NEUROPATHOLOGY OF CHRONIC TRAUMATIC BRAIN INJURY INCLUDING CHRONIC TRAUMATIC ENCEPHALOPATHY

This is not a data capture form, but a document specifying the questions and data elements approved in 2021 by the NINDS-coordinated Working Group on the Neuropathology of CTE and chronic TBI-related neurodegeneration. Site-specific data capture forms should collect all recommended CORE data elements for upload to the FITBIR form structure. The collection of additional non-core elements may be SUPPLEMENTAL HIGHLY RECOMMENDED or SUPPLEMENTAL. Additional information is available on the FITBIR website fitbir.nih.gov. Note that there is not necessarily a 1:1 mapping between questions and data elements; data elements are the building blocks for data acquisition and may be used in a combinatorial fashion to address some questions. This document is organized by the Working Group's recommended order. Skip logic must be implemented at the level of the data capture form.

MAIN GROUP

Study Name:

1. GUID (GUID, CORE): _____
2. Autopsy number (AutopsyNum, SUPP) _____
3. Autopsy date (AutopsyDate, SUPP; YYYY-MM-DD): _____
4. Subject identifier number (SubjectIDNum, NINDS CDE, SUPP): _____
5. Site Name (SiteName, NINDS CDE, CORE): _____
6. Case Control Indicator (CaseContrlInd, NINDS CDE, CORE): _Case _Control _Unknown
7. Gender type (GenderTyp, NINDS CDE, CORE) _Female _Male _Not Reported _Unknown _Unspecified
8. General notes (GeneralNotesTxt, FITBIR CDE). Optional free text.

FORM ADMINISTRATION GROUP

9. Language form administration ISO code (LangCRFAdministratISOCode, FITBIR CDE, SUPP)
   _____
10. Language form administration ISO code other text (LangCRFAdministratISOCodeOTH, FITBIR CDE, SUPP)
    _____
11. Who filled out this form? (NeuropathDataSourceTyp, FITBIR CDE, CORE). *Select one. If "Other, specify" is selected, please write in response.*
    - ○ Neuropathologist
    - ○ Neurologist
    - ○ Psychologist
    - ○ Research coordinator
    - ○ Other, specify (NeuropathDataSourceTypOTH, FITBIR CDE) _____

Users may remove non-core questions. Users are NOT allowed to insert/delete permissible values of existing questions. The variable name in FITBIR is indicated in parentheses: existing FITBIR CDEs are in default black font; new FITBIR CDEs are in blue; NINDS CDEs are in green.

SUBJECT HISTORY

DEATH INFORMATION

1. Age at death: (DeathAgeVal, NINDS CDE, C54722, CORE). The subject's age is typically recorded to the nearest full year completed, e.g. 11 years and 6 months should be recorded as 11 years.
   _____

POSTMORTEM INTERVAL

1. Postmortem interval for autopsy specimen recorded in hours:(PstmrtmIntrvlApSpecmnVal, NINDS CDE, C12227, CORE). Enter the time interval in hours.
   _____
2. How was the postmortem interval ascertained, e.g. recorded, calculated, or estimated? (PstmrtmIntrvlAscerTyp, (new FITBIR CDE, CORE). Choose one, if "Calculated" is selected, please fill out the next question:

   ○ Recorded ○ Calculated ○ Estimated ○ Unknown
3. Notes on how the postmortem interval was calculated:(PstmrtmIntrvlCalcTxt, new FITBIR CDE, SUPP). Enter free text to describe how the postmortem interval was calculated. _____
   _____
4. Agonal state (AgonalStateDur, new FITBIR CDE, SUPP). Enter the value in hours.
5. RIN (RINSpecimenVal, new FITBIR CDE, SUPP). Enter the RNA Integrity Number.
6. How was the RIN calculated? Free text. (RINValueMethodTxt, new FITBIR CDE, SUPP)
7. pH (pHTissueVal, new FITBIR CDE, SUPP). Enter the pH value between 0.00:14.00.
8. Refrigeration time (SpecimenRefridgTimeVal, new FITBIR CDE, SUPP). Enter the value in hours.

CLINICAL SUMMARY (OPTIONAL)

9. Clinical history notes (NeuropathClinHistTxt, new FITBIR CDE, SUPP). Please note that standard clinical history questions, including medical history and TBI exposure, are not included in this neuropathology form, as this content will be covered by the clinical history CDEs.
   _____
   _____

GROSS PATHOLOGY

BRAIN TISSUE AND POST-MORTEM CSF

10. Is the tissue available in repository (BioSampReposInd, NINDS CDE, C16194, CORE). Choose one.

    ○ Yes ○ No ○ Unknown

11. Frozen tissue repository information (RepositoryName, PDBP CDE, CORE if Yes to previous question). Enter the name of repository where frozen tissue(s) is located.

    _____

12. Tissue collected in the repository (BrainAutopsyTissueTyp, FITBIR CDE, CORE). Select all that apply.

Tissue type (BrainAutopsyTissueTyp)	Preservation technique used (PresrvtnTechnqUseTyp, NINDS CDE) Choose one for each tissue type.		
☐ Entire brain	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Right hemisphere	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Left hemisphere	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Portions of brain	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ DNA	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ DNA prep	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Dura	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Spinal cord	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Right eye	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Left eye	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ CSF	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Pituitary	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Skin	○ Frozen	○ Paraformaldehyde	○ Formalin
☐ Other, specify (BrainAutopsyTissueTypOTH, FITBR CDE) _____	○ Frozen	○ Paraformaldehyde	○ Formalin

13. Comments on tissue quality and preservation technique (PresrvtnTechnqUseTypOTH, new FITBIR CDE, SUPPHIGHREC). Enter any comments on tissue quality and preservation technique.

    _____

14. Known infectious tissues (InfectiousTissueInd, FITBIR CDE, CORE)? If "Yes", proceed to the next question and provide the information about infections. If "No" or "Unknown" is selected, skip to the next section.

    ○ Yes ○ No ○ Unknown

15. Specify infections (InfectiousTissueTyp, new FITBIR CDE, CORE) Select all that apply. If "Other, specify" is selected, provide the information in InfectionTissueOTH CDE. Consideration: For many banks the tissues are not tested, and for those in which testing is performed, it may not be comprehensive

    ☐ Prion disease (CJD/TSE) ☐ SARS-CoV-2 (COVID-19) ☐ HIV ☐ HBV ☐ HCV ☐ TB

16. Infectious disease comments. Enter comments text. (InfectiousTissueCommTxt, FITBIR CDE, CORE)

    _____
    _____

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PARAFFIN BLOCK INVENTORY

17. Paraffin block inventory by brain region (NeuropathROITBICoreTyp, NeuropathROITBISuppTyp, NeuropathROITBIOTH new FITBIR CDE) Core brain regions for TBI-related dementia are listed in the first table and supplemental regions are listed in the second table. Select all that apply. For each region, enter the corresponding block number and provide laterality and lesional information. Can combine into one cassette if feasible and desired. Including depth of sulcus is critically important for assessment for pathognomonic CTE neuropathological feature (depth of sulcus perivascular neuronal and glial PHF-tau). Core regions based on 1st and 2nd CTE consensus papers and NIA-AA guidance, including additional regions for evaluation in cases of high suspicion (indicated by asterisks*).

