

### Journal publications

#### Characteristic and Necessary Minutiae in Fingerprints

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**Abstract:** Fingerprints feature a ridge pattern with moderately varying ridge frequency (RF), following an orientation field (OF), which usually features some singularities. Additionally at some points, called minutiae, ridge lines end or fork and this point pattern is usually used for fingerprint identification and authentication. Whenever the OF features divergent ridge lines (e.g. near singularities), a nearly constant RF necessitates the generation of more ridge lines, originating at minutiae. We call these the necessary minutiae. It turns out that fingerprints feature additional minutiae which occur at rather arbitrary locations. We call these the random minutiae or, since they may convey fingerprint individuality beyond the OF, the characteristic minutiae. In consequence, the minutiae point pattern is assumed to be a realization of the superposition of two stochastic point processes: a Strauss point process (whose activity function is given by the divergence field) with an additional hard core, and a homogeneous Poisson point process, modelling the necessary and the characteristic minutiae, respectively. We perform Bayesian inference using an MCMC-based minutiae separating algorithm (MiSeal). In simulations, it provides good mixing and good estimation of underlying parameters. In application to fingerprints, we can separate the two minutiae patterns and verify by example of two different prints with similar OF that characteristic minutiae convey fingerprint individuality.

#### An algorithm for computing Fréchet means on the sphere

Gabriele Eichfelder, Thomas Hotz, Johannes Wieditz

*Optimization Letters*, 2019, Volume 13, Issue 7, pp 1523–1533.

<https://link.springer.com/article/10.1007/s11590-019-01415-y>

**Abstract:** For most optimisation methods an essential assumption is the vector space structure of the feasible set. This condition is not fulfilled if we consider optimisation problems over the sphere. We present an algorithm for solving a special global problem over the sphere, namely the determination of Fréchet means, which are points minimising the mean distance to a given set of points. The Branch and Bound method derived needs no further assumptions on the input data, but is able to cope with this objective function which is neither convex nor differentiable. The algorithm's performance is tested on simulated and real data.

#### Non-Asymptotic Confidence Sets for Circular Means

Thomas Hotz, Florian Kelma, Johannes Wieditz

*Entropy*, 2016, 18.10, 375.

<https://www.mdpi.com/1099-4300/18/10/375>

**Abstract:** The mean of data on the unit circle is defined as the minimizer of the average squared Euclidean distance to the data. Based on Hoeffding's mass concentration inequalities, non-asymptotic confidence sets for circular means are constructed which are universal in the sense that they require no distributional assumptions. These are then compared with asymptotic confidence sets in simulations and for a real data set.

### Reviewed conference proceedings

#### Universal, non-asymptotic confidence sets for circular means

Thomas Hotz, Florian Kelma, Johannes Wieditz

*Lecture Notes in Computer Science*, 2015, Volume 9389.

**Abstract:** Based on Hoeffding's mass concentration inequalities, non-asymptotic confidence sets for circular means are constructed which are universal in the sense that they require no distributional assumptions. These are then compared with asymptotic confidence sets in simulations and for a real data set.

### Clinical studies and trials

#### Morphine and Hydromorphone Effects, Side Effects and Variability—a Crossover Study in Human Volunteers

Konrad Meissner, Albert Dahan, Erik Olofsen, Christine Göpfert, Jane Blood, Johannes Wieditz, Evan D. Kharasch

*Anesthesiology*, 2023, 10-1097.

<https://doi.org/10.1097/ALN.0000000000004567>

**Abstract:**

- Background: Balancing between opioid analgesia and respiratory depression continues to challenge clinicians in perioperative, emergency department and other acute care settings. Morphine and hydromorphone are postoperative analgesic standards. Nevertheless, their comparative effects and side effects, timing, and respective variabilities, remain poorly understood. We tested the hypothesis that intravenous morphine and hydromorphone differ in onset, magnitude, duration and variability of analgesic and ventilatory effects.
- Methods: We conducted a randomized crossover study in healthy volunteers. Forty-two subjects received a 2-hour intravenous infusion of hydromorphone (0.05 mg/kg) or morphine (0.2 mg/kg) 1-2 weeks apart. We measured arterial opioid concentrations, analgesia in response to heat pain (maximally tolerated temperature, and verbal analog pain scores at discreet preset temperatures to determine half-maximum temperature effect), dark-adapted pupil diameter and miosis, end-expired CO<sub>2</sub>, and respiratory rate for 12 h after dosing.

