Grant agreement no. 769051

EpiCARE – a network for rare and complex epilepsies

HP-ERN-2016 European Reference Networks / Framework Partnership Agreement

D.3.1. Report on survey imaging protocols

Work Package: WP3: Neuroimaging

Due date of deliverable: 31 August 2017

Actual submission date: 08 February 2017

Start date of project: March 1, 2017 Duration: 12 months

Lead beneficiary for this deliverable: *Prof Petr Marusic and Prof Kees Braun*
Contributors: All 28 EpiCARE healthcare providers

Project co-funded by the European Commission within the HP-ERN-2016 European Reference Networks grant		
Dissemination Level		
PU	Public	X

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Table of contents

1. Version log 4
2. Definition and acronyms 5
3. Introduction 6
4. Activities carried out and results 6
5 Conclusions 10
5.1. Summary of neuroimaging practices in EpiCARE centres 10
5.2. Neuroimaging expert group 12
6 Bibliography / References 13

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1. Version log

Version	Date	Released by	Nature of Change
1.0	2017-12-22	V. Sulc (Prague)	First version
2.0	2018-02-06	P. Marusic (Prague)	Review
3.0	2018-02-09	K. Braun	Review
3.1	2018-02-09	V. Sulc	Minor Fixes
3.2	2018-02-09	P. Marusic	Final review

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2. Definition and acronyms

Acronyms	Definitions
MRI	Magnetic Resonance Imaging
SPECT	Single Photon Emission Computer Tomography
SISCOM	Subtraction Ictal-Interictal SPECT Co-registered to MRI
STATISCOM	Statistical Ictal SPECT Co-registered to MRI
ERN	European Reference Network
SPM	Statistical Parametric Mapping
FSL	FMRIB Software Library
VBM	Voxel-based Morphometry
MRS	Magnetic Resonance Spectroscopy
fMRI	Functional Magnetic Resonance Imaging
DTI	Diffusion Tensor Imaging
GM/WM blurring	Gray matter/White matter blurring
MAP07	Morphometric Analysis tool

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3. Introduction

The overall aim of the Neuroimaging work package is to promote harmonisation of best practices in neuroimaging evaluation of rare and complex epilepsies that will provide state-of-the-art procedures in the field. Creating a database of neuroimaging findings in the specific rare and complex epilepsies with further research implications.
For year 1 the work package aimed at:

- **D 3.1** Creating a charter for expert groups
- **D 3.2** Report on status quo analysis

Based on a survey conducted in 2014 on the clinical use of imaging and postprocessing methods in epilepsy surgery candidates (Mouthaan et al., 2016) an updated and extended survey was devised by the leads of Work Package 3, Prof. Petr Marusic and Prof. Kees Braun, and Dr. Pieter van Eijsden. The survey was circulated within 28 members of EpiCARE ERN between October 2017 and January 2018. The aim of the survey was to collect information on MRI imaging protocols in adult and pediatric population of epilepsy patients, post-processing methods and other neuroimaging techniques used within centres.

Furthermore, the aim of the survey was to collect information on available experts to be used in future activities of the network, namely to fulfill objectives of WP3: Creation of an expert group for re-reviewing of neuroimaging findings, participation of an expert group in research projects, development of central web based post-processing facility for surgical evaluation.

4. Activities carried out and results

Neuroimaging in patients with epilepsy is an invaluable tool in diagnosis and treatment of the disorder. Although several recommendations were published regarding specific MRI protocols with aim to maximize sensitivity of available methods, the 2014 survey reported large variation between the diagnostic workup in different European centers. Even larger variation exists in the use of post-processing MRI methods, ranging from no methods available to cutting edge technology.

The survey provides information about neuroimaging equipment available in every center as well as neuroimaging practices. This data is necessary to increase the prevalence of neuroimaging methods, including post-processing, and could potentially also lead to harmonization of basic recommended acquisition schemes and postprocessing methods in patients with epilepsy.

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The following detailed neuroimaging questionnaire was devised and circulated to all EpiCARE members.

Neuroimaging survey

I. General information about your center

1. Name of the center

2. Name, email address of person who completed this survey

3. Does your center perform epilepsy surgery?
   In adults?
   In children?

4. How many MRI scanners are in use in your center:
   1.5T
   3T
   7T

5. Do you have facilities for general anesthesia for MRI in children? If so at what MRI scanner (1.5T, 3T, ...)

6. Does your center have specific experience with imaging in certain cohorts of epilepsy patients? If so, please specify

7. Does your center have imaging databases of epilepsy patients? If so, which cohorts, and how many patients?

8. Please provide us with names/email addresses of collaborators in your center with the following specific expertise, who would like to be actively involved in EpiCARE imaging-working groups:

- Neuroradiologist with extensive experience in epilepsy who is willing to be part of a centralized MRI review team
  For adults
  For children

- Radiologist, technical engineer or other staff with expertise in image-analysis and post-processing (MRI, PET, SPECT, other – please specify). More experts can be listed.