Core Brain Region (NeuropathROITBICoreTyp NeuropathROITBIOTH new FITBIR CDE).	**Brain Block #** (BrainBlockNumber, new FITBIR CDE)	**Laterality** (LatTyp, NINDS CDE) for each brain region.		**Lesional? (**BrainTissLesionInd, new FITBIR CDE**)**		
☐ Amygdala		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Cerebellar cortex and dentate nucleus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Cingulate gyrus, anterior		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Hippocampus at level of LGN		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Entorhinal cortex		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ *Hypothalamus including mammillary body		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Inferior parietal lobule with depth of sulcus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Medulla including dorsal motor nucleus of vagus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Midbrain including substantia nigra		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Middle frontal gyrus with depth of sulcus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Occipital (calcarine – primary visual) cortex		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Pons including locus coeruleus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Superior and middle temporal gyri with depth of sulcus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ *Superior frontal gyrus with depth of sulcus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ *Temporal pole with depth of sulcus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Thalamus at level of subthalamic nucleus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Other, specify (NeuropathROITBIOTH)		○ Right	○ Left	○ Yes	○ No	○ Unknown

18. Additional blocks/brain regions for Paraffin Block Inventory, supplemental (new FITBIR CDE NeuropathROITBISuppTyp)

Supplemental Brain Region (NeuropathROITBISuppTyp NeuropathROITBIOTH new FITBIR CDEs).	**Brain Block#** (BrainBlock Number, new FITBIR CDE)	**Laterality** (LatTyp, NINDS CDE) for each brain region.		**Lesional? (**BrainTissLesionInd, new FITBIR CDE**)**		
☐ Anterior inferior frontal gyrus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Body of corpus callosum at level of midbrain		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Body of corpus callosum with fornix		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Frontoinsula		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Fusiform/inferior temporal gyrus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Genu of corpus callosum		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Hippocampus with parahippocampal sulcus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Hippocampus, CA1		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Hippocampus, CA2		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Hippocampus, CA3		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Hippocampus, CA4		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Hippocampus, dentate gyrus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Hippocampus, subiculum		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Inferior frontal gyrus – Broca's area		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Lateral parieto-occipital cortex		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Medial prefrontal cortex and white matter		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Middle cerebellar peduncle		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Occipital white matter 2 slices posterior to ventricle		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Parietal white matter at LGN		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Posterior angular gyrus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Posterior cerebellar cortex		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Posterior cingulate gyrus at LGN		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Posterior superior middle temporal gyrus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Precuneus		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Primary motor cortex		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Splenium of corpus callosum		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Superior cerebellar peduncle with vermis		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Supplementary motor cortex		○ Right	○ Left	○ Yes	○ No	○ Unknown
☐ Other, specify (BrainROITypOTH)		○ Right	○ Left	○ Yes	○ No	○ Unknown

AUTOPSY

19. Full autopsy performed? (AutopsyFullPerformedInd, FITBIR CDE, CORE). Choose one. If "Yes" proceed to the next question, if "No" or "Unknown" skip to DIAGNOSIS section.

    ○ Yes ○ No

20. Autopsy type (AutopsyTyp, FITBIR CDE, CORE). Choose one.

    ○ Medical ○ Forensic

21. Major gross neuropathological findings (NeuropathologyMajorFindingsTxt FITBIR CDE, CORE). See the final report in appendix

    _____

GROSS EXAMINATION

22. Brain weight in grams. This value should be recorded in grams (g) for all brain tissue types weighed (BrainWgtMeasr, NINDS CDE, C08158, CORE + BrainWgtMeasTyp, new FITBIR CDE, CORE)

    ○ Whole fresh ____g; Whole fixed ____g; Right fresh _____g; Right fixed _____g
    ○ Left fresh _____g; Left fixed _____g

23. Hindbrain / cerebellum weight in grams. Provide a single value for total hindbrain weight including cerebellum. (HindbrainCerebWgtVal, new FITBIR CDE; SuppHighRec) _____g

24. Hydrocephalus severity - ventriculomegaly/ventricle enlargement - hydrocephalus ex vacuo (HydrcephlsSevScl, NINDS CDE, CORE). Choose one.

    ○ None ○ Mild ○ Moderate ○ Severe ○ Not assessed ○ Unknown

25. Septal abnormalities found? (SeptalAbnormInd, new FITBIR CDE, CORE). Choose one.

    ○ Yes ○ No ○ Not assessed ○ Unknown

26. Cavum septum pellucidum present? (CSPPresenceInd new FITBIR CDE, CORE) If yes, indicate width in cm. (CSPWidthVal new FITBIR CDE, CORE)

    ○ Yes ○ No ○ Not assessed ○ Unknown

27. Fenestrations? (FenestrationPresenceInd new FITBIR CDE, CORE)

    ○ Yes ○ No ○ Not assessed ○ Unknown

28. Indicator of ventricular catheter used (VentricularCatheterInd, FITBIR CDE, CORE). Choose one.

    ○ Yes ○ No ○ Not assessed ○ Unknown

29. Evidence of neurosurgery indicator (NeurosurgInd, FITBIR CDE, CORE). Choose one.

    ○ Yes ○ No ○ Not assessed ○ Unknown

SWELLING

30. Indication of presence of clinically significant pathology - brain swelling. (BrainGrossPathInd, new FITBIR CDE, CORE). Choose one. If "Yes," proceed to the next question and assess the severity of findings. If "No"/"Not assessed"/"Unknown" selected, proceed to the next section.

    ○ Yes ○ No ○ Not assessed ○ Unknown

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31. Brain swelling severity state? (BrainSwellNeuropathStat, FITBIR CDE, CORE). Choose one. If "None", "Not assessed" or "Unknown" selected, skip to the next section

○ Right to left shift ○ Left to right shift ○ Generalized ○ Not assessed ○ Unknown

HERNIATION

32. Indication of presence of clinically significant pathology - herniation. (BrainGrossPathInd, new FITBIR CDE, CORE). Choose one. If "Yes" proceed to the next question and assess the severity of findings. If "No"/"Not assessed"/"Unknown" selected, proceed to the next section.

○ Yes ○ No ○ Not assessed ○ Unknown

33. Brain herniation extent (BrainHerniationType, FITBIR CDE, CORE). Check all that apply

☐ Central ☐ Transcalvarial/direct/extracranial ☐ Subfalcine/cingulate
☐ Cerebellar/tonsillar/transforaminal ☐ Uncal/trans-tentorial ☐ Upward transtentorial

INFARCTS

○ *Acute infarcts 1 day – 1 month, old/chronic infarcts > 1 month.*

34. Indication of presence of clinically significant pathology - infarcts. (BrainGrossPathInd, new FITBIR CDE, CORE). Choose one. If "Yes" proceed to the next question and assess the extent of findings. If "No"/"Not assessed"/"Unknown" selected, proceed to the next section.

