

Alzheimer's Disease Neuroimaging Initiative- Neuropathology Core (ADNI-NPC)

Brain Donation and Neuropathology Manual

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Introduction and ADNI-NPC Specific Aims

The Alzheimer's Disease Neuroimaging Initiative (ADNI; U01AG024904, Michael W. Weiner, PI) has as its overarching goal the development of surrogate imaging markers for the clinical progression of mild cognitive impairment (MCI) and early-stage Alzheimer's disease (AD). In pursuit of this goal, ADNI will conduct serial neuroimaging studies over 2-3 years in individuals with mild cognitive impairment (n=400), aged 55-90 years, in comparison with similarly aged non-demented individuals (n=200) and individuals with mild Alzheimer's disease (n=200) at ~50 ADNI sites. The funding period for ADNI is 9/30/04-8/31/09. Three major specific aims will be addressed by ADNI: 1) to develop uniform standards for acquiring longitudinal magnetic resonance imaging (MRI) and positron emission tomography (PET) data and, in a subset of the ADNI sample, a cerebrospinal fluid biomarker profile for MCI, AD, and non-demented aging; 2) determine those imaging methods that provide maximum power to distinguish treatment effects in trials of individuals with MCI and early-stage AD; and 3) create an accessible data repository that describes longitudinal changes in brain structure and metabolism and provides clinical, cognitive, and biomarker data to validate the imaging surrogates.

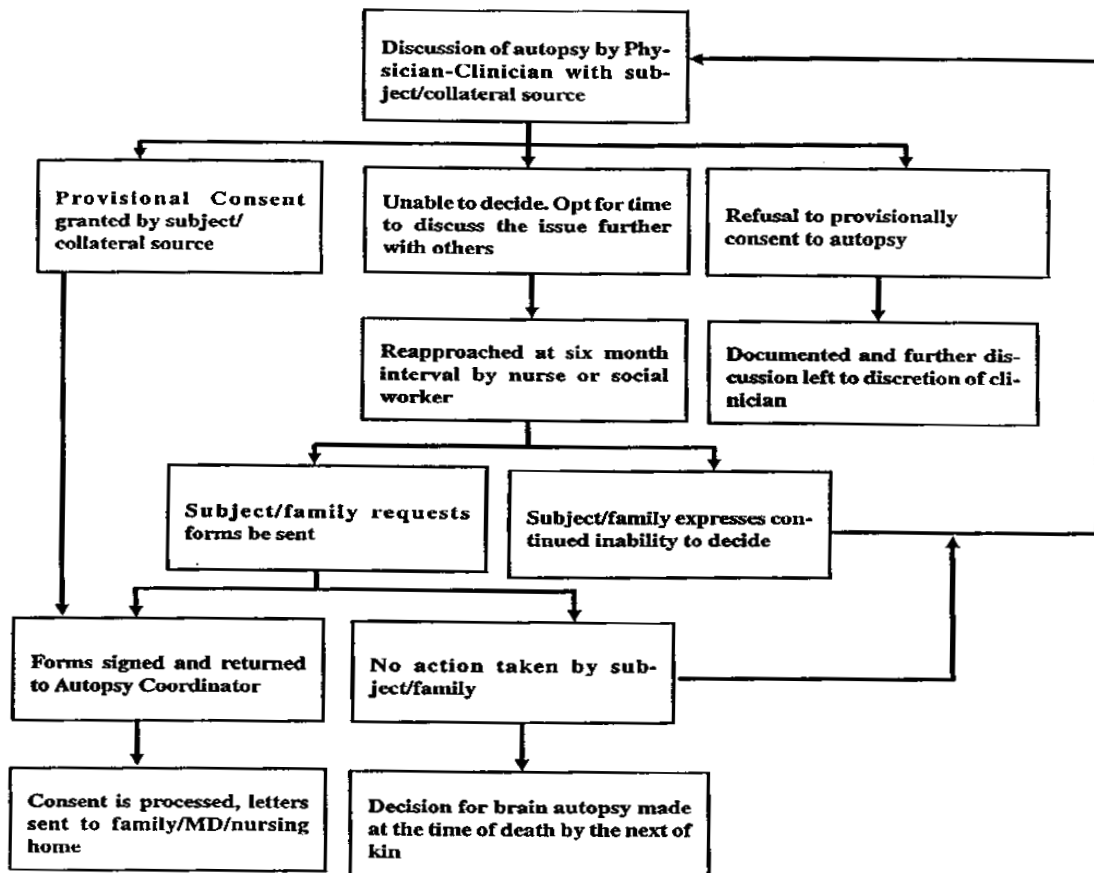
The **ADNI Neuropathology Core** (ADNI-NPC) is an extension of the ADNI specific aims in that it will provide the "gold standard" validation of the clinical diagnoses and imaging surrogates through neuropathological examination of ADNI participants who come to autopsy. The Specific Aims of ADNI-NPC are to:

