



ANNUAL RESEARCH REPORT 2022

Danish Epilepsy Centre Filadelfia

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3
Professors 

2 Ass.
Professors 

10 Ph.D.
students 

111
Publications *) 

74
Oral Presentations 

*) Papers published in peer-reviewed journals, including leading journals, such as Nature Communications, Brain, Neurology and Epilepsia.



1. Introduction – Filadelfia

Filadelfia - The Danish Epilepsy Centre - offers highly specialized health care services to epilepsy patients of all ages. Being the only tertiary referral center for comprehensive treatment of epilepsy in Denmark, we have a unique access to rare and complex epileptic syndromes on the basis of which our centre is internationally acclaimed. In 2022 Filadelfia's three professors, two associate professors, three and ten Ph.D. students published 111 papers in international and national journals and contributed with 74 oral presentations. Our researchers are affiliated to University of Copenhagen, University of Odense and University of Aarhus. They occupy positions of trust in national and international scientific societies, and participate in a series of international epilepsy research networks.

The Danish Epilepsy Center, Filadelfia is a non-profit foundation with an independent Board of Directors. In 2022 we celebrated Filadelfias 125 years anniversary. Besides the Epilepsy hospital, Filadelfia comprises a centre for neurorehabilitation, specialized institutions for mentally handicapped persons and the only special school for children and young people with epilepsy in Denmark. Filadelfia is publically funded and an integral part of the Danish Healthcare System. The Epilepsy Hospital receives patients from the five Danish Regions i.e. the public hospitals and practitioners. The specialized social institutions receive clients from the Danish Municipalities.

We are proud to publish this report and wish it to encourage further collaboration for the benefit of persons with epilepsy worldwide.


Sándor Beniczky
Professor, Head of Department


Mads Ravnborg
Medical director

2. Core Research Team 2022



Sándor Beniczky MD, Ph.D.
Professor, Head of Department
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- Editor-in-Chief, Epileptic Disorders
- Chair, EEG Task Force, ILAE Commission on Big Data
- Past-chair, Joint Taskforce on EEG of the International Federation of Clinical Neurophysiology (IFCN) and the International League Against Epilepsy (ILAE)
- Member, ILAE Commission on Diagnostic Methods
- Member, ILAE Education Council; coordinator of the Virtual Epilepsy Academy (VIREPA)
- Member, ILAE Publication Council
- Member, ILAE Congress Council



Rikke Steensbjerre Møller, Ph.D.
Professor, Head of department
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- Speaker of a thematic research column within Neuroscience Academy Denmark
- Scientific advisory board member: KCNA2 Foundation
- Scientific advisory board member: KCNT1 Foundation
- Member of EpiCARE: a European Reference Network for rare and complex epilepsies
- Member of the leadership team at Department of Regional Health Research, University of Southern Denmark, Odense, Denmark
- Member of the scientific committee of Residras; a European Registry of Dravet Syndrome



Guido Rubboli MD, Ph.D.
Professor, Senior Consultant
Email: guru@filadelfia.dk

- 2022- present: European Academy of Neurology, member of the Management Group of the Scientific Panel on Epilepsy,
- 2018 - present: ILAE Task Force "Transition in care from Childhood into Adulthood", Member,
- 2022 - present: ILAE Task Force "SNOMED-CT", Member,
- 2019 - present: "Epilessia- Fuori dall'ombra", scientific committee
- 2020 - present: KCNT1 Foundation, member of the scientific committee
- 2021 - present: KCNA2 Foundation, member of the scientific committee
- 2021 - present: VIREPA (Virtual Epilepsy Academy) ILAE, Advanced EEG Course, Director



Elena Gardella MD, Ph.D.
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- Member of the commission on Classification and Terminology of the International League against Epilepsy (ILAE)
- Director of VIREPA basic-EEG course
- Member of the board of the Danish Epilepsy Society (DES)
- Member of Molecular Therapeutic Board in Neurological Channelopathies EpiCARE: a European Reference Network for rare and complex epilepsies.
- Member of the BRIDGE team at Department of Regional Health Research, University of Southern Denmark
- Editor of Scientific advisory board member: SCN8A Italy Foundation
- Scientific advisory board member: SCL6A1 Foundation



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Allan Bayat MD, Ph.D.
Translational Researcher, Consultant
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- Post doctoral BRIDGE Translational researcher at University of Copenhagen in collaboration with Department of Clinical Genetics, Rigshospitalet and the Danish Epilepsy Center.

Research Team

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Stephan Wüstenhagen, MD, PhD
Pirgit Meritam Larsen, MD, PhD
Jesper Jeppesen, PhD
Maria Vlachou, MD
Levente Hadady, MD
Orsolya Györfi, MD, PhD
Pietro Mattioli, MD
Evy Cleeren, PhD
Aykut Kural MD, PhD
Trine Hammer, MD, PhD
Christina Fenger, PhD
Allan Bayat, MD, PhD
Anne Højte Hansen, study nurse
Nazanin Mohammad, MSc

Sabrina Neri, MD
Cristina Cioclu, MD
Margherita Aluffi Valletti (Erasmus+ mobility)
Angelica Pisati (Erasmus+ mobility)
Alessandra Rossi, MD
Roberto Previtali, MD
Alberto Cossu, MD
Morad Kamand, PhD
Francesca Furia, MD
Cathrine Gjerulfsen, MD
Benedetta Kassabian, MD
Catarina Ancora, MD
Katrine M Johannesen, MD, PhD
Carolina Alvarez, MD

3. Ph.D. projects

Completed in 2022

- Allan Bayat: Deep phenotyping, genotype-phenotype correlations and precision medicine in monogenic epilepsies. Faculty of Health Sciences, University of Southern Denmark. Main supervisor: Rikke Steensbjerre Møller, co-supervisors: Guido Rubboli; Elena Gardella.
- Bogdan Florea: Electroencephalography in patients with disturbed level of consciousness. University of Szeged, Hungary. Main supervisor: Sándor Beniczky. Co-supervisor: Péter Klivényi.
- Karin Westin: Extending the clinical applications of magnetoencephalography. Karolinska Institute, Stockholm. Co-supervisor: Sándor Beniczky. Main supervisor: Daniel Lundquist.

Ongoing

- Maria Vlachou: Evaluation of electro-clinical findings using standardised feature extraction and machine learning. Aarhus University. Main supervisor: Sándor Beniczky.
- Levente Hadady: Assessment of the clinical impact of electronic applications and wearable devices on the clinical management of patients with epilepsy. University of Szeged, Hungary. Main supervisor: Sándor Beniczky.
- Nazanin Azarinejad Mohammadi, M.Sc., Clinical and functional characterization of GABAA-receptor related disorders: translating genetic diagnostics into personalized treatment. Faculty of Health Sciences, University of Southern Denmark. Main supervisor: Rikke Steensbjerre Møller, co-supervisor: Philip Ahring.
- Marie Amanda Bust Levy, MSc. Genetic and Functional Mechanisms in Neurodevelopmental Disorders and Epilepsy. Faculty of Health Sciences, University of Copenhagen. Main supervisor: Zeynep Tümer, co-supervisor: Rikke Steensbjerre Møller.
- Tanya Ramdal Techlo, MSc. Leverage polygenic approaches to genetically diagnose idiopathic severe epilepsy and hemiplegic migraine. Faculty of Health Sciences, University of Copenhagen. Main supervisor: Thomas Folkmann Hansen, co-supervisor: Rikke Steensbjerre Møller
- Francesca Furia, MD. Deep phenotyping of monogenic epilepsies towards the identification of targeted treatments. Faculty of Health Sciences, University of Southern Denmark. Main supervisor: Elena Gardella, co-supervisors: Rikke Steensbjerre Møller, Guido Rubboli
- Frederik Nørby Friis Sørensen, MSc. Dissecting neuronal heterogeneity and epileptogenesis in focal cortical dysplasia. Faculty of Health Sciences, University of Copenhagen. Main supervisor: Konstantin Khodosevich, co-supervisor: Rikke Steensbjerre Møller.

4. Conferences and Summer School

4.1 DICE 2022 - Implementing Epilepsy Genetical In Clinical Practice

Korsør, 7-8 April 2022

Genetic testing has increasingly become an essential part of clinical practice in epilepsy to elucidate the pathogenetic role of genetic variants in different epileptic conditions, and to provide prognostic information and to guide possible targeted therapies.

At the 5th DICE, an international panel of experts have discussed the yields of genetic testing in epilepsy patients and how the use of this diagnostic tool can lead to both better management of the epilepsies and how genetics can contribute to develop novel treatment approaches. In addition, transition from pediatric to adult care, the methodology necessary to perform clinical studies in rare conditions and the current evidences suggesting that genetics can have an impact upon both selection of epilepsy surgery candidates and post-surgical prognoses have been also discussed. Finally combined endeavors of patient associations, international epilepsy networks and registries have been also debated. The Conference was complemented by case-presentations from the audience.

