

Final rapport “Bourse Foundation St-Luc”

Dear Dr.Vanoverschelde,

During my stay at the Cleveland clinic I was able to perfection my knowledge and skills in treatment of refractory epilepsy.

On educational level, I have completed a 3-month EEG and neurophysiology course organized by the Cleveland Clinic, a very well-known and established course in the USA. Attending this course was extremely useful as I was able to review the basics of EEG and epileptology, brain anatomy but also learn more about technical aspects of EEG recording systems. During this course, I accomplished homework EEG readings, which allowed me to acquire systematic reading skills. At the end, I have successfully completed the EEG and neurophysiology examination. In addition, this course also permitted me to acquire better insights how to teach in a comprehensive way neurophysiology and epileptology in general.

On clinical level, I was able to perfection my EEG readings and interpretation of semiology of epileptic seizures. For this purpose I have read under supervision multiple routine EEG's and non-invasive epilepsy monitoring unit EEGs. In addition, I co-monitored two stereo-EEG (SEEG) patients and read independently 2 SEEG cases. This reading allowed me to observe the surgical procedure of the implantation, to understand how a hypothesis of seizure localization is formed, to appreciate different types of epileptic networks and decide upon the most appropriate placement of the electrodes to prove different hypotheses. It also permitted me to perfection my anatomical knowledge as I localized all electrodes contacts in several patients using a specific atlas. Besides this reading, I also attended every monday evening the SEEG course given by Prof. Chauvel, an important French epileptologist who is actually working at the Cleveland clinic. On the level of neuro-imaging, my fellowship permitted me to get acquainted with ictal SPET and Magneto encephalography, which are not available at our center, but were of standard use in the presurgical evaluation at the Cleveland clinic. Every week, presurgical candidates were discussed at the pluridisciplinary meeting, which were very divers and extremely instructive. Fellows were given the opportunity to comment on specific cases they had monitored.

Besides my clinical work, I also attended weekly general epilepsy and pediatric epilepsy grand rounds. These lectures were always very enriching and part of our training. I have added the program of both grand rounds for your information.

I have presented two lectures, one at the Epilepsy grand rounds about advancements in the field of vagus nerve stimulation and one presentation about epilepsy in POLG 1 mutations at the Pediatric grand rounds.

On scientific level, my stay at the Cleveland Clinic was extremely successful. First of all, I performed a large retrospective study analyzing the diagnostic value of MEG and SPECT in patients that underwent a new presurgical evaluation after a previous single or multiple failed epilepsy surgery. This study permitted me to acquire knowledge about MEG and SPECT, but also to get acquainted with the program CURRY 6 (Compumedics, Charlotte, NC), which is a program that allows co-registration of different imaging modalities. By using this program I was able to co-register different sets of images: pre-surgical MRI (which contained resection from the previous surgery), MEG (dipole locations printed on top of the pre-surgical MRI), SPECT, and post-operative MRI (which contained resection of the previous surgery and the second surgery). The manuscript is in preparation for submission to Journal of Neurology, Neurosurgery and psychiatry.

In addition to this study I have written two case reports. The first case report presents a patient in which MEG was localizing and concordant with other studies in two repeated evaluations, which led to two resections, but did not render the patient seizure-free, illustrating that a single tight cluster does not always reflect correctly a possible larger epileptogenic zone. This manuscript was accepted in Clinical neurophysiology with moderate revisions. The second case report relates to a patient treated with Neuropace, which is a responsive intracranial neurostimulator, not yet available in Europe. This case report gave me the opportunity to learn about this treatment modality. The manuscript describes how a lead break of the Neuropace led to EEG artifacts which were visible on the intracranial recordings before lead impedance went high and seizure frequency deteriorated. This manuscript is in preparation for submission to Journal of Clinical Neurophysiology.

Finally, this fellowship gave me the opportunity to broaden my network within the Epilepsy community, which is an important matter when establishing international scientific and clinical collaborations.

I would like to thank La Fondation Saint Luc to help me to realize this ambitious learning experience.