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9. Does your center have databases of control scans/healthy volunteers that could be used for sharing within the consortium?
   If so, please specify: scanner, field strength, sequences, number of patients, age ranges, criteria for "control/healthy", available consent for multicenter sharing of completely anonymized/deskulled scans for research and clinical purposes.

II. Acquisition and post-processing of imaging in epilepsy

For routine MRI in children with epilepsy please indicate:

- MR Field strength:
- System (brand, e.g. Siemens, Philips etc.):
- Approximate total duration of MR scan:

Sequence	Plane (sag/trans/cor)	Resolution (mm X,Y,Z)

For routine MRI in adults with epilepsy please indicate:

- MR Field strength:
- System (brand, e.g. Siemens, Philips etc.):
- Approximate total duration of MR scan:

Sequence	Plane (sag/trans/cor)	Resolution (mm X,Y,Z)

For presurgical evaluation of children please indicate:

- MR Field strength:
- System (brand, e.g. Siemens, Philips etc.):
- Approximate total duration of MR scan:

Sequence	Plane (sag/trans/cor)	Resolution (mm X,Y,Z)

For presurgical evaluation of adults please indicate:

- MR Field strength:
- System (brand, e.g. Siemens, Philips etc.):
- Approximate total duration of MR scan:

Sequence	Plane (sag/trans/cor)	Resolution (mm X,Y,Z)

Do you do perform additional functional or structural MRI sequences in specific patient groups (e.g. MRS, presurgical DTI/fMRI, Higher field [e.g. 7T] MRI, specific sequences in neonates, etc.)?

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If so please indicate patient group, sequence and rationale:

Patient group/Indication	Sequence/Field Strength	Rationale

Do you use post-processing techniques?
(e.g. VBM for cortical thickness or GM/WM blurring detection, curvilinear reformatting etc.)?

If yes: what software packages do you use for post-processing:

In case you use a database of control patients for (automated) comparison purposes:
please indicate:

- Source of the control datasets:
- Characteristics of this dataset (field strength, sequences, resolution):
- Number of subjects in the control database:

Do you send scans to other centers for post-processing? If so, where?

Please indicate patient group, post-processing technique used and rationale:

Patient group/Indication	Technique	Rationale

Non-MR imaging in presurgical evaluation

Do you use ictal SPECT?
If so please indicate patient group, tracer and rationale:

Patient group/Indication	Tracer	Rationale

Do you use interictal PET?
If so please indicate patient group, tracer and rationale:

Patient group	Tracer	Rationale

Do you use **post-processing techniques for PET or SPECT** (e.g. SPM) or post-processing techniques that combine PET, SPECT and/or MRI (SISCOM, STATISCOM etc.)?
If so please indicate patient group, technique and rationale:

Patient group/Indication	Technique	Rationale

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In case you use a database of control patients for (automated) comparison purposes:
If so, please indicate:

- Which imaging method:
- Source of the control datasets:
- Characteristics of this dataset:
- Number of subjects in the control database:

5 Conclusions

5.1. Summary of neuroimaging practices in EpiCARE centres

All 28 EpiCare centers completed the survey. With regard to the pediatric population, all 26 centers that completed the survey offer epilepsy surgery.

In the routine examination of children
20/26 centers use 3T
89% use volumetric T1 (1mm and less)
26% use volumetric T2
67% use volumetric FLAIR
70% use SWI/T2*/other hemosiderin sequence

In the presurgical evaluation in children
21/26 centers use 3T
96% use volumetric T1
27% use volumetric T2
73% use volumetric FLAIR
77% use SWI/T2* other hemosiderin sequence
85% DTI available
73% fMRI available

In the adult population 22 out of 26 centers that completed the survey offer epilepsy surgery.

In the routine examination of adults
22/24 centers use 3T
78% use volumetric T1
9% use volumetric T2
70% use volumetric FLAIR
74% use SWI/T2* other hemosiderin sequence

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In the presurgical evaluation in adults
24/24 centers use 3T
100% use volumetric T1
13% use volumetric T2
83% use volumetric FLAIR
83% use SWI/T2* other hemosiderin sequence
100% DTI available
92% fMRI available

Although the survey was conducted among an only partly-overlapping sample of epilepsy centers, a clear shift towards the use of higher field strength and volumetric sequences is observed. The 2014 survey reported volumetric sequence with voxel size <=1mm used in 15 out of 22 centers. Similar data were observed in the availability of DTI sequence and hemosiderin imaging. This indicates that epilepsy centers have changed their imaging protocols to improve patients' outcome and safety. Dissemination of used and recommended imaging protocols might also help to justify the need for better equipment and longer acquisition times if current protocols are suboptimal.

Still, 8 out of 26 pediatric centers and 5 out of 24 adult centers do not use the latest recommended (2) slice thickness (3mm or less) in their protocols.