An audience of more than 160 people from all over the world attended the conference, participating to the lively discussions, contributing to the success of this event, and ultimately, emphasizing how the collaboration of epileptologists, geneticists, and patient representatives can be instrumental in further improving epilepsy diagnoses and management.



DICE 2022



DICE 2022

4.2 Dianalund Summer School on EEG and Epilepsy

5th edition, July 16-23, 2022

Under the auspices of the International League Against Epilepsy (ILAE), the International Federation of Clinical Neurophysiology and the Danish Epilepsy Society, we held the 5th edition of the Dianalund Summer School on EEG and Epilepsy. This biennial course addresses advanced learning objectives and it is an official core course of the ILAE.

The course was practically-oriented, with many hands-on sessions, and it was highly interactive. The main idea of the course is to bridge the gap between epileptologists and neurophysiologists. Therefore, topics both in the realm of signal analysis and topics related to seizure semiology and clinical significance of EEG findings were covered.

The theoretical presentations (in the morning) were supplemented by EEG-reading sessions (in the afternoon), where the participants were guided through video-EEG samples by the tutors. The last day of the course was dedicated to discussion of difficult cases brought by the participants.

Twenty-seven students from 16 countries attended the course in 2022. They gave a very positive evaluation of the course, using the online evaluation site of the ILAE: 92% of the students considered that the course exceeded their expectations.



Summer School 2022



Summer School 2022

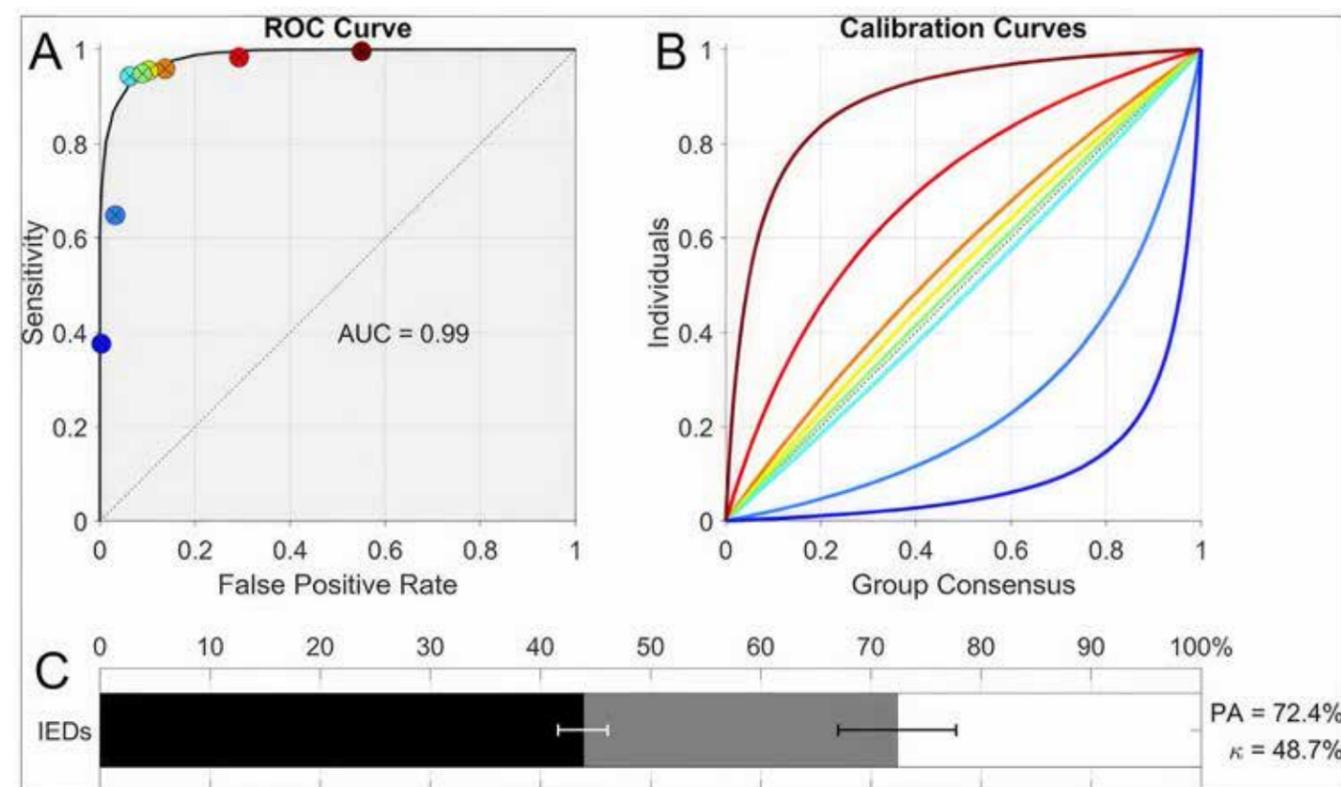
5. Research projects

5.1 Standardization and quality assurance in Clinical Neurophysiology

Standardization is essential for improving the quality of care. Clinical Practice Guidelines are important tools to achieve this goal. Guidelines must be developed using a robust methodology, based on systematic review of published evidence. Developing guidelines is resource demanding, yet much needed for clinical practice. We were happy to contribute to the clinical practice guideline on standards for inpatient long-term video-electroencephalographic monitoring. The guideline has been endorsed both by the International League against Epilepsy and the International Federation of Clinical Neurophysiology.

A significant technical impediment in clinical EEG is the lack of a universal data format. This makes shared-care and collaborative research difficult. Under the auspices of the International Federation of Clinical Neurophysiology, a working group developed a new, international standard for a universal data format, using DICOM. Our group contributed to this work.

Bias from clinical data (the text of the EEG referral) is detrimental for an objective interpretation of clinical EEG. We showed the discrepancy between what experts consider optimal, and their own clinical practice. We published a manifesto for changing the practice and improve the quality of clinical EEG interpretation.



A: Receiver operating characteristic curve fit to all experts' scores.
B: Parametric calibration curve fit to the binary scores of each expert.
C: Inter-rater reliability (IRR): Kappa (κ) values in relation to percent agreement

Papers

Vlachou M, Ryvlin P, Arbune AA, Armand Larsen S, Skraep Sidaros A, Cacic Hribljan M, Fabricius M, Beniczky S. Progressive slowing of clonic phase predicts postictal generalized EEG suppression. *Epilepsia*. 2022 Dec;63(12):3204-3211. doi: 10.1111/epi.17434. Epub 2022 Oct 29.

Vlachou M, Skrimpas GA, Kural MA, Rackauskaite G, Nikanorova N, Christensen J, Nikanorova M, Beniczky S. Electroclinical features and long-term therapeutic response in patients with typical absence seizures. *Epileptic Disord*. 2022 Apr 1;24(2):315-322. doi: 10.1684/epd.2021.1392.

Beniczky S, Tatum WO, Blumenfeld H, Stefan H, Mani J, Maillard L, Fahoum F, Vinayan KP, Mayor LC, Vlachou M, Margitta S, Ryvlin P, Philippe K. Seizure semiology: ILAE glossary of terms and their significance. *Epileptic Disord*. 2022 Jun 1;24(3):447-495. doi: 10.1684/epd.2022.1430. PMID: 35770761.

5.4 EEG Source Imaging

Using mathematical algorithms, the source of the EEG signal can be estimated in the brain. EEG Source Imaging (ESI) has been one of the research topics our group has been focusing on for more than a decade. In 2022 we continued this work, using ESI for presurgical evaluation of patients with drug-resistant focal epilepsy.

We investigated the performance of automated and semi-automated spike-detection, in relation to their localization accuracy. We found that these methods show significant agreement with visually detected spikes in the long-term recordings and concordance with the seizure onset zone. In short-term, high-density EEG, semi-automated detection of spikes is concordant with the visually detected ones, and the seizure-onset zone if high spike-counts were detected.