Sincerely,

Riem El Tahry

Appendix 1: Clinical epilepsy and clinical neurophysiology/EEG course



CLEVELAND CLINIC CLINICAL EPILEPSY & CLINICAL NEUROPHYSIOLOGY/EEG COURSE

Training Programs: Epilepsy & Clinical Neurophysiology/EEG
Program Director: Andreas V. Alexopoulos, MD, MPH

Course Structure:

The clinical neurophysiology/epilepsy course given at the Cleveland Clinic is an intensive 3-month course designed to introduce core clinical competency in clinical neurophysiology and epilepsy training. The course consists of a 7 week lecture series and 4 one-week workshops, where the students have hands-on learning in the form of case-based review & discussion of various topics pertaining to epilepsy, video-EEG & clinical neurophysiology.

Weeks 1 – 7: Didactic lecture series

During the first 9 weeks a series of didactic lectures are given to cover in depths various topics in epilepsy & clinical neurophysiology. Each week is dedicated to a main core topic that is covered during the week such as EEG technology, Normal Variants, Non-epileptic abnormalities, Epileptic patterns, Evoked Potentials, Sleep neurophysiology, etc. Each week will consist of morning lectures that cover various subjects pertinent to the core topic. In the afternoons, students will be expected to complete EEG homework or other clinical neurophysiology assignments. Also, during each week a session called "EEG Unknowns" is given to teach students how to evaluate an EEG in a logical and systematic manner. In addition, students will also observe our daily video-EEG rounds in the adult and pediatric service, and our weekly conferences (Patient Management Conference, Pediatric Epilepsy Grand Rounds, Unknown Epilepsy Case Presentations, and Epilepsy Center Grand Rounds).

Weeks 1 – 7

EEG homework (and any other assignments) will be completed individually by each student. Each student will be responsible for looking at the EEG and handing in his/her own report, so that individual performance and progress can be assessed.

Weeks 8 – 11: Workshops

The last three weeks of the course will consist of three one-week workshops focusing on video-EEG monitoring: adult, pediatric, and invasive. Homework will reflect the subjects being taught in each of the workshops and will consist of studying video-EEG cases.

Week 8

Continuous Bedside Video-EEG Workshop

The entire student group will work together on analyzing two cases, one grid and one depth; starting from the noninvasive evaluation, followed by patient management and invasive work-up, and concluding with surgery.

Weeks 9-10

Adult and Pediatric Noninvasive Video-EEG Workshops

Days 1 – 3

Students are placed in small groups with each group tasked to review a pediatric or adult EMU case. History and examination are given in written format. Video-EEG data, MRI and other data are provided without interpretation for the groups to analyze. The staff will then facilitate discussion with a specific focus in defining the patient's epilepsy making use of all aspects of these investigations in a case conference format.

Days 4-5

Discussions will focus on additional investigations required to complete the evaluation for potential epilepsy surgery, and will be convened in a patient management style format. The final day of the workshop will be spent wrapping up the topic and going over the written reports describing the evaluation handed in by each group. The instructor will provide feedback on the writing styles, traces/images being selected for figures, etc.

Week 11

Invasive Video-EEG Workshop

Appendix 2: Abstract Manuscript: Use of magnetoencephalography and ictal SPECT in patients with failed epilepsy surgery

Objective: In this study, we aim to investigate whether the noninvasive multimodal approach with MEG and ictal SPECT contributes to better seizure outcomes in patients with previous failed epilepsy surgery.

Methods: We retrospectively analyzed clinical profiles, MEG and ictal SPECT data, site of resection and pathological findings in relation to seizure outcomes in a consecutive cohort of 40 patients who have failed the initial epilepsy surgery.

Results: Seizure-freedom was achieved in 52% at 1 year of follow up after a new surgery. Majority of the pathological findings from the new surgery consisted of focal cortical dysplasia [21/40 FCD type I (52.5 %), 3/40 FCD type II (7.5%)]. Resection of MEG foci significantly correlated with seizure-free outcome, compared to the resection of hyperperfusion zones of ictal SPECT (odds ratio 7 for MEG and 3 for SPECT, $p=0.03$). MEG had a lower sensitivity compared to ictal SPECT (43 % versus 71 %) but higher specificity (90 % versus 73%), In addition, patients whose MEG and ictal SPECT were concordant on a sublobar level had a significantly higher chance of seizure freedom ($p=0.03$).