- Results: For morphine and hydromorphone, respectively: maximum miosis was less (3.9 [3.4,4.2] vs 4.6 mm [4.0,5.0],  $P < 0.001$ ; median and 25%-75% quantiles) and occurred later ( $3.1 \pm 0.9$  vs  $2.3 \pm 0.7$  h after infusion start,  $P < 0.001$ ; mean  $\pm$  SD); maximum tolerated temperature was less ( $49 \pm 2$  vs  $50 \pm 2^\circ\text{C}$ ,  $P < 0.001$ ); verbal pain scores at end-infusion at the most informative stimulus ( $48.2^\circ\text{C}$ ) were  $82 \pm 4$  and  $59 \pm 3$  ( $P < 0.001$ ); maximum end-expired  $\text{CO}_2$  was 47 [45,50] and 48 mmHg [46,51] ( $P = 0.007$ ), and occurred later ( $5.5 \pm 2.8$  vs  $3.0 \pm 1.5$  h after infusion start,  $P < 0.001$ ); respiratory nadir was  $9 \pm 1$  and  $11 \pm 2$  breaths/min ( $P < 0.001$ ) and occurred at similar times. Area under the temperature tolerance-time curve was less for morphine (1.8 [0.0,4.4]) than hydromorphone ( $5.4^\circ\text{C}\cdot\text{h}$  [1.6,12.1]  $P < 0.001$ ). Inter-individual variability in clinical effects did not differ between opioids.
- Conclusions: For morphine compared to hydromorphone, analgesia and analgesia relative to respiratory depression were less, onset of miosis and respiratory depression was later, and duration of respiratory depression was longer. For each opioid, timing of the various clinical effects was not coincident. Results may enable more rational opioid selection, and suggest hydromorphone may have a better clinical profile.

## Screening versus multidimensional assessment of symptoms and psychosocial distress in cancer patients from the time of incurability

Stefanie Solar, Johannes Wieditz, Florian Lordick, Anja Mehnert-Theuerkauf, Karin Oechsle, Birgitt Van Oorschot, Michael Thomas, Thomas Asendorf, Friedemann Nauck, Bernd Alt-Epping

*Frontiers in Oncology*, 2023, 13.

<https://www.frontiersin.org/articles/10.3389/fonc.2023.1002499>

### Abstract:

- Objective: Previous symptom prevalence studies show a diverse spectrum of symptoms and a large diversity in symptom intensities in patients being just diagnosed as having incurable cancer. It is unclear, how physical symptoms and psychosocial burden should be recorded in order to determine the variable need for palliative care and further support. Therefore, we compared two different strategies for detecting physical symptoms and psychosocial burden of patients with newly diagnosed incurable cancer and their effects on the further course of the disease.
- Methods: SCREBEL is a controlled, randomized, non-blinded, longitudinal study of the research network of the Palliative Medicine Working Group (APM) of the German Cancer Society (DKG). We compared: a less complex repeated brief *screening* for symptoms and burden in patients using the NCCN Distress Thermometer and IPOS questionnaire versus a multidimensional comprehensive *assessment* using the FACT-G and their entity-specific questionnaires, the PHQ4 scales, SCNS-34-SF, IPOS and NCCN Distress Thermometer. The primary study endpoint was quality of life (QoL), measured using FACT-G, after six months. Secondary study endpoints were QoL by using evaluation of secondary scores (NCCN DT, IPOS, PHQ4, SCNS-SF-34G) at time 6 months, the number of hospital days, the utilization of palliative care, emergency services, and psychosocial care structures. To assess effects and differences, multiple linear regression models were fitted and survival analyses were conducted.
- Results: 504 patients were included in the study. 262 patients were lost to follow-up, including 155 fatalities. There were no significant differences between the low-threshold *screening* approach and a comprehensive *assessment* with respect to symptoms and other aspects of QoL. Using the IPOS, we were able to measure an improvement in the quality of life in the low-threshold screening arm by a decrease of 0.67 points (95%-CI: 0.34 to 0.99) every 30 days ( $p < 0.001$ ). Data on the involvement of emergency facilities and on supportive services were insufficient for analysis.
- Conclusions: A comprehensive, multidimensional assessment did not significantly differ from brief screening in preserving several dimensions of quality of life. These findings may positively influence the implementation of structured low-threshold screening programs for supportive and palliative needs in DKG certified cancer centers.