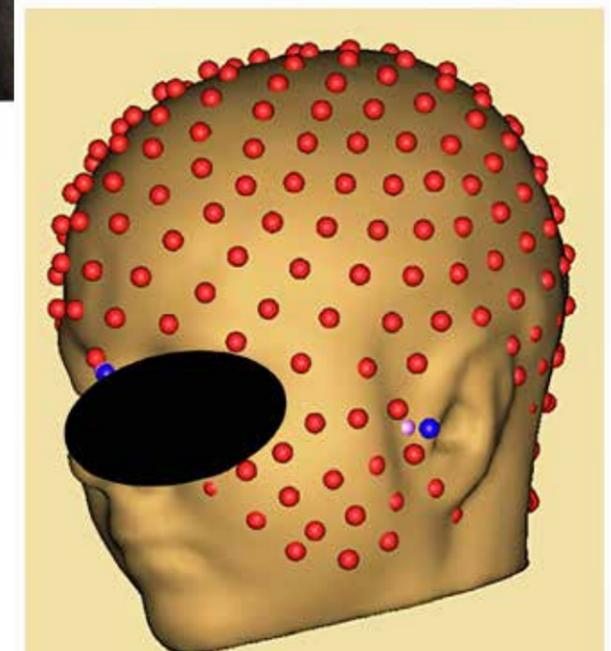
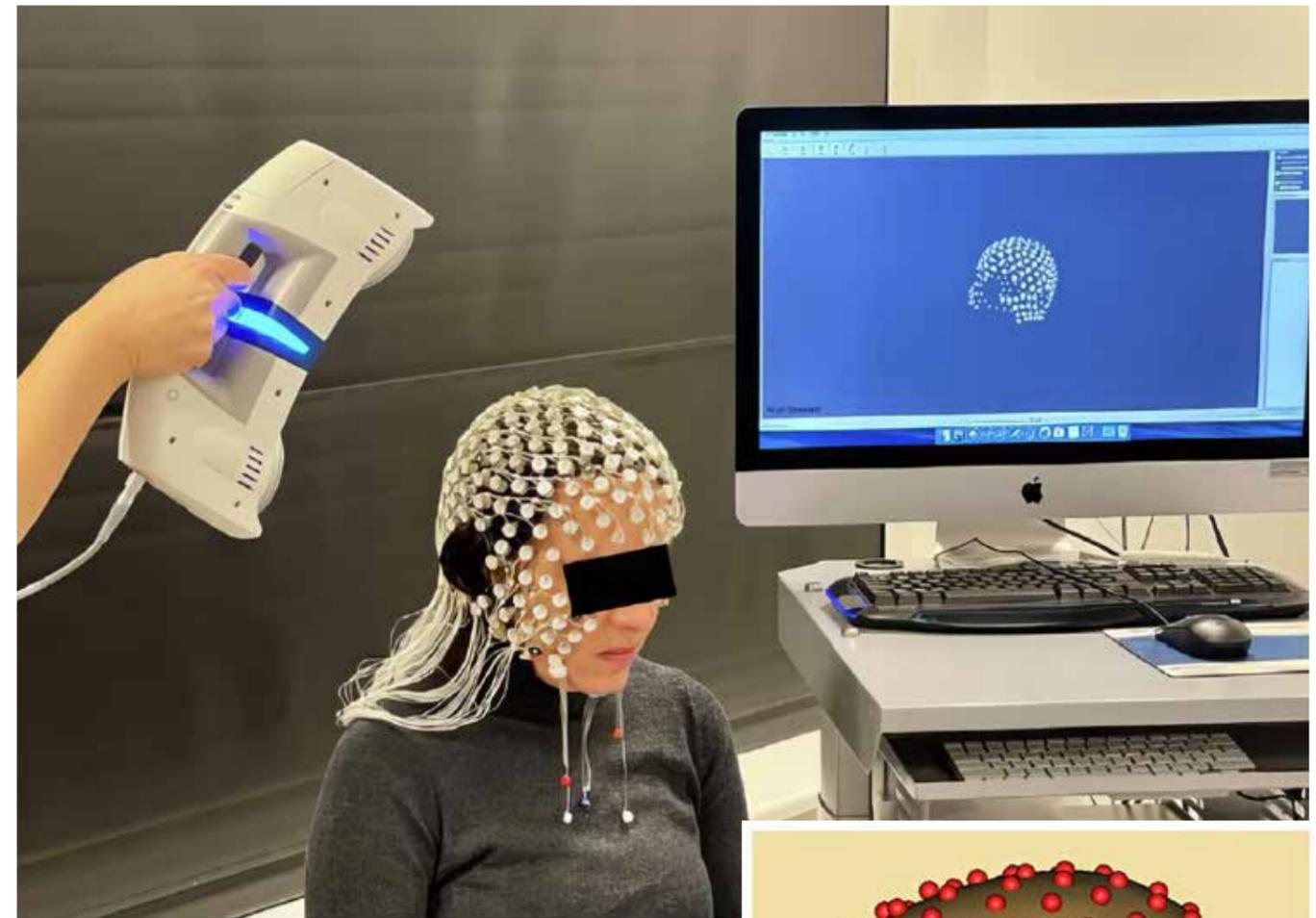
We assessed the accuracy of high-density EEG electrode position measurement, using an optical scanner compared with the classical, photogrammetry method. We found that the handheld optical scanner is more accurate and feasible, compared to the photogrammetry method. This warrants for the clinical implementation of the novel method.

We have validated the accuracy of a novel method of source localization – the relative source power (RSP) imaging of extratemporal interictal epileptiform discharge. A source region with 20 mm radius contained lesioned tissue in all cases. Using localization of the resection site and operation outcome as gold standard, we achieved a sensitivity of 82% and specificity of 50%.

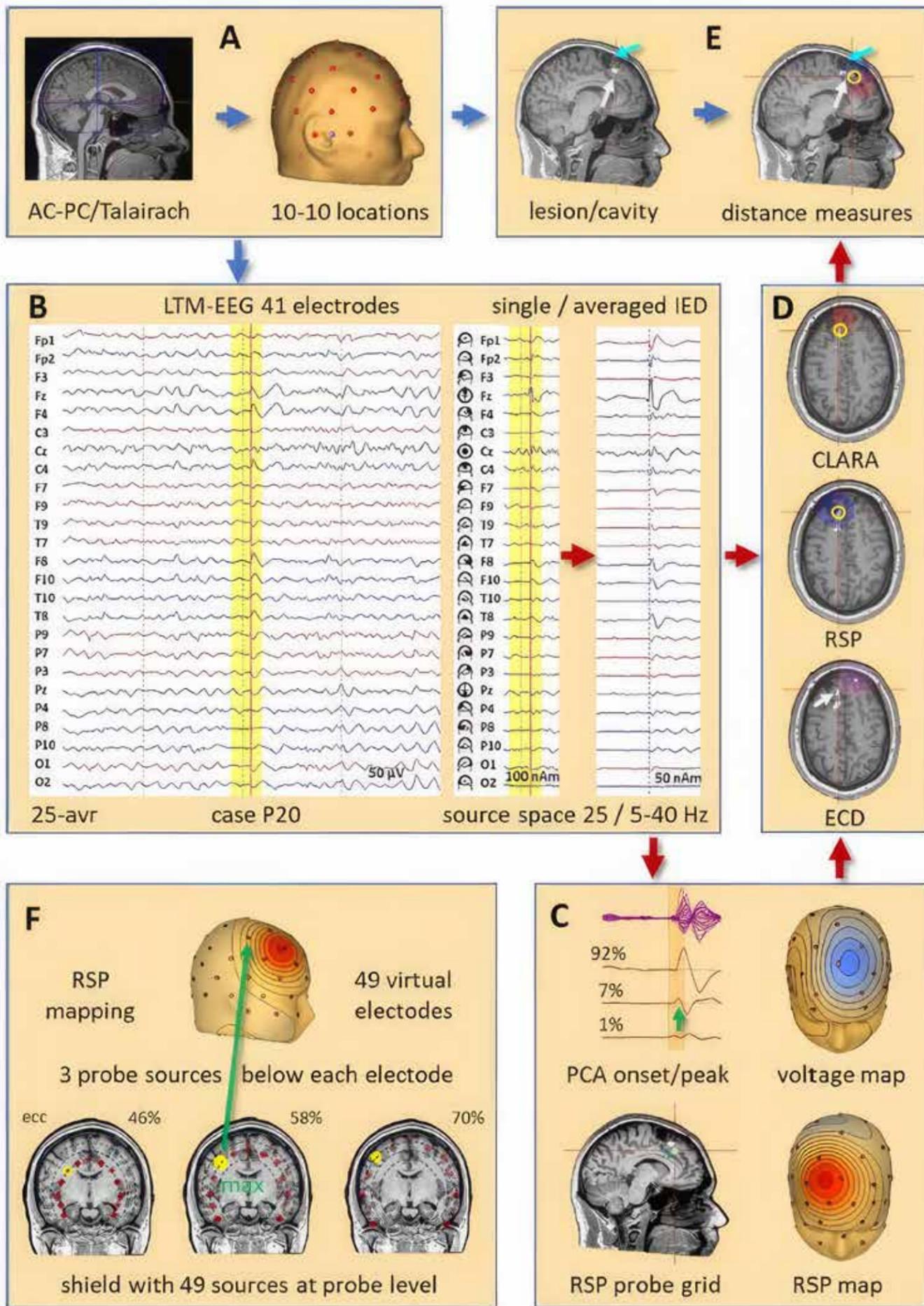
We have investigated the diagnostic utility of ESI in the presurgical evaluation of children with focal cortical dysplasia, and to compare it with other imaging techniques. Highest localization accuracy (80%) was obtained with ESI, followed by PET and ictal SPECT (75%). Our findings demonstrate that ESI using a high-density EEG array allows accurate localization of the epileptogenic zone in children with focal cortical dysplasia.