○ Yes ○ No ○ Not assessed ○ Unknown

35. Total number of infarct/lacunae found (BrainInfarctsLacunCt, FITBIR CDE, CORE). Enter up to 4-digit number_____

INFARCTS, Continued

36. Location, size, and stage of infarcts/lacunae (CORE). Select location and specify the size and axis, as well as stage (chronic vs acute). Note that the form can accommodate multiple infarcts per anatomic site (1,2,..n)

Enter the axis, size, and stage of infarcts / lacunae for each anatomic site where observed (BrainGrsPthTBIAnatSite, new FITBIR CDE). Select all that apply.	Use AnatomicAxisLocationTyp, FITBIR CDE to specify the axis (M-L, A-P, D-V). Use InfarctsLacunaMeasrVal, FITBIR CDE to specify the size of infarcts/lacunae			Indicate stage (BrainGrossPath StageTyp, new FITBIR CDE)
Multiple entries can be made per anatomic site (1..n)	Size Medial/Lateral (mm)(InfarctsLacunaMeasrVal)	Size Anterior/Posterior (mm)(InfarctsLacunaMeasrVal)	Size Dorsal/Ventral (mm)(InfarctsLacunaMeasrVal)	Acute or Chronic
☐ Brainstem (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Cerebral cortex (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Cerebellum (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Deep cerebral gray matter or internal capsule (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Subcortical white matter 1..n	• • •	• • •	• • •	o Acute o Chronic
☐ Other, specify (BrainAbnormFindAnatSiteOTH)_____	• • •	• • •	• • •	o Acute o Chronic

HEMORRHAGES

- *Acute hemorrhages 1 day – 1 month, old/chronic hemorrhages > 1 month.*

37. Indication of presence of clinically significant pathology - hemorrhages. (BrainGrossPathInd, new FITBIR CDE, CORE). Choose one. If "Yes" proceed to the next question and assess the severity of findings. If "No"/"Not assessed"/"Unknown" selected, proceed to the next section.

    o Yes o No o Not assessed o Unknown

38. Multiple or single hemorrhages? (BrainHemorStat, FITBIR CDE, CORE). Choose one.

    o Single o Multiple

39. Subdural, epidural and/or subarachnoid hemorrhage(s) (BrainHemorTyp, FITBIR CDE, CORE). Choose one.

    o Subdural o Epidural o Subarachnoid

40. Severity of primary parenchymal hemorrhage(s)) (> 5mm) (BrainHemorParenchPrimaryStat, FITBIR CDE, CORE). Choose one.

    o Mild o Moderate o Severe

41. Severity of secondary parenchymal hemorrhage(s) (e.g. tumor, vascular malformation) (BrainHemorParenchSecondStat, FITBIR CDE, CORE). Choose one.

    o Mild o Moderate o Severe

HEMORRHAGES, continued

42. Location, size, and stage of hemorrhages (CORE). Select location, then specify the size in mm for each axis (lateral, anterior/posterior, or dorsal/ventral) and indicate stage (acute or chronic).

Enter the axis, size, and stage of observed hemorrhage for each anatomic site (BrainAbnormFindAnatSite, FITBIR CDE). Select all that apply.	Use AnatomicAxisLocationTyp, FITBIR CDE to specify the axis (M-L, A-P, D-V). Use BrainHaemorMeasrVal, new FITBIR CDE to specify the size of haemorrhages			Indicate stage. BrainGrossPathStageTyp, new FITBIR CDE
Multiple entries can be made per anatomic site (1..n)	Size Medial/Lateral (mm) (BrainHaemorMeasrVal)	Size Anterior/Posterior (mm) (BrainHaemorMeasrVal)	Size Dorsal/Ventral (mm) (BrainHaemorMeasrVal)	Acute or Chronic
☐ Brainstem 1 (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Cerebral cortex 1 (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Cerebellum 1 (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Deep cerebral gray matter or internal capsule 1 (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Subcortical white matter 1 (1..n)	• • •	• • •	• • •	o Acute o Chronic
☐ Other, specify (1..n) (BrainAbnormFindAnatSiteOTH)_____	• • •	• • •	• • •	o Acute o Chronic

ATHEROSCLEROSIS

43. Indication of presence of clinically significant pathology - atherosclerosis. (BrainGrossPathInd, new FITBIR CDE, CORE). Choose one. If "Yes" proceed to the next question (table) and assess the severity of findings. If "No"/"Not assessed"/"Unknown" selected, proceed to the next section.

o Yes o No o Not assessed o Unknown

44. Severity of atherosclerosis (BrainAtherosclerAnatSite, FITBIR CDE, CORE, to indicate site and BrainAthrosclerPresStat, FITBIR CDE, CORE, to indicate severity). Select all that apply.

Indicate site of observed atherosclerosis (BrainAtherosclerAnatomicSite, FITBIR CDE). Select all that apply	Use (BrainAtherosclerPresenceStat, FITBIR CDE) to provide the atherosclerosis score		
☐ Anterior cerebral	o Mild	o Moderate	o Severe
☐ Basilar artery	o Mild	o Moderate	o Severe
☐ Internal carotid	o Mild	o Moderate	o Severe
☐ Middle cerebral	o Mild	o Moderate	o Severe
☐ Posterior cerebral	o Mild	o Moderate	o Severe
☐ Vertebral	o Mild	o Moderate	o Severe
☐ Overall	o Mild	o Moderate	o Severe

45. Presence of traumatic aneurysm (TraumatcAnrysmInd, NINDS CDE, C02484, CORE). Choose one.

o Absent o Indeterminate o Present o Premorbid

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ATROPHY

46. Indication of presence of clinically significant pathology - brain atrophy. (BrainGrossPathInd, new FITBIR CDE, CORE). Choose one. If "Yes" proceed to the next question and assess the severity of findings. If "No"/"Not assessed"/"Unknown" selected, proceed to the next section.

    ○ Yes ○ No ○ Not assessed ○ Unknown

47. Severity state of brain atrophy (BrainRegionAtrophyStat, FITBIR CDE, SUPPHIGHREC) by brain region. Select all that apply.

Atrophy/abnormality anatomic site (BrainRegionAtrophyAnatomicSite, FITBIR CDE, SUPPHIGHREC)	**Severity (**BrainRegionAtrophyStat, FITBIR CDE**)**				
☐ General Cortical	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Frontal Lobar	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Parietal Lobar	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Temporal Lobar	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Occipital Lobar	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Hippocampal	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Entorhinal	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Amygdala	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Substantia Nigra Pallor	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Locus Coeruleus Pallor	o None	o Mild	o Moderate	o Severe	o Not assessed
☐ Overall	o None	o Mild	o Moderate	o Severe	o Not assessed

CONTUSIONS/TRAUMATIC LESIONS

Acute (1 day – 1 month), old/chronic (>1 month).

48. Indication of presence of clinically significant pathology – contusions/traumatic lesions. (BrainGrossPathInd, new FITBIR CDE, CORE). Choose one. If "Yes" proceed to the next question and assess the severity of findings. If "No"/"Not assessed"/"Unknown" selected, proceed to the next section.

    ○ Yes ○ No ○ Not assessed ○ Unknown

49. Total number of contusions/ traumatic lesions (ContusionTraumaLesionTotCt, FITBIR CDE, CORE)

    _____

50. Assessment of contusions/lesions (CORE)

Enter the axis, size, coup-countrecoup, and stage of contusions/lesions for each anatomic site where observed (BrainAbnormFindAnatSite, FITBIR CDE). Select all that apply.	Use AnatomicAxisLocationTyp, FITBIR CDE to specify the axis (M-L, A-P, D-V). Use ContusTraumLesionMeasrVal, new FITBIR CDE to specify the size of contusions/traumatic lesions			Coup-Contrecoup injuries (TBICoupContrecoupTyp, FITBIR CDE)				Indicate stage using BrainGross PathStage Typ, new FITBIR CDE
Multiple entries can be made per anatomic site (1..n)	Size Medial/Lateral (mm) (ContusTraumLesionMeasrVal)	Size Anterior/Posterior (mm) (ContusTraumLesionMeasrVal)	Size Dorsal/Ventral (mm) (ContusTraumLesionMeasrVal)					Acute or Chronic?
☐ Brainstem 1 (1..n)	• • •	• • •	• • •	o Coup	o Contrecoup	o Unknown	o Not Assessed	o Acute o Chronic
☐ Cerebral cortex 1 (1..n)	• • •	• • •	• • •	o Coup	o Contrecoup	o Unknown	o Not Assessed	o Acute o Chronic
☐ Cerebellum 1 (1..n)	• • •	• • •	• • •	o Coup	o Contrecoup	o Unknown	o Not Assessed	o Acute o Chronic
☐ Deep cerebral gray matter or internal capsule 1 (1..n)	• • •	• • •	• • •	o Coup	o Contrecoup	o Unknown	o Not Assessed	o Acute o Chronic
☐ Subcortical white matter 1 (1..n)	• • •	• • •	• • •	o Coup	o Contrecoup	o Unknown	o Not Assessed	o Acute o Chronic

