Multi-centre Epilepsy Lesion Detection (MELD) Project
- *Memorandum of Understanding –*
24th May 2021

MELD Project

The MELD Project is led by Dr Konrad Wagstyl (UCL) and Dr Sophie Adler (UCL).
The e-mail address of the MELD Project is meld.study@gmail.com.
The members of the MELD Project and the participating sites are listed on the MELD Project website https://meldproject.github.io.

Anonymous individual subject level data for the MELD Project will be stored at University College London (UCL), UK. This site is hereinafter referred to as the MELD Project Data Storage Site. Anonymous individual subject level data for the MELD Project will also be stored and analysed on the Cambridge Service for Data Driven Discovery (https://www.hpc.cam.ac.uk/high-performance-computing). Individual subject level data may also be stored at sites with approved secondary proposals. Together these sites are herinafter referred to as Additional MELD Project Data Storage Sites.

In all publications that use the MELD Project data, the text "for the MELD Project", will appear the end of the author list.

Introduction

Members of the MELD Project include investigators from different centers around the world who are actively engaged in neuroimaging research in epilepsy and who have contributed MRI data, and/or features extracted from MRI data, and/or clinical / demographic data, and/or analysis / algorithm development for the purpose of multi-centre analysis, replication, and/or algorithm testing in a collaborative manner. The MELD Project's initial effort is to demonstrate the success of collaborative, systematic image analyses across multiple centers to develop methods for automated detection of focal epilepsy pathologies.

The MELD Project is expected to work collaboratively on a growing dataset of MRI data from patients with epilepsy. This database will likely be useful to investigators both within and outside of the MELD Project who may request to use parts of the dataset for secondary analyses. This wealth of data requires (1) organisation, (2) appropriate ethical approval, (3) protection of authorship rights for contributors to the primary analyses, and (4) direction for future analyses.

* Adapted from the ENIGMA MOU 21st April 2015 and ENIGMA Sleep Working Group MOU

In order to accomplish these aims, the MELD Project's scientific initiatives and policies will be guided and overseen by the overall MELD Project leaders: Dr Sophie Adler (UCL) and Dr. Konrad Wagstyl (UCL). Each MELD sub-group will also appoint a subgroup leader: typically that sub-group's principal investigator. Subgroup leaders are responsible for ensuring that work is carried out in a timely manner, and within the appropriate ethical guidelines set down for research on human subjects. Part of this responsibility is to ensure that all sites have obtained approval from their local Ethics Committees, and that such assurances are updated regularly in accordance with Office for Human Research Protections (OHRP) regulations. Additionally, the MELD Project and subgroup leaders will be responsible for oversight of authorship, determining whether a paper constitutes a MELD Project Publication, and whether the scientific contributions of the sites have been correctly and fairly acknowledged in the publication.

Data storage and sharing

Types of data
The dataset consists of:

1) Anonymised pre and post-operative MRI images from patients with focal epilepsies
2) Manually delineated lesion masks
3) Anonymised clinical (e.g. age of epilepsy onset in years, post-surgical seizure freedom) and demographic (e.g. age at scan, sex) variables extracted from electronic health records by participating sites.
4) Anonymised control MRI images from controls.

The site PIs are responsible for ensuring anonymization of their site's MR and phenotypic data. Both the site PIs who contribute data to the project as well as the project leader are responsible to comply with all relevant rules and regulations imposed by their institutions. This may mean that the project needs to be approved or declared exempt by a committee that oversees research on human subjects, e.g. a local IRB or Ethics Committee. Each subgroup will be required to provide a letter from the head of department or local R&D office confirming that they have obtained appropriate ethical approval to share the anonymised data with UCL. UCL will only receive anonymised data.

Data storage
The anonymised dataset will be stored at University College London (UCL) - the MELD Project Data Storage Site. Anonymous individual subject level data for the MELD Project will also be stored and analysed on the Cambridge Service for Data Driven Discovery (https://www.hpc.cam.ac.uk/high-performance-computing).