Significance: Noninvasive modalities are of paramount importance for the re-evaluation of patients who failed a previous resective surgery. The presence of sublobar concordant MEG and SPECT localization suggests a more favorable outcome following resective surgery. When assessing the contribution of each study individually, resection of the MEG localization rather than the SPECT result is positively associated with a favorable outcome..

Appendix 3: Program of the Epilepsy Grand rounds

<u>Date</u>	<u>Topic</u>	<u>Speaker</u>
August 8	"Can We Turn the Tide?"	Bruyn
12	"My Face Feels Weird!!"	Sivaraman
19	"Seizures in children: What's in the age? Apparently, a lot!"	Sudachan
26	"Can you turn off the light?"	Benech
September 2	"Is it Autism?"	Kantamneni
9	Redefining Epileptogenic Zone- a teenager with left temporal epilepsy"	Alanazi
16	"Epilepsy Surgery or The Cute Syndrome Search?"	Overmeyer
23	"This feels smooth"	Quist
30	"Are all Anti-Epileptic Drugs, suitable to treat children with refractory epilepsy, healing or harming?"	El Tahry
October 7	NO GRAND ROUNDS	
14	"The Importance of Cerebral Arteriopathy in Pediatric Stroke"	Friedman
21	"Polymicrogyria: When Epilepsy Surgery is Possible"	Grinenko
28	"Why are My Joints Stiff?"	Kantamneni
November 4	"Acquired Aphasia in Children"	Mahfooz
11	"Pediatric Hearing Loss"	Hopkins
18	"SUDEP"	Korabathina
25	"Things that I do not feel like doing is MOVING!!!!"	Sivaraman
December 2	"Seizure Freedom: Is It Worth The Price"	Narwani

Program of the Pediatric Epilepsy Rounds

<u>Date</u>	<u>Topic</u>	<u>Speaker</u>
June 26	"Association of Epilepsy with Cognitive Neurobehavioral and Psychiatric Comorbidities in Tuberous Sclerosis Complex (TSC)"	Bruyn
July 10	"Meg's High Temporal And Spatial Resolution, And Improved Yield Solidify A Key Role in Evaluation of Patients Being Considered for Epilepsy Surgery"	Burgess
17	"Freedom From Epilepsy In Age-Dependent Epilepsies: Cure or Remission?"	Kotagal
24	"Alternative Approaches to the Management of Paroxysmal Nonepileptic Events"	Cherian
August 7	"Cellular and Molecular Mechanisms in Epileptogenesis"	Nemes
14	"The Bases of StereoElectroEncephaloGraphy"	Chauvel
21	"Epilepsy in the Neurotrauma Patient"	Zakaria
28	"Adult Neurogenesis, mTOR signaling and the Development of Temporal Lobe Epilepsy"	Danzer
September 4	"Critical Issues in the Treatment of Conversion Disorder, Seizure Type"	Tilahun
11	"Age of Epilepsy Onset and Etiologies: Lessons Learned! The Case of FCD"	Sudachan
18	"Update on cEEG in the ICU"	Hantus
25	"Closing the loop with Responsive Neurostimulation in Epilepsy. Original observations from pre-market and post-approval use of RNS at our Center"	Alexopoulos
October 2	"Clinicopathological Conference for Harvard – A 9-year-old Girl with Acute Seizure and	Wyllie

	Encephalopathy”	
9	“Epilepsy Imaging: Current Capabilities and Perspectives”	Wang
16	Vagus Nerve Stimulation for Refractory Epilepsy: Old Device, Some New Insights!”	EITahry
23	“Pediatric Status Epilepticus – Current Practice and Future Perspectives”	Loddenkemper
30	“Language Network: Expanded Areas”	Chauvel
November 6	“Techniques in Epilepsy Surgery”	Bingaman
13	“Critical Care EEG Monitoring: Updates, Advances, and Controversies”	Hirsch
20	“New Theories, Techniques, and Technologies for Understanding Seizure Dynamics”	Stacey
December 11	“Cortical plasticity during sleep and ESES”	Gonzalez-Martinez
18	“Cortical plasticity during sleep and ESES encephalopathy”	Issa