In spite of a standardized analysis pipeline, several aspects tailored to the individual patient involve subjective decisions of the expert performing the analysis. We investigated the inter-analyzer agreement of ESI in presurgical evaluations of epilepsy, using the same software and analysis pipeline. The overall agreement among experts for the ESI methods was substantial, and there was no significant difference between the methods. Our results suggest that using a standardized analysis pipeline, newly trained experts reach similar ESI solutions, calling for more standardization in this emerging clinical application in neuroimaging.

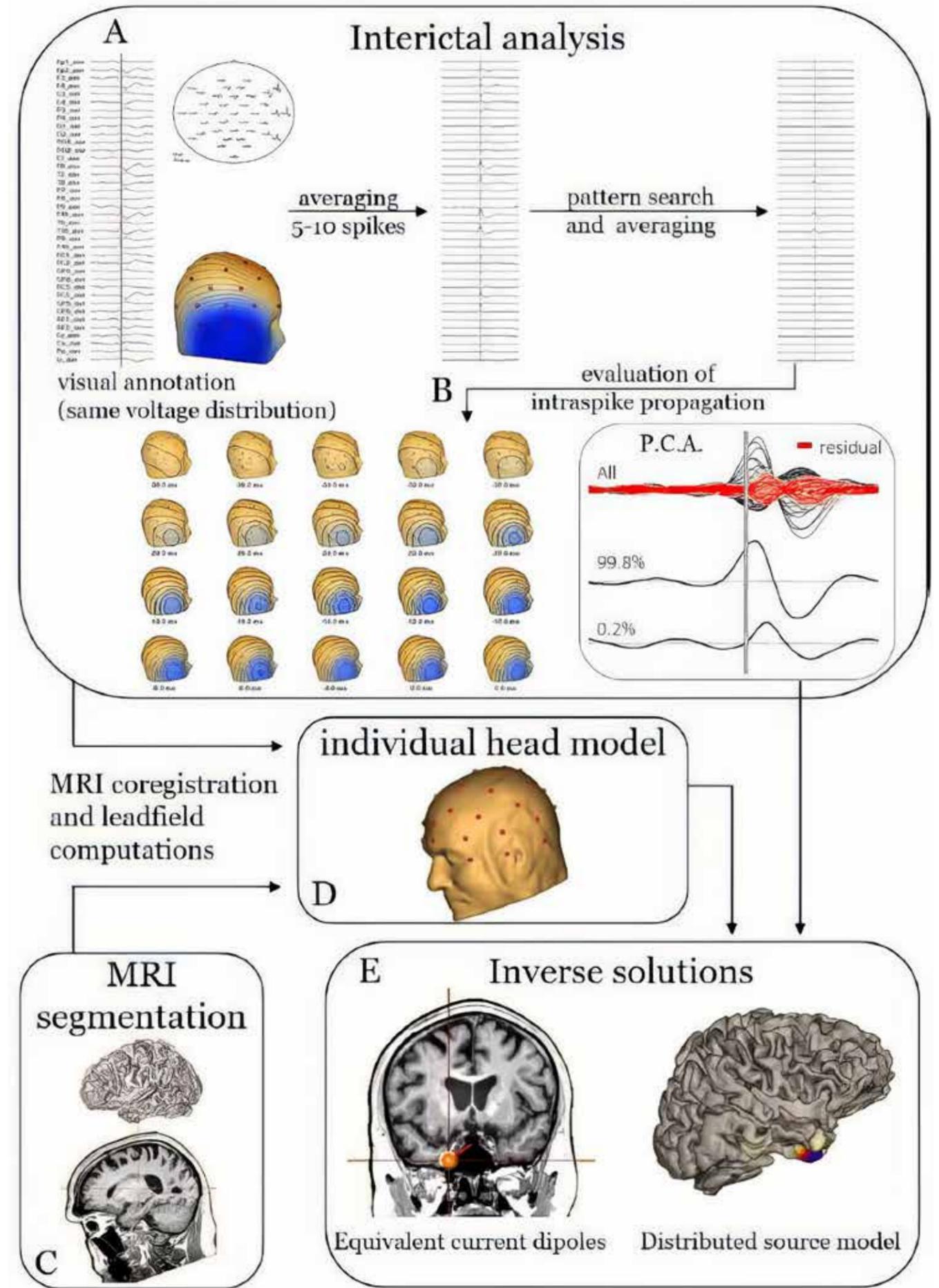
ESI requires special expertise and it is underutilized. To circumvent this, automated analysis pipelines have been previously developed and validated for the interictal discharges. In a new study published in 2022, we presented the clinical validation of an automated ESI for ictal EEG signals. The accuracy of the automated ESI was 74%. Automating the ESI of the ictal EEG signals will facilitate implementation of this tool in the presurgical evaluation.



Optical scanner for rapid and accurate measurement of the three-dimensional positions of 256 EEG electrodes in a high-density array.



Analysis pipeline of a novel ESI method: Relative Source Power.



Standardized analysis pipeline of the interictal EEG source imaging.

Publication

Heers M, Böttcher S, Kalina A, Katletz S, Altenmüller DM, Baroumand AG, Strobbe G, van Mierlo P, von Oertzen TJ, Marusic P, Schulze-Bonhage A, Beniczky S, Dümpelmann M. Detection of interictal epileptiform discharges in an extended scalp EEG array and high-density EEG-A prospective multicenter study. *Epilepsia*. 2022 Jul;63(7):1619-1629. doi: 10.1111/epi.17246.

Györfi O, Ip CT, Justesen AB, Gam-Jensen ML, Rømer C, Fabricius M, Pinborg LH, Beniczky S. Accuracy of high-density EEG electrode position measurement using an optical scanner compared with the photogrammetry method. *Clin Neurophysiol Pract*. 2022 May 2;7:135-138. doi: 10.1016/j.cnp.2022.04.002.

Scherg M, Schulz R, Berg P, Cho JH, Bornfleth H, Kural MA, Woermann FG, Bien CG, Beniczky S. Relative Source Power: A novel method for localizing epileptiform EEG discharges. *Clin Neurophysiol*. 2022 Jan;133:9-19. doi: 10.1016/j.clinph.2021.10.005.

Wanders A, Garibotto V, Spinelli L, Beniczky S, Vulliémoz S, Daniel RT, Schaller K, Bartoli A, Korff C, Seeck M. High density electric source imaging in childhood-onset epilepsy due to focal cortical dysplasia. *Clin Neurophysiol Pract*. 2022 Jul 26;7:245-251. doi: 10.1016/j.cnp.2022.07.002.

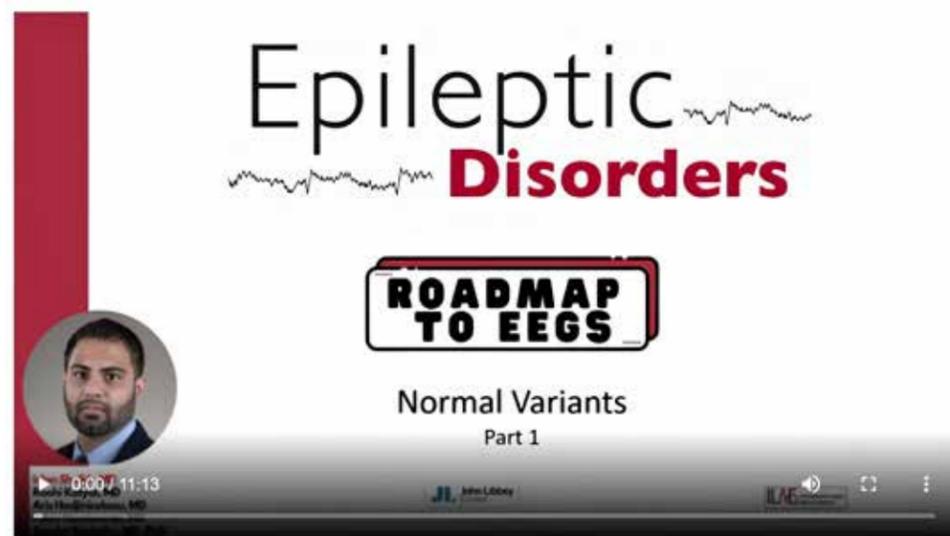
Mattioli P, Cleeren E, Hadady L, Cossu A, Cloppenburg T, Arnaldi D, Beniczky S. Electric Source Imaging in Presurgical Evaluation of Epilepsy: An Inter-Analyser Agreement Study. *Diagnostics (Basel)*. 2022 Sep 24;12(10):2303. doi: 10.3390/diagnostics12102303.

Baroumand AG, Arbune AA, Strobbe G, Keereman V, Pinborg LH, Fabricius M, Rubboli G, Gøbel Madsen C, Jespersen B, Brennum J, Mølby Henriksen O, Mierlo PV, Beniczky S. Automated ictal EEG source imaging: A retrospective, blinded clinical validation study. *Clin Neurophysiol*. 2022 Sep;141:119-125. doi: 10.1016/j.clinph.2021.03.040.