1. Provide and implement training materials and protocols to assist clinicians at ADNI sites in obtaining voluntary consent for brain autopsy in ADNI participants;
2. Establish a central laboratory to provide uniform neuropathological assessments of all autopsied ADNI participants in accordance with standard criteria and to promote clinical-neuroimaging-neuropathological correlations;
3. Maintain a state-of-the-art resource for fixed and frozen brain tissue obtained from autopsied ADNI participants to support ADNI's biomarker studies (John Q. Trojanowski, Biomarker Core Leader) and develop a process wherein investigators may have access to the tissue and data for research purposes; and
4. Interact with ADNI's Data Coordinating Center (Ron Thomas, Leader) to ensure appropriate entry of the Core's data into ADNI's database, promote data sharing and collaborative research, and integrate the ADNI-NPC with all ADNI components to support its administration, operations, and progress toward goals.

Guidelines for Obtaining Autopsy Consent

An ADNI clinician will lead a discussion about autopsy with all participants (demented and non-demented) at their initial assessment (study partners and families are welcomed in the discussion and required for AD participants). There are 3 objectives of the discussion: 1) to convey information about the value of brain autopsy in confirming the clinical diagnosis and advancing knowledge regarding MCI and AD; 2) to initiate consideration of the individual's wishes concerning an autopsy; and 3) to answer questions, misconceptions, or concerns about autopsy. The involvement of the physician in these discussions emphasizes the importance of autopsy. The discussions are repeated on an annual basis, both to ensure the participant's wishes regarding brain donation are carried out and that family members and/or participant's Durable Power of Attorney (DPOA) are aware of the participant's wishes. There is no pressure on an individual to decide; they are encouraged to involve family members, clergy, physicians, or other appropriate persons in their decision-making. Participants are assured that a decision not to have autopsy in no way jeopardizes their research participation or any other patient rights.

When voluntary consent is granted, more detailed information is provided about procedures to follow at time of death, including telephone numbers to call and other guidelines (sample forms available in manual appendix and on line). Participants are strongly encouraged to share this information with next-of-kin, legally authorized representatives (e.g. DPOA), and private physicians. In many states, final legal authorization by the DPOA or next-of-kin must be obtained at the time of death. As ADNI is a multi-center study involving sites in the US and Canada, please be sure to follow state and local laws regarding autopsy consent procedures.



Autopsy Consent Protocol

Each ADNI site is encouraged to establish an autopsy coordinator (typically a research nurse or coordinator) who processes the autopsy consent, provides information as needed, and monitors the need to update any information (e.g., change in residence) at the ADNI participant's longitudinal assessments. The coordinator also will develop procedures for that site to facilitate autopsies outside of usual hours (e.g., evenings and weekends). The actual procedures are expected to vary in accordance with local needs and resources (one model used by many Alzheimer's Disease Centers is to provide 24-hour telephone access).

At the time of death, the autopsy coordinator (or a suitable representative) facilitates arrangements to ensure the completion of the autopsy. The coordinator notifies the ADNI-NPC, which in turn verifies that the site neuropathologist has the dissection protocol and necessary materials to send the requisite tissue to the ADNI-NPC.

The ADNI-NPC, in addition to instructing site personnel at each ADNI Steering Committee Meeting in these procedures, will be available at any time to answer questions. Contact information, including a 24-hour pager, for ADNI-NPC personnel is listed on page 3. ADNI sites that already have ADRC/ADC Neuropathology Services will continue to follow their own existing protocols. For ADNI sites that do not have established neuropathology services, reasonable costs related to brain donation such as transportation costs from point of death to the autopsy suite, costs of the autopsy procedure, and shipment of materials are covered by the ADNI-NPC so that the decedent's family and the individual ADNI site do not incur extra expense.