SPINAL CORD

51. Presence of abnormalities in spinal cord (SpinalCordAbnormalityFindInd, FITBIR CDE; SUPP). Choose one.

    ○ Yes ○ No ○ Not assessed ○ Unknown

52. Presence of atrophy of ventral roots (SpinalCordVentralRtAtrophyInd, FITBIR CDE; SUPP). Choose one.

    ○ Yes ○ No ○ Not assessed ○ Unknown

EYES

If available. Refer to Tissue type availability in the repository (BrainAutopsyTissueTyp). Select all that apply for information.

53. Indication of eyes' pathology (EyesPathInd, FITBIR CDE; SUPP). Choose one.

    ○ Yes ○ No ○ Not assessed ○ Unknown

End of macroscopic section.

Users may remove non-core questions. Users are NOT allowed to insert/delete permissible values of existing questions. The variable name in FITBIR is indicated in parentheses: existing FITBIR CDEs are in default black font; new FITBIR CDEs are in blue; NINDS CDEs are in green.

MICROSCOPIC FINDINGS

Format and general instructions: Each **subsection (highlighted)** begins with a single core *synopsis* question to indicate overall presence of the feature, i.e. if it is present in any of the examined regions considered as core for the evaluation of neurodegeneration in TBI/CTE. The capture form should proceed to subsequent conditional core questions only if the answer to the synopsis indicator question is 'Yes.' Supplemental feature assessments, if relevant, are listed at the end of each section *in italics*. For each CORE feature, tables show the recommended minimum core regions of interest (ROI). Other regions, including recommended Supplemental ROIs, may also be selected for evaluation. ROIs are drawn from new FITBIR CDEs NeuropathROITBICoreTyp, CORE; and NeuropathROITBISuppTyp, SUPP, and are listed in Appendices 1 and 2.

NEURONAL TAU

1. Indication of presence of neuronal tau (pre-NFT, iNFT, gNFT) in any of the examined regions (new FITBIR CDE, NeurnPSulPTauOvrPresInd, CORE). If "Yes," proceed to next question. If "No, Not Assessed, or Unknown," skip to the next section on Glial Tau.

○ Yes ○ No ○ Not assessed ○ Unknown

1.1 Tau antibody used (TauAntibodyTyp, FITBIR CDE). Choose one. You may specify different tau antibodies for each region assessed if needed.

AT8	CP13	PHF1
Non-phospho specific	Other, specify (use TauAntibodyTypOTH)	

1.2 Evaluation of neuronal tau for core brain regions, including additional core regions (marked by *) in cases of high suspicion (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Hippocampus (If yes > Supp Y/N for subdivisions)
Entorhinal cortex	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Amygdala
Midbrain including substantia nigra	Pons including locus coeruleus
Medulla including dorsal motor nucleus of vagus	Cerebellar cortex including dentate nucleus
*Superior frontal gyrus with depth of sulcus	*Temporal pole with depth of sulcus
*Hypothalamus including mammillary body	Other, specify

1.3. Indication of presence of perivascular neuronal tau in any of the examined regions. (new FITBIR CDE NeurnPerivTauOvrPresInd, CORE). If "Yes," proceed to the next question to indicate regions and assess patterns. If "No, Not Assessed, or Unknown," skip to the next section on Glial Tau.

○ Yes ○ No ○ Not assessed ○ Unknown

Users may remove non-core questions. Users are NOT allowed to insert/delete permissible values of existing questions. The variable name in FITBIR is indicated in parentheses: existing FITBIR CDEs are in default black font; new FITBIR CDEs are in blue; NINDS CDEs are in green.

1.3.1. Evaluation of perivascular neuronal tau (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	*Superior frontal gyrus with depth of sulcus
*Temporal pole with depth of sulcus	

1.4. Indication of presence of predominant superficial pattern of neuronal tau in any of the examined regions (new FITBIR CDE NeurnPSupPTauOvrPresInd, CORE). If "Yes," proceed to the next question to indicate regions. If "No, Not Assessed, or Unknown," skip to next question on sulcal pattern.

○ Yes ○ No ○ Not assessed ○ Unknown

1.4.1. Evaluation of predominant superficial pattern of neuronal tau for core brain regions (Y/N/NA/Unknown) (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	*Superior frontal gyrus with depth of sulcus
*Temporal pole with depth of sulcus	

1.5. Indication of presence of predominant sulcal pattern of neuronal tau in any of the examined regions (new FITBIR CDE NeurnPSulPTauOvrPresInd, CORE) If "Yes," proceed to next question to indicate regions. If "No, Not Assessed, or Unknown," skip to Supplemental features (optional) or to next section on Glial Tau (required).

○ Yes ○ No ○ Not assessed ○ Unknown

1.5.1. Evaluation of predominant sulcal pattern of neuronal tau (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	*Superior frontal gyrus with depth of sulcus
*Temporal pole with depth of sulcus	

1.6. Assessment of Supplemental Highly Recommended features for perivascular neuronal tau (new FITBIR CDE NeuronalPerivTauPathTyp, SUPPHIGHREC). Select the type of observed feature. These may be assessed for any core or supplemental region using new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp, NeuropathROITBISuppTyp. Where relevant, use NeuropathROIStainTyp or TauAntibodyTyp CDEs to indicate the stain or antibody used for specific assessment.

Predominant deep pattern	*Neuropil threads*	*Other, specify (using new FITBIR CDE NeuropathPathFeatTypOTH)*
Neuropil dots	*Grains*	

GLIAL TAU

2. Indication of presence of glial tau in any of the examined regions (new FITBIR CDE GlialTauOverallPresInd, CORE). If "Yes," proceed to the next question to indicate regions. If "No, Not Assessed, or Unknown," skip to next section on Neuritic Plaques.

○ Yes ○ No ○ Not assessed ○ Unknown

2.1. Tau antibody used (TauAntibodyTyp, FITBIR CDE). Choose one. If different tau antibodies are used for specific assessments in this section, the data element may be repeated.

AT8	CP13	PHF1
Non-phospho specific	Other, specify (use TauAntibodyTypOTH)	

2.2. Evaluation of glial tau (Y/N/NA/Unknown) for core brain regions, including additional core regions (marked by *) in cases of high suspicion (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If any supplemental regions were assessed, enter these using NeuropathROITBISuppTyp before proceeding to the next question on perivascular glial tau.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Hippocampus (If yes > Supp Y/N for subdivisions)
Entorhinal cortex	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Amygdala
Midbrain including substantia nigra	Pons including locus coeruleus
Medulla including dorsal motor nucleus of vagus	Cerebellar cortex including dentate nucleus
*Superior frontal gyrus with depth of sulcus	*Temporal pole with depth of sulcus
*Hypothalamus including mammillary body	Other, specify

2.3. Indication of perivascular glial tau in any of the examined regions (CONDITIONAL CORE; new FITBIR CDE GlialPerivascTauPresInd). If "Yes," proceed to next question to indicate regions. If "No, Not Assessed, or Unknown," skip to Supplemental Highly Recommended Features (optional) or next section on Neuritic Plaques (required).