5.5 Research in postgraduate education

Postgraduate education utilizes important new knowledge in the field of adult learning. We have contributed to the development of interactive, online, self-paced learning elements, addressing the learning objectives of the ILAE curriculum in epileptology, and we have summarized these educational offerings and their performance in a paper published in 2022.

Based on a consensus discussion of a broad, international expert panel, we compiled a curriculum for the EEG patterns which neurology residents must learn during their training. We have developed an internship program at *Epileptic Disorders*, the official educational journal of the ILAE. One of the main objectives were to promote the educational activities and improve the outreach. With the interns, we developed a series of educational videos, addressing important learning objectives in EEG. These videos are available now on our YouTube channel too. We published a comprehensive, educational review paper on how to read voltage maps in EEG. We have evaluated and reported the results of the student evaluation of the educational courses which we organized at 34th International Epilepsy Congress. This content was available online too. We showed that an online interactive teaching session about the operational criteria of epileptiform discharges, significantly improved the accuracy of young trainees in interpreting EEG.



Screenshot of the online educational material on EEG normal variants.

Papers

Blümcke I, Biesel E, Bedenlier S, Händel M, Wilmshurst J, Mehndiratta MM, Yacubian EM, Cendes F, Arzimanoglou A, Beniczky S, Wolf P, Giavasi C, Baxendale S, Shisler P, Wiebe S. A structured, blended learning program towards proficiency in epileptology: the launch of the ILAE Academy Level 2 Program. *Epileptic Disord*. 2022 Oct 1;24(5):737-750. doi: 10.1684/epd.2022.1462.

Nascimento FA, Jing J, Strowd R, Sheikh IS, Weber D, Gawala JR, Maheshwari A, Tanner A, Ng M, Vinayan KP, Sinha SR, Yacubian EM, Rao VR, Perry MS, Fountain NB, Karakis I, Wirrell E, Yuan F, Friedman D, Tankisi H, Rampp S, Fasano R, Wilmshurst JM, O'Donovan C, Schomer D, Kaplan PW, Sperling MR, Benbadis S, Westover MB, Beniczky S. Competency-based EEG education: a list of "must-know" EEG findings for adult and child neurology residents. *Epileptic Disord*. 2022 Oct 1;24(5):979-982. doi: 10.1684/epd.2022.1476.

Nascimento FA, Gawala JR, Tankisi H, Beniczky S. Neurology resident EEG training in Europe. *Clin Neurophysiol Pract*. 2022 Aug 24;7:252-259. doi: 10.1016/j.cnp.2022.08.001.

Sheikh IS, Katyal R, Hadjinicolaou A, Beniczky S, Nascimento FA. Introducing the Epileptic Disorders Internship Program. *Epileptic Disord*. 2022 Dec 1;24(6):1139-1140. doi: 10.1684/epd.2022.1485.

Sheikh IS, Katyal R, Hadjinicolaou A, Nascimento FA, Beniczky S. Roadmap to EEGs: video-based e-learning modules addressing clinical EEG reading. *Epileptic Disord*. 2022 Dec 1;24(6):1132-1138. doi: 10.1684/epd.2022.1495.

Kural MA, Aydemir ST, Levent HC, Ölmez B, Özer IS, Vlachou M, Witt AH, Yilmaz AY, Beniczky S. The operational definition of epileptiform discharges significantly improves diagnostic accuracy and inter-rater agreement of trainees in EEG reading. *Epileptic Disord*. 2022 Apr 1;24(2):353-358. doi: 10.1684/epd.2021.1395.

Foged MT, Scherg M, Fabricius M, Beniczky S. Learn to interpret voltage maps: an atlas of topographies. *Epileptic Disord*. 2022 Apr 1;24(2):229-248. doi: 10.1684/epd.2021.1396.

Nascimento FA, Kural MA, Beniczky S. Learning about e-learning – the 34th International Epilepsy Congress experience. *Epileptic Disord*. 2022 Jun 1;24(3):623-625. doi: 10.1684/epd.2022.1412.

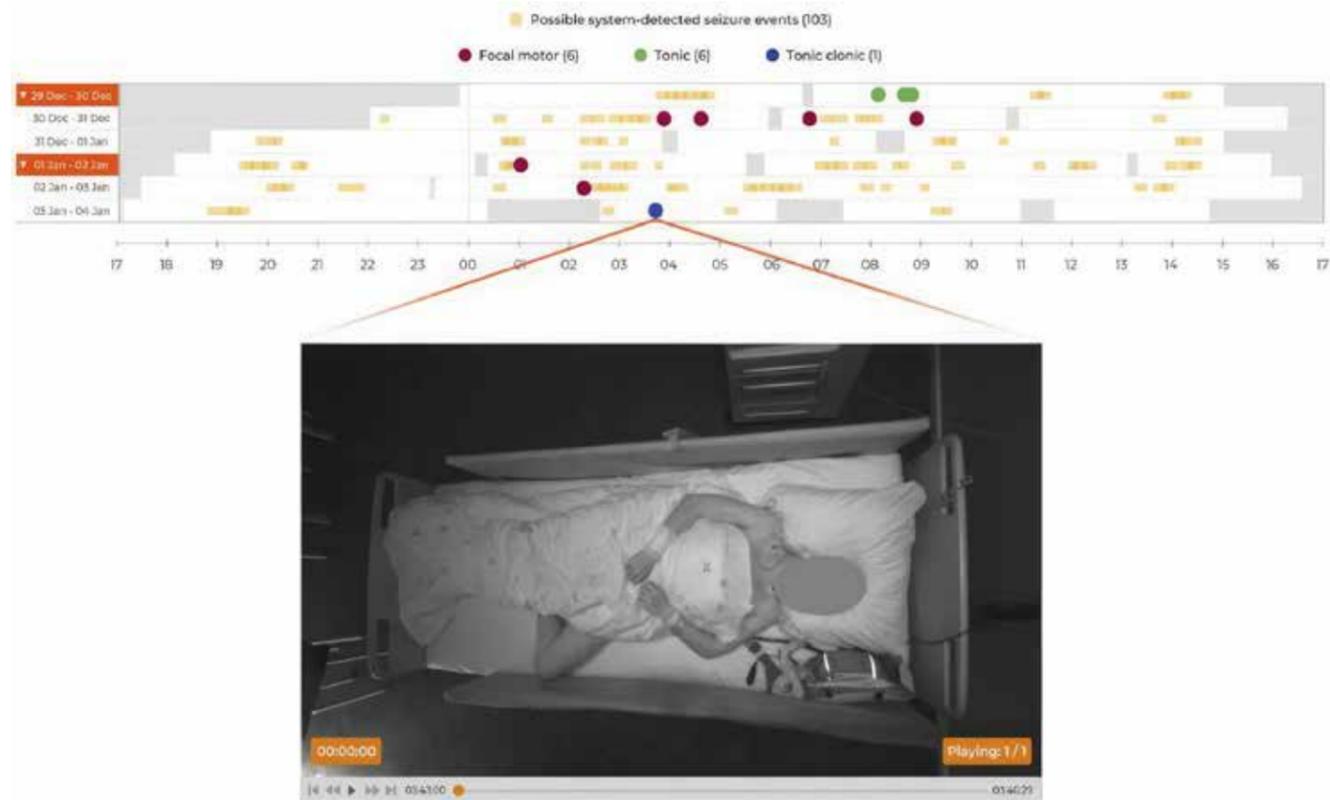
5.6 Artificial intelligence in epilepsy diagnosis and monitoring

Medical applications of artificial intelligence (AI) are likely to be a game-changer in our field too. We contributed to training and validation of AI models for automated and semi-automated analyses of videos and EEGs.

Automated video analyses was sensitive for detecting major motor seizures, such as generalized tonic-clonic seizures. However, for assessment and classification of the other seizure-types, a semi-automated ("hybrid") approach was necessary, where human experts inspected the video-epochs highlighted by the AI model. The hybrid approach significantly reduced the work-load of the human experts.

We found similar outcome for AI models detecting interictal epileptiform discharges. The fully automated application of the AI model gave high specificity, but the sensitivity was too low for clinical implementation. However, the hybrid system in which human experts inspected the automated detections, have high sensitivity and specificity, and significantly decreased the work-load.

We contributed to training and validation of an AI model which predicts impaired consciousness in absence epilepsy, based on analysis of the EEG signals.



Graphical user interface view of the video-analysis system using artificial intelligence

Papers

Armand Larsen S, Terney D, Østerkjerhuus T, Vinding Merinder T, Annala K, Knight A, Beniczky S. Automated detection of nocturnal motor seizures using an audio-video system. *Brain Behav.* 2022 Sep;12(9):e2737. doi: 10.1002/brb3.2737.

