# Minutes - ERN CRANIO craniosynostosis workgroup meeting

17 November 2023

## Attendees

| Centre/Affiliation | Name |
|---|---|
| Hospital Universitario 12 Octubre Madrid | Ana María Castaño |
| Helsinki University Hospital | Anna Ronkainen |
| Alder Hey Children's Hospital | Chris Parks |
| Hospital de Santa Maria – Centro Hospitalar Lisboa Norte | Claudia Faria |
| Uppsala University Hospital | Daniel Nowinski |
| Regional specialised children's hospital, Olsztyn. Poland | Dawid Larysz |
| Oslo University Hospital | Bernt Johan Due-Tønnessen |
| Children's Health Ireland | Dylan Murray |
| Erasmus MC | Elin Weissbach |
| Hospital Universitario 12 Octubre Madrid | Emma Miñes |
| Erasmus MC | Esther Vermeer |
| San Gerardo Hospital | Fabio Mazzoleni |
| Hospices Civils de Lyon | Federico Di Rocco |
| AOU Meyer di Firenze | Federico Mussa |
| Fondazione Policlinico Universitario A. Gemelli | Gianpiero Tamburrini |
| Hôpital Universitaire Necker Enfants-Malades | Giovanna Paternoster |
| Fondazione Policlinico Universitario A. Gemelli | Giulia Petruccini |
| Aarhus University Hospital | Gorm von Oettingen |
| Radboud UMC | Guido de Jong |
| Erasmus MC | Henri Vrooman |
| Erasmus MC | Irene Mathijssen |
| Erasmus MC | Jochem Spoor |
| Aarhus University Hospital | Johan Blomlof |
| University Hospital Salzburg | Jörn Wittig |
| GOSH | Juling Ong |
| Helsinki University Hospital | Junnu Leikola |
| Headlines UK | Karen Wilkinson-bell |
| Children's Health Ireland | Katerina Papadopoulou |
| Children's Health Ireland | Katie Geraghty |
| Sahlgrenska University Hospital | Lars Kolby |
| Fondazione Istituto Neurologico "C.Besta" | Laura Valentini |
| Universitätsklinikum Tübingen | Lea Longerich |
| Hôpital Universitaire Necker Enfants-Malades | Leslie Hemar |
| Erasmus MC | Linda Gaillard |
| GOSH | Luke Smith |
| Universitätsklinikum Tübingen | Maite Aretxabaleta |
| Erasmus MC | Marie-Lise van Veelen-Vincent |
| LAPOSA | Mariët Faasse |
| Sahlgrenska University Hospital | Marizela Kljajic |
| EAS Apert | Markus Richter |
| Children's Health Ireland | Matylda Sheenan |

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|---|---|
| Hôpital Universitaire Necker Enfants-Malades | Maxime Taverne |
| Sahlgrenska University Hospital | Niclas Löfgren |
| Children's Health Ireland | Pramila Mohan |
| Hospital Universitario 12 Octubre Madrid | Pablo Martin Munarriz |
| Regional specialised children's hospital, Olsztyn. Poland | Patrycja Larysz |
| University Medical Centre Ljubljana, Slovenia | Miha Verdenik |
| AOP University of Padua | Renzo Manara |
| AOP University of Padua | Roberto Faggin |
| Fondazione Istituto Neurologico "C.Besta" | Sabrina Mariani |
| Uppsala University Hospital | Sara Magnéli |
| Children's Health Ireland | Shirley Bracken |
| Hospices civils de Lyon | Sofia Guernouche |
| Fondazione Policlinico Universitario A. Gemelli | Stella Caterina |
| Oslo University Hospital | Stine Alvinussen |
| Erasmus MC | Tareq Abdel Alim |
| Radboud UMC | Titiaan Dormaar |
| Charité Universitätsmedizin Berlin | Ulrich Thomale |
| Oslo University Hospital | Ulrikke Wiig |
| Fondazione Istituto Neurologico "C.Besta" | Veronica Saletti |
| Hospices de Lyon | Vildan Ulker |
| Hôpital Universitaire Necker Enfants-Malades | Virginie Gaudin |
| Les p'tits courageux | Virginie Kauffman |
| Fondazione Policlinico Universitario A. Gemelli | Wanda Lattanzi |