○ Yes ○ No ○ Not assessed ○ Unknown

2.3.1. Evaluation of perivascular glial tau (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	*Superior frontal gyrus with depth of sulcus
*Temporal pole with depth of sulcus	

*Assessment of **Supplemental Highly Recommended** features for glial tau*

2.4. Indication of astroglial tau in any of the examined regions? (Y/N/Not Assessed/Unknown; new FITBIR CDE AstroglialTauPresInd, SUPPHIGHREC). If yes, continue to next item to select subtypes. If "No, Not Assessed, or Unknown," skip to next question on oligodendroglial tau (optional) or to next section on Neuritic Plaques (required)

○ Yes ○ No ○ Not assessed ○ Unknown

2.4.1. Select astroglial tau subtypes (new FITBIR CDE AstroglialTauPathTyp, SUPPHIGHREC). Associate with brain regions using new FITBIR CDEs NeuropathROITBICoreTyp and NeuropathROITBISuppTyp.

Subpial astroglial tau	*Periventricular astroglial tau*	*Tufted astrocytes*	*Astrocytic plaques*	*Other, specify (using new FITBIR CDE NeuropathPathFeatTypOTH)*
GAI	*Thorn-shaped astrocytes*	*GFA*	*Ramified astrocytes*	

2.5. Indication of oligodendroglial tau in any of the examined regions? (new FITBIR CDE OligodndglialTauPresInd, SUPPHIGHREC) If yes, continue to next question. If "No, Not Assessed, or Unknown," skip to next section on Neuritic Plaques.

○ Yes ○ No ○ Not assessed ○ Unknown

2.5.1. Select oligodendroglial tau subtypes (new FITBIR CDE OligodndglialTauPathTyp, SUPPHIGHREC). Associate with brain regions using new FITBIR CDEs NeuropathROITBICoreTyp and NeuropathROITBISuppTyp.

Globular oligo inclusions	*Coiled bodies*	*Other, specify (using new FITBIR CDE NeuropathPathFeatTypOTH)*

Users may remove non-core questions. Users are NOT allowed to insert/delete permissible values of existing questions. The variable name in FITBIR is indicated in parentheses: existing FITBIR CDEs are in default black font; new FITBIR CDEs are in blue; NINDS CDEs are in green.

NEURITIC PLAQUES

3. Indication of presence of neuritic plaques in any of the examined regions (new FITBIR CDE NeuriticPlaqOvrlPresInd, CORE). If "Yes," proceed to next question to indicate stains and regions. If "No, Not Assessed, or Unknown," skip to next section on CAA.

○ Yes ○ No ○ Not assessed ○ Unknown

3.1. Type of stain used to assess neuritic plaques (recommended from new FITBIR CDE NeuropathROIStainTyp, CORE*)*

Amyloid-beta immunostain	Congo red	Gallyas	Modified Bielschowsky
Other silver	Thioflavin S	Other, specify (use NeuropathROIStainOTH)	

3.2. If amyloid-beta used, indicate antibody. Choose one. (new FITBIR CDE ABetaAntibodyTyp, CORE*)*

10D5	4G8	6E10	Other, specify

3.3. Evaluation of neuritic plaques (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Hippocampus (If yes > Supp Y/N for subdivisions)
Entorhinal cortex	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Cerebellar cortex including dentate nucleus	*Superior frontal gyrus with depth of sulcus
*Temporal pole with depth of sulcus	*Hypothalamus including mammillary body

Assessment of Supplemental Highly Recommended features for neuritic plaques

3.4. Indication of presence of Diffuse plaques (new FITBIR CDE DiffusePlaquesPresInd, SUPPHIGHREC). Associate with brain regions using new FITBIR CDEs NeuropathROITBICoreTyp and NeuropathROITBISuppTyp.

○ *Yes* ○ *No* ○ *Not assessed* ○ *Unknown*

CEREBRAL AMYLOID ANGIOPATHY

4. Indication of presence of Cerebral Amyloid Angiopathy (CAA) in any of the examined regions (new FITBIR CDE CAAOverallPresInd, CORE) If "Yes," proceed to next question to indicate stains and regions. If "No, Not Assessed, or Unknown," skip to next section on Synucleinopathy.

○ Yes ○ No ○ Not assessed ○ Unknown

4.1. Stain used (recommended from new FITBIR CDE *NeuropathROIStainTyp, CORE)*

Amyloid-beta immunostain	Congo red	Gallyas	Modified Bielschowsky
Other silver	Thioflavin S	Other, specify (use NeuropathROIStainOTH)	

4.2. If amyloid-beta used, indicate antibody. Choose one.

10D5	4G8	6E10	Other, specify

4.3. Evaluation of CAA (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	Cerebellar cortex including dentate nucleus

4.4. Assessment of Supplemental Highly Recommended features for CAA (new FITBIR CDE CAAPathTyp, SUPPHIGHREC). Select the type of observed feature. These may be assessed for any core or supplemental region using new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp, and NeuropathROITBISuppTyp). Where relevant, use NeuropathROIStainTyp or AbetaAntibodyTyp CDEs to indicate the stain or antibody used for specific assessment.

Intraparenchymal CAA	*Leptomeningeal CAA*	*Other, specify (using new FITBIR CDE NeuropathPathFeatTypOTH)*

SYNUCLEINOPATHY

5. Indication of presence of Synucleinopathy in any of the examined regions (new FITBIR CDE SynucleinopthOvrPresInd, CORE)**.** If "Yes," proceed to next question. If "No, Not Assessed, or Unknown," skip to next section on TDP-43.

○ Yes ○ No ○ Not assessed ○ Unknown

5.1. Alpha-synuclein antibody type (new FITBIR CDE AlphaSynucleinAbTyp, CORE):

phospho-specific	non-phospho specific	other, specify (use AlphaSynucleinAbTypOTH)

Users may remove non-core questions. Users are NOT allowed to insert/delete permissible values of existing questions. The variable name in FITBIR is indicated in parentheses: existing FITBIR CDEs are in default black font; new FITBIR CDEs are in blue; NINDS CDEs are in green.

5.2. Indication of presence of Neuronal inclusions in any of the examined regions (Lewy bodies) (new FITBIR CDE NeuronInclusionsPresInd, CORE). If "Yes," proceed to next question to indicate regions. If "No, Not Assessed, or Unknown," skip to next section on TDP-43.

○ Yes ○ No ○ Not assessed ○ Unknown

5.2.1. Evaluation of neuronal inclusions (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	Amygdala
Midbrain including substantia nigra	Pons including locus coeruleus
Medulla including dorsal motor nucleus of vagus	Cerebellar cortex including dentate nucleus

5.3. Assessment of Supplemental Highly Recommended features for Synucleinopathy. Select the type of observed feature (new FITBIR CDE SynucleinopathyTyp, SUPPHIGHREC). These may be assessed for any core or supplemental region using new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp, and NeuropathROITBISuppTyp. Where relevant, use NeuropathROIStainTyp or AlphaSynucleinAbTyp CDE to indicate the stain or antibody used for specific assessment.