The UCL MELD study team will have initial exclusive use of the data for 18 months after data are received or until the first preprint is made available, whichever is sooner.

Projects and publications

What Constitutes a MELD Project *Publication?*
MELD Project publications are papers or abstracts based on investigations that: (1) rely on intellectual resources of the MELD Project or (2) use data collected through the efforts of the MELD Project, or (3) rely, in whole or in part, on information obtained through MELD Project membership.

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In agreeing to contribute data to a MELD Project analysis or meta-analysis, the MELD members at that site must also sign an agreement (below) that they will not publish or publicise (to the media or on the Internet) the results of the analysis prior to its publication. Prior to publication, findings may be presented at conferences or made available as a preprint only after consulting in advance with the MELD Project leaders. This consultation is designed to ensure that they comply with embargo policies of top-tier journals, protecting the interests of other MELD Project members. In addition, secondary analyses based on the findings of the MELD Project (for example, correlating structural MRI results with neuropsychological findings in people with epilepsy), may not be submitted to journals for publication until after the primary MELD Project paper is accepted for publication. This is intended to avoid the risk of duplicate submissions that may jeopardize a MELD Project publication.

Any participating site may choose to publish and present the results of an MRI study conducted at their own site, which does not contain analyses conducted as part of the MELD Project. These publications *do not* constitute MELD Project publications. If a MELD Project analysis is proposed and a group is already engaged in a similar analysis for that same phenotype, the site agrees to disclose their participation in the ongoing project(s) if they wish to participate in the MELD analysis. This is also intended to avoid the risk of duplicate submissions that may jeopardize a MELD Project publication.

MELD Project publications may be classified as primary or secondary publications. Primary publications of the MELD Project are those for which an analysis is conducted for the first time by the MELD Project on a phenotype of interest (for example an analysis using surface-based vertex-wise data to automatically detect focal cortical dysplasias). Secondary publications are those that solely rely upon data collected in primary publications (for example re-analyzing the per-vertex surface-based data using a novel analysis technique).

Guidelines for Authorship on Primary Publications of the MELD Project
The MELD Project will be listed as an author on all MELD Project publications, including manuscripts on which all contributing MELD Project members are listed by name. The text "for the MELD Project" will appear the end of the author list.

Authorship credit should be based on substantial contribution to at least one of the following: (1) the measurement of structural Magnetic Resonance Imaging (sMRI) phenotypes for the analysis / meta-analysis; (2) contributions or generation of data for the analysis; (3) contributions to the conception, design, analysis and/or interpretation of the data; and (4) final approval of the manuscript version to be published. All co-authors are also expected to help draft the manuscript and/or revise it critically for important intellectual content.

Based upon the level of contribution, authorship at each site may vary from one publication to another. For each discrete publication, each site PI is responsible for preparing the authorship and acknowledgment list for their site. Each subgroup leader will have final responsibility to adjudicate who contributed enough to their respective group's analysis to be considered a co-author.

Authorship for all MELD Project papers will be weighted by current effort and contribution rather than on past contribution to MELD Project research. MELD Project members will be reasonable and self-critical in their claims for authorship. If a question arises regarding the appropriateness of authorship of a member(s), other MELD Project members will be asked to advocate for these members in order to avoid putting members in the awkward position of having to advocate for themselves.

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Guidelines for secondary analyses of data collected as part of the MELD project
Each proposal for a project using MELD Project data by a MELD subgroup will be submitted to the MELD Project leads using the MELD Project Proposal form that can be requested from the MELD Project leads. All MELD Project members are encouraged to submit such proposals. Non-MELD Project members will be asked to complete a more detailed proposal and sign a Memorandum of Understanding regarding authorship and publishing.

The MELD Project leads (Dr Sophie Adler and Dr Konrad Wagstyl) will screen the proposals for scientific interest, quality, overlap with other plans, appropriateness and feasibility of the proposed timeline, and whether the proposed resources committed to the project are sufficient.