Peltola J, Basnyat P, Armand Larsen S, Østerkjaerhuus T, Vinding Merinder T, Terney D, Beniczky S. Semiautomated classification of nocturnal seizures using video recordings. *Epilepsia.* 2022 Feb 23. doi: 10.1111/epi.17207.

Kural MA, Jing J, Furbass F, Perko H, Qerama E, Johnsen B, Fuchs S, Westover MB, Beniczky S. Accurate identification of EEG recordings with interictal epileptiform discharges using a hybrid approach: Artificial intelligence supervised by human experts. *Epilepsia.* 2022 May;63(5):1064-1073. doi: 10.1111/epi.17206.

Springer M, Khalaf A, Vincent P, Ryu JH, Abukhadra Y, Beniczky S, Glauser T, Krestel H, Blumenfeld H. A machine-learning approach for predicting impaired consciousness in absence epilepsy. *Ann Clin Transl Neurol.* 2022 Oct;9(10):1538-1550. doi: 10.1002/acn3.51647.

5.7 Wearable devices in epilepsy monitoring

One of the main research topics of our group is development and validation of wearable devices for automated seizure detection and characterization. In 2022 we continued working on numerous projects in this area.

We have validated an artificial intelligence-based algorithm for automated detection of absence seizures, using a wearable non-invasive EEG device. In a proof of principle study, we demonstrated the feasibility and clinical utility of automated behavioral testing triggered by automated seizure detection. We contributed to a multicenter study on detection of temporal lobe seizures using ultra-long term monitoring with a subcutaneously implanted EEG device. Our findings demonstrated that semi-automated seizure detection/review process can be performed with high sensitivity and clinically applicable specificity. In a large, international survey study on the ultra-long-term experience of patients with using wearable devices, we showed the clinical utility of these devices, and we found that the devices formally validated in phase-3 studies performed better than the other devices.



Graphical user interface view of the video-analysis system using artificial intelligence

Papers

Japaridze G, Loeckx D, Buckinx T, Armand Larsen S, Proost R, Jansen K, MacMullin P, Paiva N, Kasradze S, Rotenberg A, Lagae L, Beniczky S. Automated detection of absence seizures using a wearable electroencephalographic device: a phase 3 validation study and feasibility of automated behavioral testing. *Epilepsia.* 2022 Feb 17. doi: 10.1111/epi.17200.

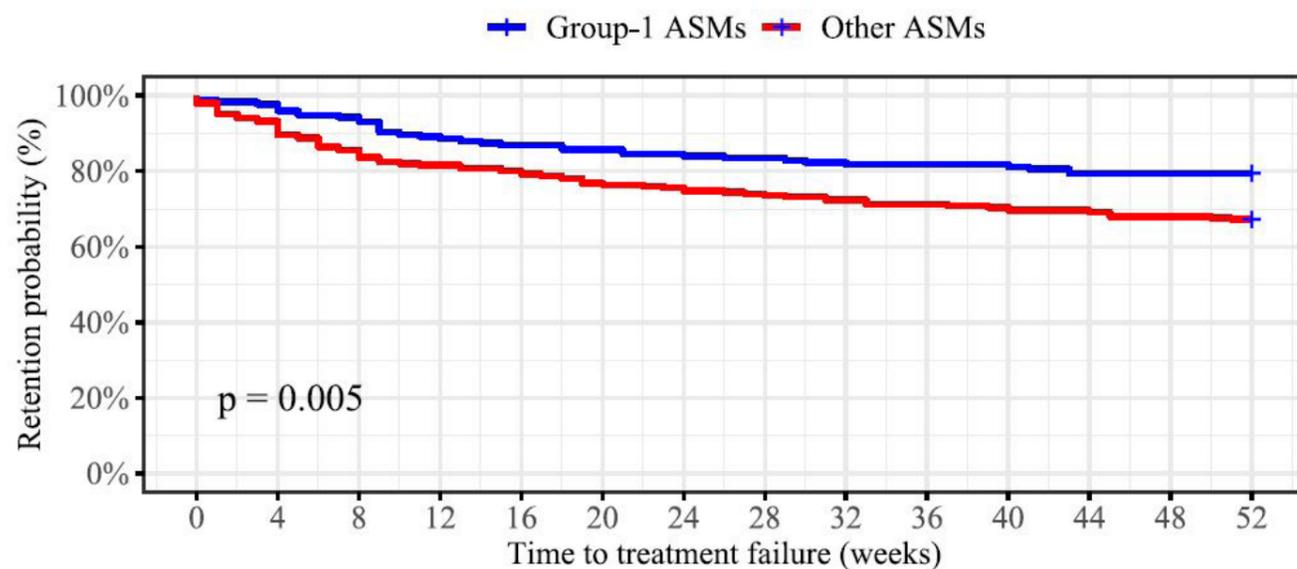
Remvig LS, Duun-Henriksen J, Furbass F, Hartmann M, Viana PF, Kappel Overby AM, Weisdorf S, Richardson MP, Beniczky S, Kjaer TW. Detecting temporal lobe seizures in ultra long-term subcutaneous EEG using algorithm-based data reduction. *Clin Neurophysiol.* 2022 Oct;142:86-93. doi: 10.1016/j.clinph.2022.07.504.

Hadady L, Klivényi P, Fabó D, Beniczky S. Real-world user experience with seizure detection wearable devices in the home environment. *Epilepsia.* 2022 Feb 23. doi: 10.1111/epi.17189.

5.8 Epipick: a web-based decision support system for optimal, patient-tailored choice of antiseizure medication

We developed the Epipick - a freely accessible web-based application (<https://epipick.org>) to help health care professionals select the most appropriate, patient-tailored antiseizure medication (ASM) in patients with epilepsy (seizure onset at 10 years of age or older). EpiPick considers seizure types and patient-specific variables to provide treatment recommendations, ranking ASMs in order of appropriateness based on the available scientific evidence and expert judgement. The app also provides a summary of prescribing information for each of the ASMs being suggested.

After the original publication of the application in 2021, we continued monitoring the published evidence and we updated the application accordingly in 2022. We completed a large-scale validation study on 425 consecutive patients with newly diagnosed epilepsy, who were followed for at least 1 year after starting medication. ASMs classified by the algorithm as best options had a significantly higher retention rate, higher seizure freedom rate and lower rate of discontinuation due to adverse effects than ASMs ranked as less desirable by the algorithm. We concluded that the use of the freely available decision support system is associated with improved outcomes. This drug selection application can provide valuable assistance to health care professionals prescribing medication for individuals with epilepsy.



Kaplan–Meier analysis of the time to treatment failure. Patients treated with best option antiseizure medications (ASMs) recommended by the algorithm (Group 1) versus patients treated with other drugs

Papers

Hadady L, Klivényi P, Perucca E, Rampp S, Fabó D, Bereczki C, Rubboli G, Asadi-Pooya AA, Sperling MR, Beniczky S. Web-based decision support system for patient-tailored selection of antiseizure medication in adolescents and adults: An external validation study. *Eur J Neurol.* 2022 Feb;29(2):382-389. doi: 10.1111/ene.15168.

Asadi-Pooya AA, Beniczky S, Rubboli G, Sperling MR, Rampp S, Perucca E. The EpiPick algorithm to select appropriate antiseizure medications in patients with epilepsy: Validation studies and updates. *Epilepsia.* 2022 Jan;63(1):254-255. doi: 10.1111/epi.17129.

5.9 GABA-A receptor related epilepsies

Developmental and Epileptic Encephalopathies (DEEs) are devastating early-onset conditions associated with intractable epilepsy, intellectual disability, developmental delay/regression, movement, and autism spectrum disorders. The condition is highly debilitating for both the impacted children and their caretakers. Genetic factors play a major role in the underlying cause of DEEs, and pathogenic variants in subunits of the γ -aminobutyric acid type A receptor (GABAAR), the major inhibitory protein of the brain, are found to be a common cause of DEE. Until recently these were assumed to lead to loss-of-function (hypoactive) receptors supporting a hypothesis that reduced GABAergic inhibition causes overexcitation in the brain leading to epilepsy.

Recently, we have published exciting new data that contradicts the belief that only loss-of-function GABAARs cause DEE. We discovered that the functional assessment of pathogenic variants from a subset of GABAAR subunits, led to an equal distribution of loss- and gain-of-function receptors. It is currently unknown how increased GABAAR function leads to DEE, however, the paradoxical finding of gain GABAARs has subsequently been confirmed by others. Furthermore, we discovered that patient phenotypes were linked to the functional outcome of the variants and that gain variants are associated with more severe forms of treatment resistant epilepsy.

Papers

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5.10 GRIA-related disorders

Developmental and Epileptic Encephalopathies (DEEs) are rare and severe neurological conditions often associated with intellectual disability, developmental delay, autism spectrum disorders and movement disorders. Seizures often begin in early infancy, and patients are often resistant to antiepileptic treatment.