# Contents

## 1. The MRC national Mouse Genetics Network

*Irene Mathijssen*

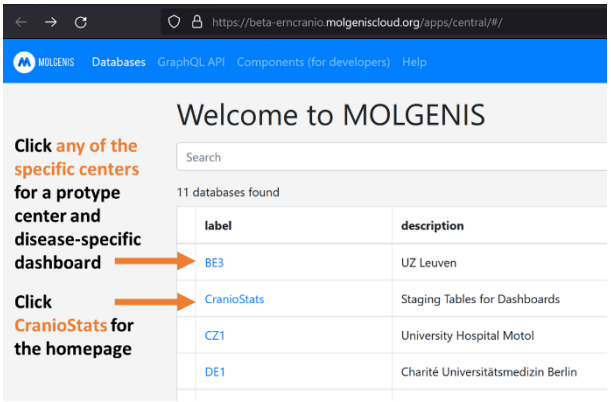
The MRC national mouse genetics network is a package of distinctive research clusters drawing from the specialist facilities of the Mary Lyon Centre at MRC Harwell. The congenital anomaly cluster aims to create mouse models of prioritized gene variants identified from patients with craniosynostosis to establish causality and disease mechanisms.
If there is a VUS of interest in your center, please contact: dr. Stephen Twigg MRC Weatherall Institute of Molecular Medicine / University of Oxford.
Email : Stephen.Twigg@imm.ox.ac.uk
Additional information: https://nmgn.mrc.ukri.org/clusters/congenital-anomalies/

## 2. Update on the ERN CRANIO registry, research

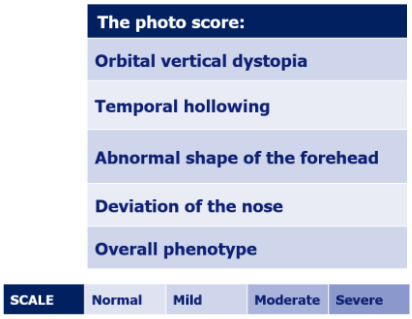
*Linda Gaillard*

There are two workstreams currently ready to start inclusion in the registry: craniosynostosis and cleft lip and palate. Craniofacial macrosomia is nearly finished, and congenital deafness and orodental are currently being developed.

The registry team is working together with Molgenis to update the registry. This update is focused on improving user-friendliness and includes the creation of the dashboard. The aim is to be able to include real data from January 2024 onwards. Workshops will be organized together with Molgenis focused on data entry (manual and bulk) and the SPIDER tool (mandatory pseudonimsation tool developed by ERICA).
Link to prototype dashboard:
https://beta-erncranio.molgeniscloud.org/




Update on research
Two papers on suture-specific photo scores (sagittal synostosis and metopic synostosis)have been published in Journal of Craniofacial Surgery *(doi: 10.1097/SCS.0000000000009732 and 10.1097/SCS.0000000000009773*).
We will develop a photo score of unicoronal synostosis next. The research proposal was discussed last year. The photos can be shared via CPMS. We aim to begin scoring in January 2024.
If you would like to participate in the photo scoring study, please contact:
Meike Tjaberinga and / or Linda Gaillard
M.tjaberinga@erasmusmc.nl
L.Gaillard@erasmusmc.nl
For questions on the registry and dashboard please contact:
ern-cranioregistry@erasmusmc.nl



## 3. Update on 3D working group

*Tareq Abdel Alim, Guido De Jong, Maxime Taverne*

The 3D working group was set up during the annual meeting in 2022. The key objective is to lay down best practices and standardize data acquisition and processing for facilitating seamless execution of large multi-center studies. After the meeting last year a questionnaire was sent out with the main objective to identify key approaches and differences in current standards, which may, to a greater or lesser extent, influence the outcomes of collaborative studies. Things that may contribute to variance and image quality are: Type of setup, system resolution, acquisition protocol, registration and processing differences.

Questionnaire outcomes:

*Acquisition of data*

Differences in used hardware between centers:

- Fixed setup 58.3%
- Portable 2%
- Both 16.7%

The first study of the 3D working group will focus on accuracy by validating different systems in different centers. A high accuracy mannequin will be 3D printed to assess how different set ups affect results (i.e. whether differences are in the respectable error margin). This approach will be used to validate different systems in different centers.

A limitation of 3D data acquisition is that you need someone for consistency, who understands 3D data and, integration within your patient file. Someone who is available temporarily is insufficient. It is advised to keep personnel involved to improve quality and consistency of data.

*Data storage : output options and accessibility*

If you have the option to choose an output format use .obj or .ply. These are widely used formats and there is a possibility to embed texture information. Most outputs are convertible and there are very few scanners that only capture shape.