Analysis plans should include a proposal for publication of a specific scientific paper, not for multiple papers on a more general topic or for a "line of work". This implies that the analysis plan should include specific research questions and hypotheses and a detailed plan for data analysis to answer those specific research questions. To attempt to avoid overlap between papers resulting from different analysis plans, the data analyses and results reported in the manuscript are limited to those described in the analysis plan. For additional analyses not described in the analysis plan a new analysis plan needs to be submitted, also if this concerns a similar topic but different data or different analyses on the same data.

When the analysis plan is approved by the MELD Project leads, the proposal will be circulated amongst MELD Project members. MELD Project members will have 14 days from the time of the posting to opt-out, ask for clarification, voice concerns or objections and/or give feedback to the proposal.

If the author of the proposal agrees to the authorship and publication policies of the MELD Project, the project proposal will be approved. One of the MELD Project leaders will be assigned as a project liaison. The MELD Project liaison will be responsible for providing the data and answering any queries relating to the project, and providing the contributing site PIs with updates. *For access to the data see the data sharing section.*

Submission of a proposal implies actual plans for a publication, which will be worked on within a reasonable time frame specified in the proposal. When within 6 months after submitting a proposal there are no provable activities in that direction, the subject can be released for other interested parties.

Manuscripts using data obtained via this mechanism will be considered secondary MELD Project publications provided no new data is required. We will request that the 'MELD Project' and the MELD Project leads be listed as co-authors. The MELD Project on the byline will reference the PIs of each study, in addition to contributors at their site. In this way the authors contributing data to the MELD Project will be appropriately acknowledged on any publication.

Data sharing
The dataset is divided into 3 categories:
1) Full anonymised MRI dataset
2) Derived data without an accompanying manuscript
3) Derived data supporting a manuscript

Guidelines for access to the full MRI dataset (Category 1):

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Each subgroup will be required to provide a letter from the head of department or local R&D office confirming that they have obtained appropriate ethical approval to share the anonymised data requested with the subgroup leading the secondary analysis. No site data will be shared without written approval. The MELD project liaison will provide the approved data to the Additional MELD Project Data Storage Site for the secondary analysis. The project leader of an approved analysis plan is required to keep track of ethical approval of each participating cohorts when Category 1 data is being shared.

Guidelines for access derived data without an accompanying manuscript (Category 2):
Any MELD Project member (or non-member) wishing to access derived data or group-level summaries will need to complete a project proposal. The project proposal will clearly state which variables will be included in the analysis, and thus what data is requested from each of the participating sites. The level of data-sharing will also be mentioned in the analysis plan, so that it is clear whether individual structural or functional imaging measures derived from software packages including, but not limited to, FreeSurfer (hereinafter referred to as "individual data"), and/or clinical / demographic data or group level summaries will need to be shared for the project.
Access to unpublished derived datasets (Category 2) will be managed by MELD Project leads. No site data will be shared if the PI opts out.

Guidelines for access derived data supporting a manuscript (Category 3):
Metadata and accompanying code (Category 3) relevant to each publication will be available through the UCL data repository service without restricted access.

The project leader of an approved analysis plan is not allowed to share the data of participating cohorts (**Category 1 or 2 data**) to third parties inside or outside the MELD Project. Individuals who will have access to the data during the project, the location of data storage and a timeline for finishing the project shall all be stated in the Analysis Plan. The project leader shall keep a document stating who has access to these data. At the end of the proposed timeline, the individual level data can continue to be stored on the project leader's local data storage for archival purposes, but no additional statistical analyses on the data from participating MELD Project members beyond the scope of the approved analysis (i.e., analyses that have not been explicitly described in the approved analysis plan). Shall a cohort PI determine to withdraw from a project they had previously enrolled in and committed data towards, the project leader will comply and remove the dataset in question from all future analyses. Prior to this, all efforts would be made by MELD Project leads to address any concerns the withdrawing PI may have and to determine if the project has deviated from proposed plans.