Genetic factors play a major role in the underlying cause of many DEEs, and the identification of the causative genes have disclosed unique information on the different pathomechanisms and opened novel therapeutic perspectives. Recently, human variants in the α -amino-3-hydroxy-5methyl-4-isoxazole propionic acid receptor (AMPA) have been reported to cause of DEE. This receptor is important as it helps to maintain normal brain activity and variants in GRIA genes that encode the AMPAR will cause changes to normal brain function.

The overall aim of this proposal is to establish specific correlations between phenotype, genotype, functional effects and therapeutic response to translate genetic diagnostics into therapy. Knowing the functional effect of a genetic variant can assist clinicians to avoid ineffective or even disease-aggravating treatments. Our findings will help change the current paradigm of treating patients with DEE currently uses a trial-and-error approach to one that utilizes precision medicine based on a patient's genetic, functional and clinical diagnoses (Figure 1).

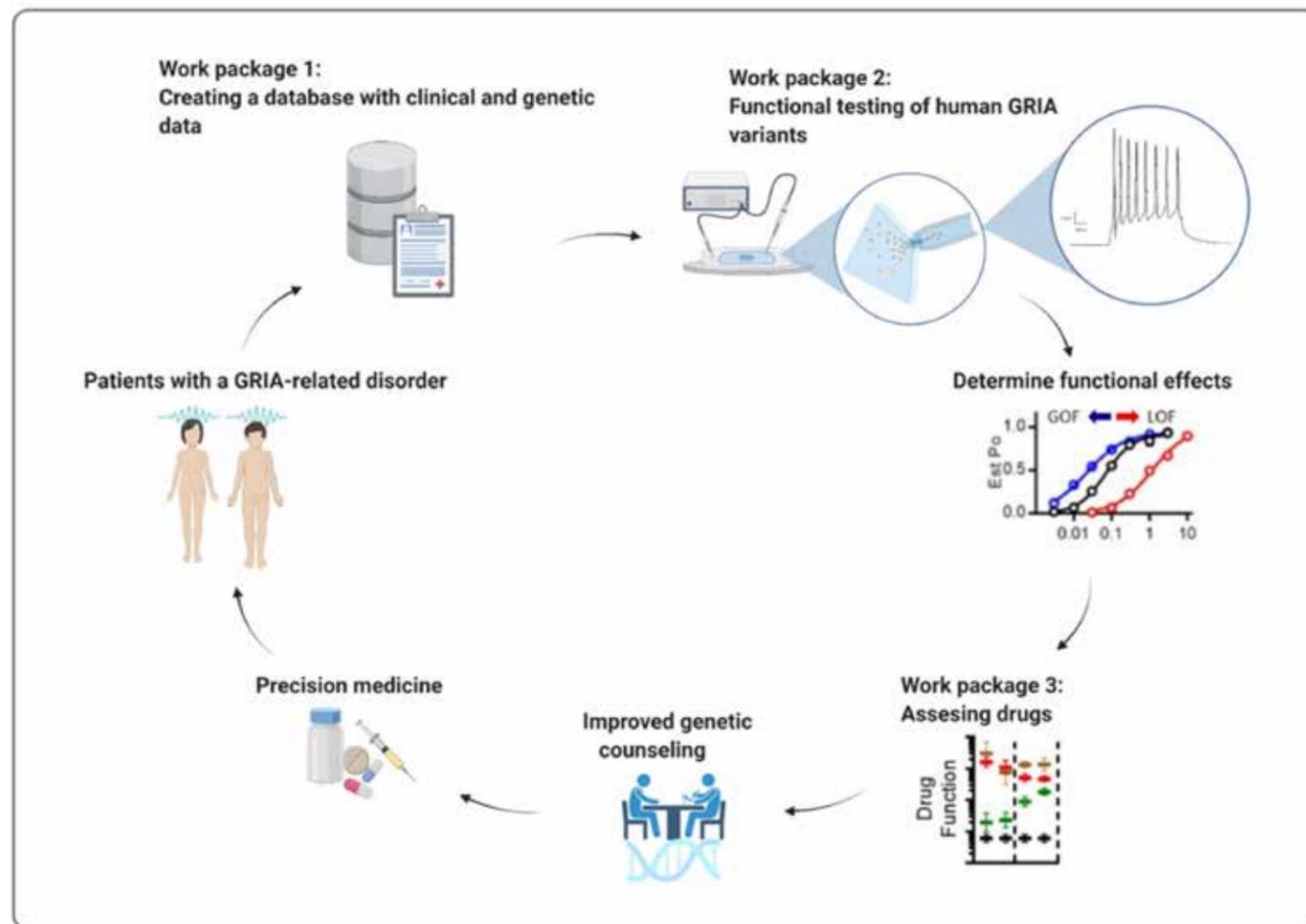


Illustration of the research strategy and how the three work packages bridge the translational gap and ultimately enable precision therapy.

5.11 Ultra-long sub-cutaneous EEG monitoring: reliability,, safety and impact on clinical management in uncontrolled epilepsies

In epileptology, seizure classification and quantification are among the main parameters that contribute to define the degree of severity of an epileptic condition, and they are crucial to guide individual treatments. However, patient self-evaluation compared with objective evaluation by videoEEG monitoring or long-term ambulatory EEG revealed that patients' self-assessment is highly imprecise, documenting fewer than 50% of their seizures, on average. Recently, a novel EEG recording device consisting of an EEG electrode designed for subcutaneous implantation (subcutaneous EEG, 24/7 EEG™ SubQ) connected to an external device has been shown to be able to record EEG for periods of time up to 3 months. We have initiated a study in drug-resistant epilepsy patient using sqEEG with the purposes of:

- assess the sensitivity, reliability and safety of the 24/7 EEG™ SubQ device for recording seizures over longer periods (over 1 month) in people suffering from either focal or generalized uncontrolled epilepsy
- assess sensitivity and reliability of automated seizure recognition software in the 24/7 EEG™ SubQ equipment
- evaluate how and whether data collected with the 24/7 EEG™ SubQ equipment can influence the clinical treatment of the participating subjects

In 2021-2022, 3 patients have been implanted, showing that sqEEG can be a promising technique for long-term seizure recording and possibly for drug effects assessment.

5.12 The Human Related Conversation and the Professional Tension Between Diaconia and Nursing

The article explores how nurses experience tension in a professional collaboration between nursing and work with a diaconal profile in Filadelfia, Denmark. Filadelfia was founded in 1897 as a diaconal institution with a hospital and deaconess house. Today, Filadelfia appears primarily as a highly specialized Epilepsy Hospital unrelated to diaconia. The collaboration this article investigates is called The Human Related Conversation (hereafter THRC). It is a practice developed within a diaconal unit of the institution, Filadelfia Uddannelse, and performed by nurses at Filadelfia Epilepsy Hospital. The article is based on a discourse analysis of five interviews conducted using THRC. The analysis finds that the nurses' experience of THRC generates different discourses, including a nursing discourse and a legitimacy discourse, and encourages them to work in a more value-conscious way.

Papers

Hjelm, Conny (2021 [2022]): The Human Related Conversation and the Professional Tension Between Diaconia and Nursing. *Diaconia*, vol. 12, p. 137-160. doi:10.13109/diac.2021.12.2.137



Conny Hjelm
Deacon and Ph.d. stud.

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7. Lectures - oral presentations in 2022

Sándor Beniczky:

- ILAE Residential Comprehensive Epilepsy Surgery Course: 11th EPODES (online, January 25, 2022) Scalp video-EEG monitoring in adults
- American Clinical Neurophysiology Society Annual meeting (Orlando, January 30 2022). Quantitative Analysis of Surface EMG in Functional Seizures
- Annual Meeting of the European Reference Network for epilepsy: EpiCare (Lyon, February 17, 2022) Update on the Clinical Neurophysiology work-package
- 16th World Congress on Controversies in Neurology (CONY) (online, March 26, 2022) Do seizure detection devices have a significant role in managing people with epilepsy?
- The Triennial Course of the British Society of Clinical Neurophysiology (Oxford, March 28, 2022) Identifying interictal epileptiform EEG discharges
- Clinical and Scientific Meeting of the Irish Society of Clinical Neurophysiology (Dublin, April 1, 2022) EEG in Critically Ill Patients
- Fourth International Taiwanese Congress of Neurology (Taiwan, April 15, 2022) EEG source image in clinical practice
- 63rd Annual Meeting of the Japanese Society of Neurology (Tokyo, May 18, 2022) Automated seizure detection using wearable device
- Electroencephalography Teaching Course (Santander, May 26-27, 2022) EEG in status epilepticus EEG in critically ill patients
- BrainDrugs Annual Meeting (Snekkersten, June 10, 2022) Epipick: a web-based algorithm for optimal, patient-tailored choice of antiseizure medication
- ICTALS 2022 – The tipping point (Bern, July 8, 2022) Devices for epilepsy