Acknowledgement of Autopsy Authorization

Once the Participant has given consent (provisional or otherwise) the Acknowledgement of Autopsy Authorization letter and wallet cards (see appendix) should be sent to the following persons:

1. Participant and/or family and/or applicable other (e.g., Durable Power of Attorney)
2. Nursing home (include chart cover sheet)
3. Funeral home/transport service (as requested)
4. Private Physician (as requested)

Autopsy Costs to Family

The ADNI-Neuropathology Core (ADNI-NPC) will cover brain autopsy costs, with the following limitations:

1. ADNI sites **with** existing ADRC/ADC neuropathology arrangements in place for handling ADNI Participant brain donations will continue to make their own arrangements for brain autopsies.
2. ADNI sites **with no** arrangements in place for handling ADNI Participant brain donations:
 - a. Local transportation costs will be paid by ADNI-NPC if arrangements are set-up by ADNI-NPC (see the Out-of-Town Arrangements list); if not, ADNI-NPC will pay up to \$200 unless the charges are approved (see last paragraph).
 - b. Brain removal performed out-of-state or out of local area: Transportation costs will be paid by ADNI-NPC if arrangements are set-up by ADNI-NPC. Transportation costs will be limited to \$500. Any costs for transportation above \$500 will be incurred by the deceased's estate. The additional costs are to be communicated to the participant or his/ her next-of-kin prior to transport. Brain removal costs will be paid by ADNI-NPC if arrangements are arranged by ADNI-NPC. Brain removal costs will be limited to \$500. Any costs for brain removal above \$500 will be incurred by the deceased's estate. Again, the additional costs are to be communicated to the participant or his/her next-of- kin prior to brain removal. Brain shipping expenses will be paid by ADNI-NPC. There are a few cases in rural areas where a local funeral home may transport the body to the nearest ADRC/ADC with Neuropathology Services for brain removal. In these cases, the total cost for transport to the center may be less than the cost of transport to a private pathologist (\$200) and the pathologist's fees (\$500). This is generally reasonable as long as the total cost is less than \$700.

Death certificates and related paperwork and transport to funeral home or body donor programs post-autopsy are not covered by ADNI-NPC.

Exceptions: Any exceptions to the above costs should be approved by the Director or Co-Director of the local ADC/ADRC or ADNI-NPC. However, if a death occurs after regular business hours or if the Director or Assistant Director of ADNI-NPC is not in the office, the radiopager carrier is empowered to allow charges of up to \$1000 (for transportation and brain removal) if the expenses seem justified. As a rule, we do not have the funds to pay this much and so this cost should be for the extreme exception. Please inform the transporter/ pathologist that ADNI-NPC is a research study with limited funds and suggest a cost reduction. If the expenses are above \$1000, please attempt to contact the ADNI-NPC Director or Co-Director at home for permission to proceed. If you are unable to reach them, you are empowered to decide based on the importance of the case. In all cases of additional expense, the next-of-kin should be notified of this and allowed to determine if they wish to proceed.

ADNI-NPC Neuropathology Protocols

Where possible, each center will undertake its own brain assessment and forward a standard set of fixed tissue blocks or sections and frozen tissue to ADNI-NPC (see below). For sites that do not routinely undertake neuropathologic studies, a separate brain removal protocol is listed in the Appendix.

Financial Assistance with Block Sampling, Preservation, and Shipping Costs

The ADNI-NPC will fund all costs in shipping frozen and fixed tissue samples to St. Louis. To assist participating centers and neuropathologists with the costs of obtaining frozen tissue blocks and/or formalin-fixed paraffin wax-embedded tissue the following costs will be reimbursed, if requested:

1. Harvesting of frozen tissue and/or formalin-fixed paraffin wax-embedded tissue blocks (*see list of brain regions below) \$300.
2. Harvesting formalin-fixed paraffin wax-embedded tissue sections or frozen sections (*see list of brain regions below) \$100.