## Modeling iatrogenic intraoperative hyperthermia from external warming in children: A pooled analysis from two prospective observational studies

Clemens Miller, Anselm Bräuer, Johannes Wieditz, Katharina Klose, Carla Pancaro, Marcus Nemeth

*Pediatric Anesthesia*, 2022, 33.2, 114-122.

<https://onlinelibrary.wiley.com/doi/full/10.1111/pan.14580>

### Abstract:

- Background: Maintenance of normothermia is an important quality metric in pediatric anesthesia. While inadvertent hypothermia is effectively prevented by forced-air warming, this therapeutic approach can lead to iatrogenic hyperthermia in young children.
- Aims: To estimate the influence of external warming by forced air on the development of intraoperative hyperthermia in anesthetized children aged 6 years or younger.
- Methods: We pooled data from two previous clinical studies. Primary outcome was the course of core temperature over time analyzed by a quadratic regression model. Secondary outcomes were the incidence of hyperthermia (body core temperature  $>38^\circ\text{C}$ ), the probability of hyperthermia over the duration of warming in relation to age and surface-area-to-weight ratio, respectively, analyzed by multiple logistic regression models. The influence of baseline temperature on hyperthermia was estimated using a Cox proportional hazards model.
- Results: Two hundred children (55 female) with a median age of 2.1 [1st-3rd quartile 1-4.2] years were analyzed. Mean temperature increased by  $0.43^\circ\text{C}$  after 1h,  $0.64^\circ\text{C}$  after 2h, and reached a peak of  $0.66^\circ\text{C}$  at 147min. Overall, 33 children were hyperthermic at at least one measurement point. The odds ratios of hyperthermia were 1.14 (95%-CI: 1.07-1.22) or 1.13 (95%-CI: 1.06-1.21) for every 10min of warming therapy in a model with age or surface-area-to weight ratio (*ceteris paribus*), respectively. Odds ratio was 1.33 (95%-CI: 1.07-1.71) for a decrease of 1 year in age and 1.63 (95%-CI: 0.93-2.83) for an increase of 0.01 in the surface-to-weight-area ratio (*ceteris paribus*). An increase of  $0.1^\circ\text{C}$  in baseline temperature increased the hazard of becoming hyperthermic by a factor of 1.33 (95%-CI: 1.23-1.43).
- Conclusions: In children, external warming by forced-air needs to be closely monitored and adjusted in a timely manner to avoid iatrogenic hyperthermia especially during long procedures, in young age, higher surface-area-to-weight ratio, and higher baseline temperature.

## Ventilatory Ratio, Dead Space, and Venous Admixture in Acute Respiratory Distress Syndrome

Roberta Maj, Paola Palermo, Simone Gattarello, Serena Brusatori, Rosanna D'Albo, Carmelo Zinnato, Mara Velati, Federica Romitti, Mattia Busana, **Johannes Wieditz**, Peter Herrmann, Onnen Moerer, Micheal Quintel, Konrad Meissner, Barnaby Sanderson, Davide Chiumello, John J. Marini, Luigi Camporota, Luciano Gattinoni  
*British Journal of Anaesthesia*, 2022, 130.3, 360-367.