Ensuring data is accessible to clinicians is challenging and accessibility of 3D is limited in most centers at the moment. Data is accessible but rarely embedded within the electronic patient records. If your center has a solution to embed 3D into electronic patient records or otherwise ensure easy access to 3D data for clinicians, please contact one of the 3D working group leads:

t.abdelalim@erasmusmc.nl
guido.dejong@radboudumc.nl
maxime.taverne@aphp.fr

*Analysis*

Several centers do not use the collected 3D data and a significant number of centers limit themselves to linear anthropometric measurements, not utilizing full 3D potential. The majority of centers use the 3D data for research only.

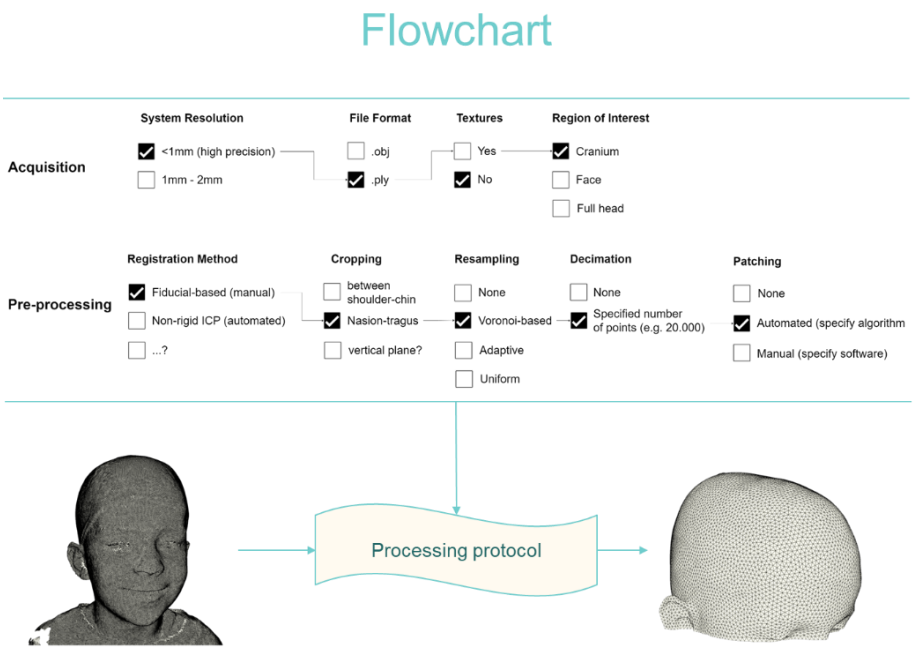
*Multicenter endpoints*

Ideal endpoints would be to: assess the outcome of surgical techniques, improve own techniques, define a population normal (balanced set of normal data required), to do an external validation of own measurements (different ages, ethnicity, type of data) and to define new measurements /indices / methods (in addition to head circumference).

Local and global endpoints were discussed. Local endpoints are endpoints that can be used internally for clinical practice and research and can optionally match global ERN endpoints ore benefit from tools/data derived from ERN endpoints. ERN (global) endpoints include (open) clinical and scientific goals, are collaborative in nature and may provide guidelines, tools and data.

*Concerns regarding data sharing*
Data can be shared through anonymized representation. Without the uncoding key, data cannot be reconstructed into a face. You can also crop part of the face/head. Shape can be converted for 3D analysis of morphology.

A guideline/flowchart for the ERN was shown:




Processing protocol should be defined for every study. Centers should have golden standard of data (to be defined).

Technician meeting outcomes

1. Technician meeting was mainly focused on research applications, which indirectly finds its way to clinical practice fundamental findings and published results. Hopefully it will also translate to direct use (e.g surgical planning or severity assessment). To allow for direct clinical use, the pipeline from raw to interpretable data needs to be automated and there should be a standardized data structure with attributes to ease data collection in collaborative studies.
2. Sharing within ERN might present risks of patient's data leakage: this must be addressed in details. Especially, more control on our data may be possible if all centers use the same anonymization method.
3. The maintenance of databases should be anticipated on the long-term
4. Consider including 3D soft-tissue reconstruction from CT-scans.
5. A global agreement within the ERN should be set as soon as possible. Is certification mandatory in the case where data is directly used for clinical decision?
6. Timing of data acquisition throughout patient's managements should be standardized.
7. Involve photographer (or person responsible for acquisition) in research projects
8. Download files as .ply or .obj, which embed texture information
9. Naming conventions, for example: PatientID_DoB_AcqDate [YYYY_MM_DD]
10. Contact local IT dept about storage and accessibility solutions
11. Storage of 3D data for clinical use could be done as 3D PDF.

