Tractography under the microscope: Protocol for a diagnostic test accuracy systematic review and network meta-analysis of intraoperative tractography

Citation

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Review question

To compare the diagnostic accuracy of DTI- and FOD-based tractography in visualising the corticospinal tract as determined by subcortical mapping in individuals undergoing surgery for motor eloquent lesions.

Searches

A systematic search using pre-defined search strings will be conducted in the databases MEDLINE Ovid (1946 to date of search), Embase Ovid (1974 to date of search), and Web of Science. Keywords used for the search include inter alia surg*, tractography*, and motor function. Following the recommendations of the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Deeks et al., 2023), no filters will be applied to the search. The search will not be restricted by language or date of publication. To ensure a comprehensive search of the literature, forwards and backwards citation tracking of included articles will be conducted using citationchaser (https://estech.shinyapps.io/citationchaser/) to identify relevant articles in addition to the systematic search of databases. Relevant unpublished articles will be searched for using the title search in the database BASE Bielefeld with the search terms: tractograph* AND map* AND motor.

References

Deeks, J. J., Bossuyt, P. M., Leeflang, M. M., & Takwoingi, Y. (2023). Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy. John Wiley & Sons.

Types of study to be included

We will include cross-sectional studies that use subcortical stimulation during surgery of motor eloquent lesions to determine the accuracy (sensitivity, specificity, positive predictive value, negative predictive value) of at least one tractography method.

Condition or domain being studied

Tractography of the corticospinal tract for as applied in neurosurgical practice

Participants/population

Patients of any age undergoing neurosurgical intervention with neuromonitoring for motor-eloquent lesions near the

corticospinal tract. We will not exclude studies on the basis of type of lesion, exact lesion location, or neuromonitoring protocol, provided some form of intraoperative neuromonitoring was present.

As this is a diagnostic test accuracy systematic review, the PIRD framework will be used: Population, Index test, Reference test, Diagnosis/Outcome (Munn et al., 2018). Since the pre-registration form uses the PICO/PECO framework, the PIRD framework will be adopted for the pre-registration. The systematic review itself, however, will follow the PIRD framework.

References

Munn, Z., Stern, C., Aromataris, E., Lockwood, C., & Jordan, Z. (2018). What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences. BMC Medical Research Methodology, 18(1), 5. https://doi.org/10.1186/s12874-017-0468-4

Intervention(s), exposure(s)

Studies employing subcortical mapping to identify the location of the corticospinal tract and using this, determine the accuracy of pre-operative tractography of the corticospinal tract. If studies do not report either the distance between positive/negative stimulation points and the tract and/or a measure of accuracy (sensitivity, specificity, positive predictive value, negative predictive value), the corresponding author will be contacted. If the data could not be obtained by such means, the study will be excluded.

Comparator(s)/control

We will compare the accuracy of diffusion tensor imaging (DTI)- and Fibre Orientation Distribution (FOD)-based tractography methods (index tests). We will include studies that use subcortical mapping (reference test) to determine the accuracy of either DTI-based or FOD-based tractography or both.

Main outcome(s)

Outcomes indicating the accuracy of tractography methods are of primary interest. Accuracy may be indicated through sensitivity, specificity, positive predictive value, and negative predictive value.

Additional outcome(s)

Of secondary interest are reports of (1) mean distances between the tract and positive and negative stimulation points, (2) correlations between stimulation strength and measured distances, and (3) post-operative motor function of the patients.

Data extraction (selection and coding)

Record Selection

Article screening will be performed using CADIMA. In CADIMA, articles identified in the literature search will be de-duplicated and screened using the PIRD-defined inclusion/exclusion criteria in two stages: (1) title/abstract, and (2) full-text screening. All articles will be screened independently by two independent reviewers at both the title/abstract and full-text stage to ensure concordant application of the inclusion criteria (based on the PIRD framework). Weekly meetings will be held to discuss potential questions and resolve discrepancies amongst the original reviewers. If discrepancies cannot be resolved via discussion amongst reviewers, a third independent reviewer with knowledge of the topic will be consulted for arbitration. An overview of screening decisions, including reasons for article exclusion at the full-text stage, will be provided using the PRISMA flow diagram.