Lewy Neurites	*Oligodendroglial: Coiled bodies*	*Oligodendroglial: Papp-Lantos bodies*	*Other, specify (using new CDE NeuropathPathFeatTypOTH)*

TDP-43

6. Indication of presence of Neuronal or glial TDP-43 in any of the examined regions (new FITBIR CDE TDP43OverallPresInd, CORE). If "Yes," proceed to next question to indicate antibodies/regions. If "No, Not Assessed, or Unknown," skip to next section on Microhemorrhages.

○ Yes ○ No ○ Not assessed ○ Unknown

6.1. TDP-43 antibody:

phospho-specific	non-phospho specific	other, specify

6.2. Evaluation of neuronal or glial TDP-43 (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Hippocampus (If yes > Supp Y/N for subdivisions)

Users may remove non-core questions. Users are NOT allowed to insert/delete permissible values of existing questions. The variable name in FITBIR is indicated in parentheses: existing FITBIR CDEs are in default black font; new FITBIR CDEs are in blue; NINDS CDEs are in green.

Entorhinal cortex	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Amygdala
Midbrain including substantia nigra	Pons including locus coeruleus
Medulla including dorsal motor nucleus of vagus	*Superior frontal gyrus with depth of sulcus
*Hypothalamus including mammillary body	*Temporal pole with depth of sulcus

MICROHEMORRHAGES

7. Indication of presence of Microhemorrhages (acute or chronic) in any of the examined regions (CORE) (new FITBIR CDE BrainMicroHemOvrPresInd, CORE). If "Yes," proceed to next question to address acute and chronic questions. If "No, Not Assessed, or Unknown," skip to next section on white matter pathology.

○ Yes ○ No ○ Not assessed ○ Unknown

7.1. Indication of presence of acute microhemorrhages in any of the examined sections (new FITBIR CDE BrainMicrHemAcutPresInd, CORE). If "Yes," proceed to next question to indicate stain/regions. If "No, Not Assessed, or Unknown," go chronic microhemorrhages.

○ Yes ○ No ○ Not assessed ○ Unknown

7.1.1.Histochemical stain type (recommended from new FITBIR CDE NeuropathROIStainTyp, CORE)

H and E	H and E/Luxol Fast Blue	Other, specify (use NeuropathROIStainOTH)

7.1.2. Evaluation of acute microhemorrhages (Y/N/NA/Unknown) in core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Pons including locus coeruleus

7.2. Indication of presence of chronic microhemorrhages in any of the examined regions (CONDITIONAL CORE) (new FITBIR CDE BrainMicrHemChrnPresInd, CORE). If "Yes," proceed to next question to indicate regions. If "No, Not Assessed, or Unknown," skip to next section on White Matter Pathology.

○ Yes ○ No ○ Not assessed ○ Unknown

7.2.1. Histochemical stain type (recommended from new FITBIR CDE NeuropathROIStainTyp, CORE)

H and E	H and E/Luxol Fast Blue	Other, specify

Users may remove non-core questions. Users are NOT allowed to insert/delete permissible values of existing questions. The variable name in FITBIR is indicated in parentheses: existing FITBIR CDEs are in default black font; new FITBIR CDEs are in blue; NINDS CDEs are in green.

7.2.2. Evaluation of chronic microhemorrhages (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Pons including locus coeruleus

WHITE MATTER PATHOLOGY

8. Indication of presence of White matter pathology in any of the examined regions (new FITBIR CDE BrainWMPathOvrlPresInd, CORE). If yes, continue to next question. If no, proceed to next section on Microvascular Disease.

○ Yes ○ No ○ Not assessed ○ Unknown

8.1. Indication of presence of White matter rarefaction/pallor in any of the examined regions (new FITBIR CDE BrainWMROverallPresInd, CORE). If "Yes," proceed to next question to indicate regions. If "No, Not Assessed, or Unknown," skip to next section.

○ Yes ○ No ○ Not assessed ○ Unknown

8.1.1. Stain type (recommended from new FITBIR CDE NeuropathROIStainTyp, CORE)

H and E	H and E/Luxol Fast Blue	Other, specify (use NeuropathROIStainOTH)

8.1.2. Evaluation of white matter rarefaction/pallor (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	

8.2. Indication of presence of Macrophage infiltration, perivascular, in any of the examined regions (new FITBIR CDE BrainMcphgInfOvrPresInd, CORE). If "Yes," proceed to next question to indicate regions. If "No, Not Assessed, or Unknown," skip to Spheroids (optional) or next section on Microvascular Disease (required).

○ Yes ○ No ○ Not assessed ○ Unknown

8.2.1. Stain type (recommended from new FITBIR CDE NeuropathROIStainTyp, CORE)

H and E	H and E/Luxol Fast Blue	Other, specify

8.2.2 Evaluation of macrophage infiltration, perivascular (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	

8.3. Assessment of Supplemental highly recommended features for white matter pathology. Select the type of observed feature (new FITBIR CDE NeuropthPthFeatWMSupTyp, SUPPHIGHREC). These may be assessed for any core or supplemental region using new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp, and NeuropathROITBISuppTyp. Where relevant, use NeuropathROIStainTyp to indicate the stain or antibody used for specific assessment.

Spheroids	*Other, specify (using new FITBIR CDE NeuropathPathFeatTypOTH)*

MICROVASCULAR DISEASE

9. Indication of presence of microvascular disease in any of the examined regions (new FITBIR CDE BrainMVDOverallPresInd, CORE). If "Yes," proceed to next question to indicate stains/regions. If "No, Not Assessed, or Unknown," skip to next section.

○ Yes ○ No ○ Not assessed ○ Unknown

9.1. Stain type (recommended from new FITBIR CDE NeuropathROIStainTyp, CORE)

H and E	H and E/Luxol Fast Blue	Iron	Other, specify (use NeuropathROIStainOTH)

9.2 Evaluation of microvascular disease (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Pons including locus coeruleus
Cerebellar cortex including dentate nucleus	

9.3. Indication of presence of Chronic microinfarcts in any of the examined regions? (new FITBIR CDE BrainMInfChrnOvrPresInd, CORE). If "Yes," proceed to next question to indicate regions. If "No, Not Assessed, or Unknown," skip to next section on hypoxic/ischemic change.

○ Yes ○ No ○ Not assessed ○ Unknown

9.3.1. Evaluation of chronic microinfarcts (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Pons including locus coeruleus
Cerebellar cortex including dentate nucleus	

9.4. Indication of presence of Arteriolosclerosis in any of the examined regions (new FITBIR CDE BrainArtiolscOvrPresInd, CORE). If "Yes," proceed to next question to indicate regions. If "No, Not Assessed, or Unknown," skip to next section on hypoxic/ischemic change.

○ Yes ○ No ○ Not assessed ○ Unknown

9.4.1. Evaluation of arteriolosclerosis (Y/N/NA/Unknown) for core brain regions (new FITBIR CDEs BrainMicroscPathTBIInd, NeuropathROITBICoreTyp). If additional regions were assessed, enter these using other values of NeuropathROITBICoreTyp or NeuropathROITBISuppTyp before proceeding to the next question.

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Pons including locus coeruleus
Cerebellar cortex including dentate nucleus	

ACUTE HYPOXIC / ISCHEMIC CHANGE

10. Indication of presence of Acute Hypoxic/Ischemic Change in any of the examined regions (new FITBIR CDE BrainIschmChgOvrPresInd, CORE). Only the synopsis answer is required; regional evaluations are optional and may be entered by specifying regions using NeuropathROITBICoreTyp or NeuropathROITBISuppTyp. If "Yes" to presence in any region, proceed to next question to indicate stain.