The workgroup determined a number of work packages for the coming year:

- 2024.1 Legal
- 2024.2 Research methodologies: *Registration method, Reference planes / templates, etc.*
- 2024.3 Accuracy validation (different setups) à collaborative paper
- 2024.4 Writing of Guidelines à aimed to present next ERN
- 2024.5 Data sharing and storage opportunities
- 2024/25 Software / tool development

There was a question on existing commercial solutions and supporting members. It was discussed that commercial solutions are not transparent, for example you would not know to what extent smoothing affect volumes. Supporting members get access to the same protocols.

## 4. Redo surgery for sagittal synostosis; redo after redo

*Marie-Lise van Veelen – Vincent*

In patient with sagittal synostosis the incidence for a first redo for raised ICP is 1.4-23.5% depending on follow-up time and technique. However, there are no studies on recurrent raised ICP after second cranial enlargement. Three cases of sagittal synostosis patients who underwent a second redo were discussed. As there is no literature on this problem, it was discussed that a study will be started to assess second redo cases. Patients will be collected from the ERN CRANIO network. All redo cases relative to the total number of sagittal synostosis patients will be collected. The follow-up of redo cases will be assessed with respect to symptoms and ICP (Dr van Veelen (Rotterdam) and prof Thomale (Berlin) and Sara Magneli (Uppsala)). Cases can be shared via CPMS.

For questions, please contact Marie-Lise van Veelen: m.l.c.vanveelen@erasmusmc.nl

## 5. Therapeutic patient education new approach for patients parents

*Giovanna Paternoster*

Therapeutic patient education improves patient management protocols, understanding of disease mechanisms and treatment, acceptance of disease and quality of life for patients. It was initially developed for chronic disease. Customized patient education programs are created that incorporate:

1. Educational diagnosis: discusses beliefs, fears, hopes etc.
2. educational objectives: skills and knowledge that a patient needs appropriate for their age
3. Acquisition of skills: demo, educative tools, collective workshops, individual sessions, personalized action plan
4. Assessment

There are multiple target populations that have therapeutic patient education during different timepoints in their treatment protocols: children <5 years, children 8-18 years, parents of children or adolescents, siblings 5-10 years, siblings >10 years. The idea is to start with an educational diagnosis for patients, siblings and parents, when beliefs, fears and hopes are discussed. Objectives are defined (for example more surgical explanation, more psychological assistance), and applied. Finally there is an assessment to assess if everything is accomplished. For the monobloc and Le Fort III patients, a big meeting day is organized to discuss different aspects of surgery. This day is for patients (children, teenagers), parents and sibling.

The Necker hospital developed a video for parents and patients which shows how the surgery will happen, a tour of all different aspects that are involved when a patient undergoes surgery. It was discussed that this video could be translated to other languages. If you would like the video to be translated to your language, please contact paternoster.gio@gmail.com

## 6. Patient partnership ERN CRANIO

*Mariët Faasse, Karen Wilkinson-Bell*

Patient partnership in the ERNs can be defined as a mutual relationship between patients and health professionals where input from people living with a rare disease or caring for someone with a rare disease routinely and formally informs the Networks' collaborative activities and decision-making. Patient partnership implies considering health professionals and patients involved in the Networks as equal partners in all ERN activities and domains. This highlight the importance of including patients.

There can be a multitude of areas of collaboration including: network strategy and management, healthcare, education and training, clinical research and registries, information and outreach.

Examples of patient-clinician collaboration in ERN CRANIO include:

- Video on genetics à collaboration between patient representatives and geneticists
- Research collaborations
- Communication materials on visible differences, à collaboration between patient representatives and psychologists
- Guideline consensus statement development à clinical and patient versions
- Patient – clinician engagement groups
- National collaborations

Brainstorm session: ideas for collaborations discussion

- Disability charities have looked into how to better inform patients with cognitive disabilities on medical treatment. This may be useful for patients in the ERN CRANIO as well.
- Nurse specialist should also be involved as it may be perceived as easier for patients to communicate with nurses compared to physicians.
- There was a UK headlines top 10 research topics, an update would be useful.

## 7. Quality of life assessments

*Marizela Kljajić*

Quality of life is a multidimensional *construct* that considers physical, mental, and social components that describes well-being depending on number of factors. It is a subjective concept. Treating a patient aims to improve QoL. The QoL could be affected by the condition but could also be affected by the treatment itself. Quality of life can be measures with questionnaires: which can be generic and disease-specific. For craniofacial conditions the FACE-Q is available. Be aware of what each measure actually measures, how long an assessment may be valid and who responds (child, parent, both). Consider if the questionnaire is appropriate for your patients, if it is a valid questionnaire, and if it measures what it is intended to measure, if the questionnaire uses self-report and if it is being used to identify patients with need or to evaluate care that is provided.