Authorships
Specific authorship policies for:

Manuscript:
1. We request that manuscripts resulting from approved analysis plans will be submitted to the MELD Project leads prior to circulating it to all co-authors and prior to submitting to a journal. This review is intended to ensure that provisions described in the analysis plan are correctly implemented and to avoid overlap with other MELD Project proposals/manuscripts. The MELD Project leads maintain confidentiality of the manuscript and will complete its review within 2 weeks.
2. Authorship credit should be based on substantial contribution to (1) the measurement of structural Magnetic Resonance Imaging (sMRI) phenotypes for the analysis / meta-analysis; (2) contributions or

generation of data for the analysis; (3) contributions to the conception, design, analysis and/or interpretation of the data; and (4) final approval of the manuscript version to be published.

3. The phrase "for the MELD Project" can be included on the author line of the manuscript if there is a restriction on the total number of co-authors. The MELD Project website can be used as the affiliation, which will include a list of all people involved in MELD Project.

4. Funding for the MELD Project will be acknowledged in the support acknowledgement section of the manuscript.

5. All authors get to inspect and comment on the article before it is submitted to a journal.

6. It is the responsibility of the first author that the authorship guidelines are followed, that the sample and the research-methodology are described correctly and that references to former relevant MELD Project Group publications where appropriate are made.

Conference poster and talk abstracts:

1. Include as co-authors the project leaders / major contributors, as well as the MELD Project leads and the statement "for the MELD Project ".

2. If not all authors can be listed, consider putting in the abstract "Contributing Authors are listed on the MELD Project Website".

3. Regardless of the names listed on the abstract, it is best to list all contributors on the conference poster and/or the conference acknowledgement slide. PDF copies of the conference abstracts can be used by all MELD Project members to list abstracts on CVs.

Symposium submissions:

1. List the presenting author, and if possible, on behalf of the MELD Project. Again, if possible consider putting in the abstract "Contributing Authors are listed on the MELD Project Website".

2. Regardless of the abstract, all contributors should be listed on the symposium talk acknowledgement slide.

Participation in the MELD Project

New and existing MELD Project members will sign a Memorandum of Understanding indicating that they agree with the policies listed here.

Expulsion from the MELD Project

Expulsion from the MELD Project will be considered when a site fails to uphold this Memorandum of Understanding, or does not contribute significantly to the work of the MELD Project either in data collection, data analyses, or its goals. It is the responsibility of the MELD Project subgroup leaders to assemble evidence and present the reasons for possible expulsion to the PIs. Expulsion from the MELD Project will require a simple majority vote of the PIs.

A site may request to withdraw from the MELD Project. The withdrawing site will need to agree in writing to a moratorium on publication of any data that were obtained in the context of the MELD Project work, or where the interpretation of the data relies in any part on unpublished MELD Project work.

MELD Project Membership is contingent upon signing the following statement:

I AGREE:
1. To consider participation in analyses, meta-analyses and secondary analyses proposed by the MELD Project, subject to constraints or limitations that I can impose in each case.

2. To abide by the guidelines for authorship and publication, and other guidelines described in this document.

3. Not to distribute or communicate any privileged information to individuals who are not members without consent of the MELD Project leads. This includes any other existing collaborators who are not members of the MELD Project. Privileged information includes results of any unpublished analyses completed by members of the MELD Project.

4. Not to distribute or copy any data collected by the Project without prior written consent of the MELD Project leads.

5. That the MELD Project leads will review and evaluate future scientific opportunities, and will make recommendations regarding the needed expertise and research program to maximize those opportunities in the best possible way.

6. That failure to uphold this agreement may result in my expulsion from the MELD Project (but I will still be bound by publication moratorium on MELD Project work, as described above).

I, as subgroup leader of my site, consent to participate in the MELD Project with (tick all that apply):

☐ Anonymised data matrices derived from MRI based computational anatomy (no sharing of raw MRI data)

☐ Anonymised clinical demographic information (no sharing of identifiable patient information e.g. name, DOB or hospital ID)

☐ Anonymised MRI data

Signature   Date

_____   _____

Please print name   Institute

_____   _____

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