○ Yes ○ No ○ Not assessed ○ Unknown

10.1. Stain type (recommended from NeuropathROIStainTyp)

H and E	H and E/Luxol Fast Blue	Other, specify (use NeuropathROIStainOTH)

End of microscopic section

DIAGNOSIS

Classification for CORE/SUPPLEMENTAL HIGHLY RECOMMENDED/SUPPLEMENTAL is indicated in parentheses, *by section*.

TAU PROTEINOPATHY (SECTION IS CORE)

1. CTE neuropathologic change (from 1st and 2nd consensus papers) (NeuropathCTEChangeInd, New FITBIR CDE)
   - ○ Yes ○ No ○ Suggested features not sufficient for diagnosis ○ Not assessed ○ Missing/Unknown

2. CTE neuropathologic stage (from 2nd consensus paper) (NeuropathCTEStageTyp, New FITBIR CDE)
   - ○ Low ○ High

3. Other tau proteinopathy? (TaupthyDegenOtherInd, New FITBIR CDE). Choose one.
   - ○ Yes ○ No ○ Not assessed ○ Missing/Unknown

4. Tau proteinopathy type:

Type of FTLD-tau or other tau proteinopathy (TaupthyDisTyp)	Presence (TaupthyProtnpthyPathInd FITBIR CDE)			
	No	Yes	Not assessed	Missing/Unknown
FTLD-tau, Pick's disease (PiD)-3R	o	o	o	o
Other 3R tau proteinopathy (includes *MAPT* tauopathy)	o	o	o	o
Argyrophilic grain disease (AGD)-4R	o	o	o	o
FTLD-tau, Corticobasal degeneration (CBD)-4R	o	o	o	o
FTLD-tau, Progressive Supranuclear Palsy (PSP)-4R	o	o	o	o
FTLD-tau, Globular glial tauopathies (GGT)-4R	o	o	o	o
Aging-related tau astrogliopathy (ARTAG)-4R	o	o	o	o
Other 4R tau proteinopathy (includes *MAPT* tauopathy)	o	o	o	o
Primary age-related tauopathy (PART)-3R+4R	o	o	o	o
ALS/Parkinsonism/Dementia Guam-3R+4R	o	o	o	o
Other 3R + 4R tau proteinopathy (includes *MAPT* tauopathy)	o	o	o	o
Tau immunoreactivity not sufficient to meet diagnostic criteria	o	o	o	o

ALZHEIMER'S DISEASE (SECTION IS CORE)

5. Thal phase for amyloid plaques by immunohistochemistry (A score) (ThalPhaseTyp). Choose one.
   - ○ Phase 0 ○ Phase 1 ○ Phase 2 ○ Phase 3 ○ Phase 4 ○ Phase 5 ○ N/A ○ Unknown

6. Braak stage for neurofibrillary degeneration (AtrBraakNeurfibStageTyp). Choose one. If 'Unknown,' optional additional text can be supplied using BraakStageTextOTH, new FITBIR CDE.
   - ○ Not assessed
   - ○ Unknown
   - ○ Stage II (B2)
   - ○ Stage III (B3)
   - ○ Stage IV (B4)
   - ○ Stage V (B5)
   - ○ Stage VI (B6
   - ○ Tauopathy other than AD precludes staging

Users may remove non-core questions. Users are NOT allowed to insert/delete permissible values of existing questions. The variable name in FITBIR is indicated in parentheses: existing FITBIR CDEs are in default black font; new FITBIR CDEs are in blue; NINDS CDEs are in green.

7. CERAD score for density of neuritic plaques (C score) (CERADNeuritcPlqDenScore). Choose one.
   - ○ No neuritic plaques (C0)
   - ○ Sparse neuritic plaques (C1)
   - ○ Moderate neuritic plaques (C2)
   - ○ Frequent neuritic plaques (C3)
   - ○ Not assessed
   - ○ Unknown

8. CERAD score for density of diffuse plaques (CERADDiffPlqDenScore). Choose one.
   - ○ No diffuse plaques (C0)
   - ○ Sparse diffuse plaques (C1)
   - ○ Moderate diffuse plaques (C2)
   - ○ Frequent neuritic plaques (C3)
   - ○ Not assessed
   - ○ Unknown

9. NIA-AA Alzheimer's Disease neuropathological change (NPADNC). Choose one.
   - ○ High AD neuropathological change
   - ○ Intermediate AD neuropathological change
   - ○ Low AD neuropathological change
   - ○ Not AD
   - ○ Not assessed
   - ○ Unknown

10. Cerebral amyloid angiopathy (AmyldAngpthySevScl). Choose one.
    - ○ None
    - ○ Moderate
    - ○ Not Assessed
    - ○ Mild
    - ○ Severe
    - ○ Unknown

11. Vessel type for cerebral amyloid angiopathy (CerebrlAmylAngpthVesTypp, NEW FITBIR CDE, SUPPLEMENTAL). Choose one.
    - ○ Capillaries (Type 1)
    - ○ Middle/Large Vessels (Type 2)

MICROVASCULAR DISEASE (SECTION IS CORE)

Old microinfarcts? (MicroinfarctsInd). Choose one (applies to all blocks assessed).
- ○ No
- ○ Yes
- ○ Not assessed

12. Old microbleeds? (MicrobleedsInd). Choose one. If "No", "not assessed", or "Missing/unknown" skip to question on Arteriolosclerosis.
    - ○ No
    - ○ Yes
    - ○ Not assessed
    - ○ Missing/Unknown

13. Old microinfarcts and microhemorrhages/microbleeds?

Anatomic site of old microinfarcts and microbleeds (BrainAbnormFindingsAnatomicSite)	Microinfarct count (MicroinfarctsCt)					Microhemorrhages/microbleeds count (MicrohemorrhagesCt)				
	None	One	Two	Three or more	#	None	One	Two	Three or more	#
Cerebral cortex	o	o	o	o		o	o	o	o	
Subcortical gray matter	o	o	o	o		o	o	o	o	
Subcortical white matter	o	o	o	o		o	o	o	o	
Other, specify (BrainAbnormFindingsAnatomicSiteOTH)	o	o	o	o		o	o	o	o	

14. Arteriolosclerosis? (ArtrScalersisSevScl). Choose one.
    - ○ None
    - ○ Mild
    - ○ Moderate
    - ○ Severe
    - ○ Not assessed
    - ○ Missing/Unknown

15. Other vascular pathology not previously mentioned? (IschHemVasclPathInd). Choose one.
    - ○ Yes
    - ○ No
    - ○ Not assessed
    - ○ Missing/Unknown

16. Other vascular pathology (IschHemVasclPathFindTyp). Select all that apply.
    - o Acute gross hemorrhage
    - o Acute infarcts
    - o Acute microhemorrhage
    - o Acute microinfarcts
    - o Acute neuronal necrosis
    - o Aneurysm
    - o CADASIL
    - o Laminar necrosis
    - o Mineralization of blood vessels
    - o Vascular malformation
    - o Vasculitis
    - o Other, specify(IschHemVascPthFndTypOTH)_____

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SYNUCLEINOPATHY (SECTION IS CORE)

17. Lewy body pathology present (LewyBdyPathlgyInd)? Choose one
    - ○ Yes ○ No ○ Not assessed ○ Unknown

18. Lewy body pathology location (LewyRltdPathAnatSite). Select all that apply.
    - ○ Brainstem predominant ○ Limbic/transitional ○ Neocortical/diffuse ○ Amygdala predominant ○ Olfactory bulb