Twenty-three centers apply some form of MRI postprocessing to their data. Methods used are widely different and include use of specialized software and experimental methods (such as SPM, FSL, Freesurfer, 3D Slicer, EpiNav). Most widely used is curvilinear reformatting available in some MRI and hospital workstations and MAP07.

Twenty-six centers perform either PET or SPECT imaging, although some centers are able to provide access to the methods only in cooperation with other institutions. PET use is more widespread than SPECT (15/28 SPECT, 24/28 PET). Only one epilepsy center offers neither PET nor SPECT.

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5.2. Neuroimaging expert group

Representatives of centers within the network nominated radiologists and post-processing specialists willing to participate in the future network activities as stated above.

Radiologists (adult patients)

- Philippe Demaerel, Leuven
- Ritva Vanninen, Päivi Koskenkorva, Kuopio
- Ludovico D'Incerti, Milan
- Mario Mascalchi, Florence
- Mcamilla Rossi, Daniela Longo, Rome
- Anna Federica Marliani, Bologna
- Jan Willem Dankbaar, Gerard de Kort, Utrecht
- Bruno César, Pereira Moreira, Porto
- Rui Pedro Pais, Coimbra
- Carlos Morgado, Lisboa
- Nuria Bargallo, Barcelona Hospital Sant Joan de Déu
- Lars Jönsson, Gothenburg
- Roxana Gunny, London GOSH
- Kirsten Forbes, Glasgow
- Martin Kyncl, Prague

Pediatric radiologists

- Philippe Demaerel, Leuven
- Volodia Dangouloff–Ros, Paris
- Horst Urbach, Freiburg
- Luisa Chiapparini, Ludovico D'Incerti, Laura Farina, Milan
- Anna Pichiecchio, Pavia
- Mario Mascalchi, Florence
- Francesco Toni, Bologna
- Jan Willem Dankbaar, Gerard de Kort, Utrecht
- Elzbieta Jurkiewicz, Warsaw
- Daniel Carvalho Dias ,Porto
- Rui Pedro Pais, Coimbra
- Oreste Straciuc, Bucharest
- Jordi Muchart, Barcelona Hospital Sant Joan de Déu
- Lars Jönsson, Gothenburg
- Roxana Gunny, Dr Felice D'Arco, London GOSH
- Kirsten Forbes, Glasgow
- Martin Kyncl, Prague

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Expert group on postprocessing

- Karolien Goffin, Patrick Dupont, Leuven
- Michal Mikl, Radek Mareček, Martin Kojan, Pavel Říha, Brno
- Vlastimil Sulc, Jan Sanda, Prague
- Mervi Könönen, Kuopio
- Hansjörg Mast, Freiburg
- Peter Trautner, Bonn
- Ileana Zucca, Domenico Aquino, Cristina Rosazza, Francesco Ghielmetti, Francesco Deleo, Milan
- Simona Albergati, Anna Pichiecchio, Claudia Gandini, Pavia
- Matteo Lenge, Florence
- Antonio Napolitano, Rome
- Sander Diederen, Matea Rados, Utrecht
- Sylwia Chelstowska, Warsaw
- Luís Filipe Botelho Casal dos Santos, Cristina Maria Giesta Ramos, João Eduardo Paiva Ramalheira, Joel Freitas, Porto
- Daniela Jardim Pereira, João Castelhano, Catarina Duarte, Maria João Cunha, Jorge Isidoro, Coimbra
- Oreste Straciuc, Bucharest
- Anna Calvo, Jose Pariente, Xavier Setoain, Barcelona Hospital Sant Joan de Déu
- Juan Carlos Martínez Martínez, Valencia
- Pär-Arne Svensson, David Krysl, Gothenburg
- Roxana Gunny, Felice D'Arco, Lorenzo Biassoni, Torsten Baldeweg, David Carmichael, Chris Clark, Sara Lorio, Sophie Adler, London GOSH
- Natalie Voets, Oxford
- Roman Rodionov, Sjoerd Vos, London UCL

Conclusion: Both deliverables have been achieved. Status quo analysis on neuroimaging techniques and imaging protocols used within EpiCARE centers has been performed. Expert groups were created.

6 Bibliography / References

(1) Mouthaan, B E, M Rados, P Barsi, P Boon, D W Carmichael, E Carrette, D Craiu, et al. 2016. "Current Use of Imaging and Electromagnetic Source Localization Procedures in Epilepsy Surgery Centers across Europe." *Epilepsia* 57 (5): 770–76. doi:10.1111/epi.13347.

(2) Wellmer, Jörg, Carlos M. Quesada, Lars Rothe, Christian E. Elger, Christian G. Bien, and Horst Urbach. 2013. "Proposal for a Magnetic Resonance Imaging Protocol for the Detection of Epileptogenic Lesions at Early Outpatient Stages." *Epilepsia* 54 (11): 1977–87. doi:10.1111/epi.12375.

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