromonitoring are (processed) electroencephalography [EEG] (60%), near infrared spectroscopy (40%), evoked potentials (50%), and transcranial doppler (17%). EEG is the preferred neuromonitoring modality for type A aortic dissection repair (38%), elective surgery on the thoracic and thoraco-abdominal aorta (34% and 32% respectively), and in carotid surgery dissection repair (38%), elective surgery on the thoracic and thoraco-abdominal aorta (34% and 32% respectively), and in carotid surgery dissection repair (38%), elective surgery on the thoracic and thoraco-abdominal aorta (34% and 32% respectively), and in carotid surgery dissection repair (38%).

**Conclusion:** TAVI has good haemodynamic results and a risk-adjusted mortality similar to that of surgical AVR. Transfemoral TAVI can be done in LA-MAC in up to 90% of cases; conversion to GA and/or CPR may be necessary in ≤10%. Elective GA is required for transapical TAVI and selected indications; it was associated with more vasopressor and resource use, but no different mortality.

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**Comparison of bedside and central laboratory ROTEM®-measurements**

**Background and objectives:** Major blood loss during surgery can lead to coagulopathy. Pre- and postoperative prompt and balanced haemostatic resuscitation. Rotation thrombelastometry by ROTEM® provides a fast and differentiated blood clotting analysis. If ROTEM® measurements are done in the central laboratory, duration until first values are available is delayed. This study aimed to evaluate time savings and reliability of bedside versus central laboratory ROTEM® values.

**Material and methods:** Blood samples for both bedside and central laboratory ROTEM® delta analysis were simultaneously drawn from children undergoing major surgery with anticipated major blood loss. Blood samples were immediately sent to the central laboratory and analysis was started at the same time in the operating theatre. Time saving between availability of bedside versus central laboratory ROTEM® values was recorded. Paired ROTEM® values were compared using Bland-Altman analysis and Spearman correlation.

**Results and discussion:** Fourteen patients aged between 0.7–15.3 yrs (median 5.9) weighing 5.5 to 63.0 kg (14.5 kg) undergoing craniofacial (n = 4), spine (n = 7) or tumour surgery (n = 3) were included. Median of time by bedside ROTEM® was 11 min and ranged from 2 to 28 min. Bias and precision of Bland-Altman analysis and Spearman correlation of ROTEM® parameters of 49 paired blood samples were as followed:
Spearman correlation was very high and ranged from 0.904 to 0.981 (p <0.01), except for CT in all tests, where it ranged from 0.511 to 0.853 (p <0.01). The reliability in our study is comparable to interrater reliability testing of ROTEM® in piglets [1], where CT was also shown to be less reliable than the other parameters.

**Conclusion:** Bedside ROTEM® measurements save valuable time during surgery with major blood loss. Considerable differences in some of the ROTEM® results demand further studies evaluating rapid versus slow processing of blood samples.

**Reference**

**No Wrong Site/Patient Surgery for 18 month after Implementation of a Checklist: Is everything all right?**

Pascale Ablinger*, Stephanie Hackethal*, Sandra Gautsch*, Burkhardt Seifert*, Thomas Hess*

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**Introduction:** Safety in surgery and perioperative care has evolved as an important quality control measure and outcome over the last decade. In order to improve patient safety at our institution [1, 2] we implemented a surgical checklist called the “4-step-protocol” hypothesizing we would improve team communication and consistency of care.

**Methods:** We retrospectively reviewed our charts of patients undergoing a surgical procedure over a 52 months period from May 2005 through August 2008 for wrong site/wrong patient surgery. In order to prevent any further incidents we designed and implemented a 13-item surgical safety checklist called the “4-step-protocol” and prospectively we collected data for 18 months from September 2008 through February 2010 for all patients undergoing a surgical procedure at our hospital. The checklist is mandatory for every patient undergoing a surgical procedure in our OR. The primary end-point of this study was the incidence of wrong site surgery. To ensure correct data collection and quality we evaluated the accuracy on 2 different occasions with a sample of 600 surgeries.

**Results:** The rate of wrong site surgery upon baseline was 5 cases in 52 months resulting in an incidence of 1/4901 cases. None of these patients sustained a noticeable damage. After implementation of a surgical safety checklist the rate declined to 0 cases over the 18 month period (p <0.05). Using Fisher’s exact test (p = 0.318) after the rule of three [3] with a confidence interval of 95% our actual incidence of a wrong site surgery is <1/3520 cases.

**Conclusion:** No wrong site/patient surgery has occurred after the implementation of a specifically designed surgical safety checklist for 18 months. If nothing goes wrong, is everything all right? [3] To be sure that everything is all right, we have to continue error free with 14700 surgeries or another 32 month without a mixed up patient. Since the checklist is part of our daily practice we believe that we are on the road to safer surgery.

**References**
2 Schweizerische Stiftung für Patientensicherheit: Empfehlungen zur Prävention von Eingriffverwechslungen.