19. Multiple system atrophy pathology? (NeuropthMulSysAtrphyInd, new FITBIR CDE) Choose one
    - ○ Yes ○ No ○ Not assessed ○ Missing/Unknown

TDP-43 PROTEINOPATHY (SECTION IS CORE)

20. TDP-43 immunoreactive lesions present (TDP43ImmunLesionsInd)? Choose one.
    - ○ Yes ○ None ○ Not assessed ○ Unknown

21. TDP-43 immunoreactive lesions location (TDP43ImmuLesionAnatSite). Select all that apply.
    - ○ Amygdala ○ Entorhinal/inferior temporal cortex ○ Hippocampus ○ Neocortex ○ Spinal Cord

22. FTLD with TDP-43 pathology (TaupthyFTLDTDP43PathInd)? Choose one.
    - ○ Yes ○ No ○ Not assessed ○ Missing/Unknown

23. Limbic-predominant age-related TDP-43 encephalopathy (LATE)? (LATEInd, new FITBIR CDE) Choose one.
    - ○ No ○ Stage 1 (amygdala)
    - ○ Not assessed ○ Stage 2 (hippocampus)
    - ○ Missing/Unknown ○ Stage 3 (isocortex)

24. ALS/MND? (ProteinopathyALSMNDInd, FITBIR CDE). Choose one.
    - ○ Yes, TDP inclusions in motor neurons ○ Yes, FUS inclusions in motor neurons ○ Yes, no specific inclusions in motor neurons ○ No
    - ○ Missing/Unknown ○ Yes, SOD1 inclusions in motor neurons ○ Yes, with other inclusions ○ Not assessed

FTLD-FUS (SECTION IS SUPPLEMENTAL HIGHLY RECOMMENDED)

25. FTLD-FUS pathology. Select all that apply

Type of FUS pathology (FTLDFUSPathologyTyp)	Presence of pathology (FTLDPathologyInd). Choose one			
	No	Yes	Not assessed	Missing/Unknown
○ Atypical FTLD-U	o	o	o	o
○ Neuronal intermediate filament inclusion disease (NiFID)	o	o	o	o
○ Basophilic inclusion body disease (BIBD)	o	o	o	o

26. Other FTLD pathology. Select all that apply.

Type of FUS pathology (FTLDPathologyOTHTyp)	Presence of pathology (FTLDPathologyInd). Choose one			
	No	Yes	Not assessed	Missing/Unknown
○ FTLD-ubiquitin proteasome system (FTLD-UPS)	o	o	o	o
○ FTLD-Not otherwise specified (FTLD-NOS)	o	o	o	o

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27. Other pathological diagnosis, specify (PathologyDiagnosTypOTH)_____
_____
_____

OTHER PATHOLOGIC DIAGNOSES (SECTION IS SUPPLEMENTAL)

28. Other pathologic diagnoses. Select all that apply.

Type of other pathologic diagnoses (PathologyDiagnosTyp). Select all that apply.	Presence of other pathologic diagnoses (PathologyDiagnosInd). Choose one. Skip remaining questions if "No", "Not assessed" or "Missing/unknown" is selected.			
	No	Yes	Not assessed	Missing/Unknown
o AD-related genes, dominant	o	o	o	o
o Contusion/TBI, acute	o	o	o	o
o Contusion/TBI, chronic	o	o	o	o
o FTLD-related genes, dominant	o	o	o	o
o Herniation	o	o	o	o
o Infection	o	o	o	o
o Malformation of cortical development	o	o	o	o
o Metabolic/storage disorder	o	o	o	o
o Neoplasm, primary	o	o	o	o
o Neoplasm, metastatic	o	o	o	o
o Pigment spheroid degeneration	o	o	o	o
o Prion disease	o	o	o	o
o Trinucleotide repeat disease	o	o	o	o
o Trisomy 21	o	o	o	o
o WM disease, leukodystrophy	o	o	o	o
o WM disease, multiple sclerosis or other demyelinating	o	o	o	o

29. Other pathological diagnosis not listed #1, specify (BrainPathDiagTypOTH)_____
_____
_____
_____
_____

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Primary references

- McKee AC, Cairns NH, Dickson DW, Folkerth RD, Keene CD, Litvan I, Perl DP, Stein TD, Vonsattel J-P, Stewart W, Tripodis T, Crary JF, Bieniek KF, Dams-O'Connor K, Alvarez VE, Gordon WA, TBI/CTE group. The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy. *Acta Neuropathol.* 2016, 131:75-86.
- Bieniek KF, Cairns NH, Crary JF, Dickson DW, Folkerth RD, Keene CD, Litvan I, Perl DP, Stein TD, Vonsattel J-P, Stewart W, Dams-O'Connor K, Gordon WA, Tripodis T, Alvarez VE, Mez J, Alosco ML, McKee AC, TBI/CTE Research Group. The Second NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy. J Neuropathol Exp Neurol. 2021, 80(3):210-219.

Appendix 1: List of brain regions that are CORE for gross pathology and for microscopic neuropathologic evaluation. *Indicates area

Middle frontal gyrus with depth of sulcus	Superior and middle temporal gyrus with depth of sulcus
Inferior parietal lobule with depth of sulcus	Hippocampus (If yes > Supp Y/N for subdivisions)
Entorhinal cortex	Cingulate gyrus, anterior
Occipital (calcarine – primary visual) cortex	Basal ganglia at level of nucleus accumbens, with basal nucleus of Meynert
Thalamus at level of subthalamic nucleus	Amygdala
Midbrain including substantia nigra	Pons including locus coeruleus
Medulla including dorsal motor nucleus of vagus	Cerebellar cortex including dentate nucleus
*Superior frontal gyrus with depth of sulcus	*Temporal pole with depth of sulcus
*Hypothalamus including mammillary body	Other, specify

Appendix 2: List of brain regions that are supplemental for gross pathology and for microscopic neuropathologic evaluation. For any regions not presently listed, use the value 'Other, specify' and the accompanying free text CDE NeuropathROITBIOTH to indicate the region assessed.

Supplemental Brain region (NeuropathROITBISuppTyp, NeuropathROITBIOTH ,new FITBIR CDE).
☐ Anterior inferior frontal gyrus
☐ Body of corpus callosum at level of midbrain
☐ Body of corpus callosum with fornix
☐ Frontoinsula
☐ Fusiform/inferior temporal gyrus
☐ Genu of corpus callosum
☐ Hippocampus with parahippocampal sulcus
☐ Hippocampus, CA1
☐ Hippocampus, CA2
☐ Hippocampus, CA3
☐ Hippocampus, CA4
☐ Hippocampus, dentate gyrus
☐ Hippocampus, subiculum
☐ Inferior frontal gyrus – Broca's area
☐ Lateral parieto-occipital cortex
☐ Medial prefrontal cortex and white matter
☐ Middle cerebellar peduncle
☐ Occipital white matter 2 slices posterior to ventricle
☐ Parietal white matter at LGN
☐ Posterior angular gyrus
☐ Posterior cerebellar cortex
☐ Posterior cingulate gyrus at LGN
☐ Posterior superior middle temporal gyrus
☐ Precuneus
☐ Primary motor cortex
☐ Splenium of corpus callosum
☐ Superior cerebellar peduncle with vermis
☐ Supplementary motor cortex
☐ Other, specify (BrainROITypOTH)