[https://www.bjanaesthesia.org/article/S0007-0912\(22\)00624-9/](https://www.bjanaesthesia.org/article/S0007-0912(22)00624-9/)

### Abstract:

- Background: Ventilatory ratio (VR) has been proposed as an alternative approach to estimate physiological dead space. However, the absolute value of VR, at constant dead space, might be affected by venous admixture and CO<sub>2</sub> volume expired per minute (VCO<sub>2</sub>).
- Methods: This was a retrospective, observational study of mechanically ventilated patients with acute respiratory distress syndrome (ARDS) in the UK and Italy. Venous admixture was either directly measured or estimated using the surrogate measure PaO<sub>2</sub>/FiO<sub>2</sub> ratio. VCO<sub>2</sub> was estimated through the resting energy expenditure derived from the Harris-Benedict formula.
- Results: A total of 641 mechanically ventilated patients with mild (n=65), moderate (n=363), or severe (n=213) ARDS were studied. Venous admixture was measured (n=153 patients) or estimated using the PaO<sub>2</sub>/FiO<sub>2</sub> ratio (n=448). The VR increased exponentially as a function of the dead space, and the absolute values of this relationship were a function of VCO<sub>2</sub>. At a physiological dead space of 0.6, VR was 1.1, 1.4, and 1.7 in patients with VCO<sub>2</sub> equal to 200, 250, and 300, respectively. VR was independently associated with mortality (odds ratio [OR]=2.5; 95% confidence interval [CI], 1.8–3.5), but was not associated when adjusted for V<sub>D</sub>/V<sub>Tphys</sub>, VCO<sub>2</sub>, PaO<sub>2</sub>/FiO<sub>2</sub> (OR<sub>adj</sub>=1.2; 95% CI, 0.7–2.1). These three variables remained independent predictors of ICU mortality (V<sub>D</sub>/V<sub>Tphys</sub> [OR<sub>adj</sub>=17.9; 95% CI, 1.8–185; P<0.05]; VCO<sub>2</sub> [OR<sub>adj</sub>=0.99; 95% CI, 0.99–1.00; P<0.001]; and PaO<sub>2</sub>/FiO<sub>2</sub> (OR<sub>adj</sub>=0.99; 95% CI, 0.99–1.00; P<0.001)).
- Conclusions: VR is a useful aggregate variable associated with outcome, but variables not associated with ventilation (VCO<sub>2</sub> and venous admixture) strongly contribute to the high values of VR seen in patients with severe illness.

## Blood Culture Headspace Gas Analysis Enables Early Detection of Escherichia coli Bacteremia in an Animal Model of Sepsis

Maximilian Euler, Thorsten Perl, Isabell Eickel, Anna Dudakova, Esther Maguilla Rosado, Carolin Drees, Wolfgang Vautz, **Johannes Wieditz**, Konrad Meissner, Nils Kunze-Szikszay  
*Antibiotics*, 2022, 11.8, 992.

<https://www.mdpi.com/2079-6382/11/8/992>

### Abstract:

- Background: Automated blood culture headspace analysis for the detection of volatile organic compounds of microbial origin (mVOC) could be a non-invasive method for bedside rapid pathogen identification. We investigated whether analyzing the gaseous headspace of blood culture (BC) bottles through gas chromatography-ion mobility spectrometry (GC-IMS) enables differentiation of infected and non-infected.
- Methods: BC were gained out of a rabbit model, with sepsis induced by intravenous administration of E. coli (EC group; n = 6) and control group (n = 6) receiving sterile LB medium intravenously. After 10 h, a pair of blood cultures was obtained and incubated for 36 h. The headspace from aerobic and anaerobic BC was sampled every two hours using an autosampler and analyzed using a GC-IMS device. MALDI-TOF MS was performed to confirm or exclude microbial growth in BCs.
- Results: Signal intensities (SI) of 113 mVOC peak regions were statistically analyzed. In 24 regions, the SI trends differed between the groups and were considered to be useful for differentiation. The principal component analysis showed differentiation between EC and control group after 6 h, with 62.2% of the data variance described by the principal components 1 and 2. Single peak regions, for example peak region P<sub>15</sub>, show significant SI differences after 6 h in the anaerobic environment (p < 0.001) and after 8 h in the aerobic environment (p < 0.001).
- Conclusions: The results are promising and warrant further evaluation in studies with an extended microbial panel and indications concerning its transferability to human samples.