- ILAE - European Epilepsy Congress (Geneva, July 9-12, 2022) Interactive, half-day EEG teaching course EEG source imaging: basic principles and clinical applications
- Dianalund Summer School on EEG and Epilepsy (5th edition, July 16-23, 2022) Systematic approach to clinical EEG reading Standardized Computer-based Organized Reporting of EEG Electromagnetic Source Imaging
- ILAE – Epilepsy Summer School (Slanic Prahova, September 2, 2022) Seizure semiology: ILAE glossary of terms and their significance
- International Congress of Clinical Neurophysiology (Geneva, September 3-8, 2022)
- How to Use Voltage Maps to Estimate the Source Interictal Epileptiform Discharges: What’s New for This Old Stuff? Automated and Semi-Automated Source Imaging
- Epilepsy colloquium (Lausanne, September 14-16, 2022) Pitfalls in ictal scalp-EEG interpretation Wearable devices for automated seizure detection
- The 55th Annual Congress of the Japan Epilepsy Society (Sendai, September 21, 2022) A pragmatic algorithm to classify seizures without EEG
- ILAE – Latin-American Epilepsy Congress (Medellin, October 4, 2022) Electric Source Imaging of scalp recordings: impact on patient management.
- Annual meeting of the ILAE British Chapter (Cardiff, October 13, 2022) The Salzburg consensus criteria for non-convulsive status epilepticus
- 4th International video-EEG course in pediatric epilepsies (Madrid, October 29, 2022) The role of source analysis in epilepsy surgery
- Annual meeting of the Danish Epilepsy Society (Copenhagen, November 4, 2022). Is this epilepsy? Or not? An interactive video-EEG session.
- ILAE - Asian & Oceanian Epilepsy Congress (online, November 18, 2022) Can seizure detection devices reduce mortality?
- Forum of Excellence in Epilepsy (London, November 19, 2022) AI interpretation of EEG in epilepsy
- Epilepsy symposium (Szeged, November 24-25, 2022) EEG interpretation in clinical practice Seizure semiology and classification
- Annual meeting of the American Epilepsy Society (Nashville, December 6, 2022) What is an epileptiform discharge?
- Conference of the Egyptian Epilepsy Society (online, December 23, 2022). Accurate identification of interictal epileptiform discharges.

Rikke Steensbjerre Møller:

- Personalized medicine in epilepsy – upcoming new treatments, Annual Meeting of the Danish Society of Epileptology, Copenhagen, Denmark
- Importance of epilepsy genetics for diagnosis, treatment, and prognosis. 4th Annual Meeting between the Danish and the Norwegian Epilepsy Centre, Copenhagen, Denmark
- Genotype-phenotype correlations in SCN8A-related disorders reveal prognostic and therapeutic implications. Childhood Epilepsy and Movement Disorders Workshop, Barcelona, Spain
- Experience with precision medicine for epilepsy in a Danish tertiary reference center. Impact and hurdles. SEED conference 2022, Tunis, Tunisia
- Future perspectives of genetics in epilepsy. Educational course. The Chilean Society of Neurology and Psychiatry of Childhood and Adolescence (SOPNIA) (Virtual)
- Precision Medicine in Genetic Epilepsies: Challenges and Opportunities. 60th Annual Meeting of the German Society of Epileptology, Leipzig, Germany
- Utility of genetic testing for therapeutic decision-making in individuals with epilepsy. University of Washington, Saint Louis (Virtual)
- Sodium channelopathies (SCN2A-SCN8A). Genetic Epilepsies and Precision Medicine, EPIGENS (Virtual)
- Developmental and epileptic encephalopathies: genetic diagnosis in adolescents and adults. Curso de Invierno de Epilepsia, La Granja, Spain

Guido Rubboli:

- “Group Discussion on Topics: Surgery”, Speaker at the Nordic Experience Sharing Meeting, Korsør, 6 April 2022.
- “ESES: an update”, speaker, virtual meeting, University of Padova, 31 May 2022.
- “Genetics in epilepsy - children and adults. The clinician’s perspective.” National Anniversary symposium Oslo 9-10 June, 2022
- “Half-day Teaching Course: Genetic testing: whom, when and what to test”, European Epilepsy Congress, Geneva 9 July 2022
- “Ultra-long sub-cutaneous EEG monitoring: reliability, safety and impact on clinical management in uncon-

trolled epilepsies. Our experience with 24/7 EEG SubQ24: preliminary results. Speaker in collaboration with S. Beniczky. Meeting sponsored by UNEEG at the European Epilepsy Congress, Geneva, 11 July 2022

- “Teaching Session: Video session – adult”, European Epilepsy Congress, , Geneva 13 July 2022
- “Polygraphic recordings” at the 5th ed. Dianalund Summer School on EEG and Epilepsy, Dianalund, 16-23 July 2022, in collaboration with E. Gardella.
- “Erfaringer med PER som tidlig tillæg i klinisk praksis” webinar meeting, Speaker 6 september 2022
- “Understanding pathophysiology and improving outcomes in Electrical Status epilepticus during Sleep (ESES)”, 8th London-Innsbruck Colloquium on status epilepticus and acute seizures, Salzburg, 17-20 September 2022
- “EPI_PED course. Genetic and EEG comparison in pediatric epilepsy”, speaker and tutor, Bologna, 9-13 October 2022.
- “Photosensitivity in epileptic syndromes” and “From bench-to-bedside II. Interactive presentation of cases. Cases with absences, tonic, atonic and myoclonic seizures”, Video-EEG in pediatric epilepsies, “From seizures to syndromes”, Madrid, 27-29 October 2022.
- “La classificazione neurofisiologica del mioclono - circuiti sottesi”, Diagnostic working group of the Italian League Against Epilepsy, Rome, 17-18 November 2022.
- “Introduction” at the 4th Annual Meeting Danish Epilepsy Center and Norwegian Epilepsy Center “Epilepsy syndromes 2022”, Copenhagen , 10 November 2022

Elena Gardella:

- Fuori dall'ombra, Padova, Italy
- 5th Dianalund International Conference on Epilepsy (DICE), Køge, Denmark
- LEGOLAS annual meeting, Amsterdam, The Nederland
- 14th European Epilepsy Congress (EEG); Geneva, Switzerland
- STXBP1 Summit and family meeting
- 4th Annual Meeting DEC and NEC, Copenhagen, Denmark
- Nordic Epilepsy Sharing meeting on personalized medicine (part VI)- Natural History Studies and drug trials readiness, Copenhagen, Denmark
- Annual Meetig of the CUTE syndrome foundation / American Epilepsy Society meeting, Nashville, USA
- 5th Dianalund Summer School on EEG and Epilepsy (DSSEES), Dianalund, Denmark
- 9th International Residential Course on Drug Resistant Epilepsies, Tagliacozzo, Italy
- EPIPED-EEG course “Genetic and EEG comparison in pediatric epilepsy”, Bologna, Italy
- EpiCARE Workshop: Childhood Epilepsy and Movement Disorders Translational Medicine and Novel Therapeutic Approaches; Barcelona, Spain
- Video-EEG in pediatric epilepsies Madrid

Marina Nikanorova:

- How do we choose ASMs for refractory epilepsies in childhood – online meeting with Finnish neuropediatricians, 08.03.22
- Clinical experiences with Fenfluramin in Denmark – Advisory Board, 28.06.22
- Early adjustment of Perampanel in refractory epilepsy in children and adults – Advisory Board, 06.09.22
- ILAE Epiwebtutorial – 20.09.22 (Case-oriented learning)
- 15th Baltic Sea Summer School on Epilepsy – Case-oriented learning, 3 online sessions, September 2022
- Epileptic encephalopathies of childhood: outcome in adults – meeting of the Lithuanian ILAE Chapter, 14.10.22
- Diagnosing, treating and managing patients with Lennox-Gastaut syndrome – online Nordic meeting for neuropediatricians and neurologists (Denmark, Finland, Norway, Sweden), 25.10.22

Allan Bayat:

- GRIA3 related disorders. ILAE-Europe Epilepsy workshop. Rome.
- Two electrode voltage clamping – TEVC. ERN-ITHACA Research workgroup. Budapest.
- Understanding GPI anchoring disorders, precision medicine and unwinding the cause of a high childhood mortality. LEGOLAS-meeting, Amsterdam.
- Impact of genetic testing on therapeutic decision making in childhood-onset epilepsies. European conference on epilepsy, ILAE, Geneve, Switzerland.
- Pyridoxine or pyridoxal-5-phosphate treatment for seizures in glycosylphosphatidylinositol deficiency: A cohort study. European conference on epilepsy, ILAE, Geneve, Switzerland.
- Phenotypical and functional assessment of four novel KCNQ2 gain-of-function variants and effects of amitriptyline treatment. The 5th Dianalund International Conference on Epilepsy.

8. Acknowledgements

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