Data Extraction

Data extraction will be performed using pre-define data extraction forms. Data extraction will be performed by two independent reviewers. Prior to initiation of data extraction, we will pilot our extraction form which will be revised until

it achieves >85% agreement between reviewers. We will perform a pilot data extraction of two studies to revise our data extraction spreadsheet if necessary. After final data extraction, the standardised data extraction spreadsheet will be used for analysis.

The extraction variables include the following: sample characteristics (e.g., age, pathology), sample size, methodological detail (e.g., imaging parameters, tractography approach, subcortical stimulation parameters, intraoperatively monitored muscles, method for brain shift correction), and outcome measures (sensitivity, specificity, positive predictive value, negative predictive value). In case of uncertainties regarding the data or methods, the authors will be contacted via email. In total, two weeks will be granted for authors to reply. In case of no response, a follow-up email will be sent one week after initial contact.

Risk of bias (quality) assessment

Risk of bias of articles that passed the full-text screening stage will be evaluated by two independent reviewers using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool (Whiting et al., 2011). The reviewers are blinded to each other's decisions and familiar with the topic.

Discrepancies that arise will be resolved via consensus amongst reviewers. If discrepancies cannot be resolved via original reviewer consensus, a third reviewer will be consulted for arbitration. The critical appraisal tool was selected by consulting the Quality Assessment and Risk of Bias Tool Repository (https://osf.io/ws824/).

References

Whiting, P. F., Rutjes, A. W. S., Westwood, M. E., Mallett, S., Deeks, J. J., Reitsma, J. B., Leeflang, M. M. G., Sterne, J. A. C., Bossuyt, P. M. M., & the QUADAS-2 Group. (2011). QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies. Annals of Internal Medicine, 155(8), 529–536. https://doi.org/10.7326/0003-4819-155-8-201110180-00009

Strategy for data synthesis

We plan to conduct a meta-analysis to compare the accuracy of DTI- and FOD-based tractography depending on (1) sufficient data being retrieved by the literature search, (2) heterogeneity in study design, and (3) heterogeneity in outcome measures. Firstly, we plan to meta-analyse the accuracy of DTI- and FOD-based tractography individually using bivariate analyses. Secondly, we will compare the pooled sensitivity and specificity of DTI- and FOD-based tractography.

Of the secondary outcomes, the mean distance between the tract and (positive/negative) stimulation points will be compared between DTI- and FOD-based tractography using a Wilcoxon-Mann-Whitney test. The same statistical approach will be applied to analyse the post-operative motor function of patients, assuming the motor function was assessed across studies using the same clinical scales. Finally, correlations between stimulation strength and measured stimulation point-to-tract distances will be compared between DTI- and FOD-based tractography.

If sufficient data are retrieved but study design and/or outcomes measures are too heterogeneous to pool data, studies will be sub-grouped by study design (e.g., by dMRI acquisition parameters, or by subcortical mapping protocols) and/or outcome measures (e.g., motor function of patients). Publication bias will be visually assessed using funnel plots.

Data will be extracted and synthesised in tables showing (1) patient demographics (age, pathology, location of pathology), (2) dMRI acquisition parameters, (3) method of tractography generation (e.g., algorithm, software, seeding regions of interest), (4) subcortical mapping parameters and protocol (e.g., number of subcortical stimulation sites, stimulation strength, interval between successive stimulations, protocol for adjusting the stimulation strength), (5) intraoperative monitoring protocol (e.g., monitored muscles), (6) accuracy of tractography (e.g., sensitivity, specificity), and (7) method for correction of brain-shift. The robustness of the reported evidence will be evaluated. The results will be reported following the PRISMA 2020 statement for reporting systematic reviews.

All analyses will be conducted using Python (https://www.python.org) and R Studio (https://posit.co/download/rstudio-desktop/).

Analysis of subgroups or subsets

Not applicable

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Type and method of review

Systematic review, Other

Anticipated or actual start date

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None

Conflicts of interest

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English

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Germany

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Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

MeSH headings have not been applied to this record

Date of registration in PROSPERO

17 September 2024

Date of first submission

06 September 2024

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

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