***ADNI-NPC Block Sampling**

Resources to defray the costs of sampling, tissue, processing, administration, and transport will be made available to each center already undertaking neuropathology. These resources are to facilitate the provision of the standard set of blocks for ADNI-NPC. To minimize the burden on participating centers, formalin-fixed, paraffin wax-embedded tissue blocks from the following 16 areas from the left cerebrum will be forwarded to ADNI-NPC:

1. Middle frontal gyrus
2. Superior and middle temporal gyri
3. Inferior parietal lobe (angular gyrus)
4. Occipital lobe to include the calcarine sulcus and peristriate cortex
5. Anterior cingulate gyrus at the level of the genu of the corpus callosum
6. Posterior cingulate gyrus and precuneus at the level of the splenium
7. Amygdala and entorhinal cortex
8. Hippocampus and parahippocampal gyrus at the level of the lateral geniculate nucleus
9. Striatum (caudate nucleus and putamen) at the level of the anterior commissure
10. Lentiform nuclei (globus pallidus and putamen)
11. Thalamus and subthalamic nucleus
12. Midbrain
13. Pons
14. Medulla oblongata
15. Cerebellum with dentate nucleus
16. Spinal cord

In the unusual situation where it is impractical to forward a tissue block (e.g., if the block is used for stereology), 10 paraffin wax sections (4-8 μm) from each block will be provided to ADNI-NPC for systematic neuropathology and diagnosis.

Frozen Tissue

To provide tissue for biochemical studies and to advance the aims of the Biomarkers Study, snap frozen tissue will be dissected, frozen, and sent to ADNI-NPC. The following coronal hemibrain slices (0.5 to 1cm thick), where possible, will be taken:

1. Frontal lobe to include striatum;
2. Frontal and temporal lobe at the level of the mamillary body;
3. Temporal and parietal lobes at the level of the lateral geniculate nucleus;
4. Occipital lobe to include the calcarine sulcus.

Histology

In all cases, the following stains will be performed at the ADNI-NPC lab on the blocks indicated above, and/or as requested by the neuropathologist: hematoxylin and eosin and a modified Bielschowsky silver impregnation. Routine immunohistochemistry will be performed using the following antibodies: ubiquitin (Dako), tau (PHF1 and/or AT8), β -amyloid (4G8 and/or 10D5), and α -synuclein (LB509). In cases with ubiquitin-positive inclusions, the following additional IHC will be performed: TDP-43, α -internexin or phosphorylated neurofilament (SMI 31).

Histology Review

Dr. Cairns reviews the histological slides in a systematic manner. The data are entered into the National Alzheimer's Coordinating Center (NACC) Neuropathology Data Form and transmitted by Dr. Grant (Biostatistics Core) to the ADNI Coordinating Center. The final neuropathologic diagnosis and neuropathologic report will be forwarded to ADNI for entry into the central database and to the center that made available the tissue.

Neuropathologic Assessment and Diagnostic Criteria

The operational criteria for the classification of AD and other pathologies defined by NACC will be applied to all ADNI-NPC cases (and are currently applied to all WU ADRC cases). The neuropathologic diagnosis will be determined by Dr. Cairns and Dr. Robert Schmidt (Division of Neuropathology, WUSTL) using consensus neuropathologic criteria for AD, and for non-AD disorders. The NACC Neuropathology Form includes an entry for the diagnosis of AD by each of the 3 sets of criteria: CERAD, NIA-Reagan, and Khachaturian. ADNI-NPC cases thus will be diagnosed in accordance with each of these sets of criteria, as no consensus currently exists in favor of one set in relation to the others (particularly for the incipient stages of AD addressed by the ADNI study). This will allow investigators maximal utility in applying the neuropathological diagnoses most appropriate to their research aims.

Procedures for Accessing Autopsy Data and Tissue from the ADNI Neuropathology Core

Data Data generated by the ADNI-NPC will be transmitted securely to the ADNI Coordinating Center for storage, management and distribution according to the ADNI procedures. These de-identified data will be available with the relevant clinical, biological and imaging data on the Coordinating Center's public access web site.

Tissue The process by which investigators request access to ADNI-NPC tissue is based on the established and successful procedures in place at the WU ADRC. Qualified investigators will initiate requests for ADNI autopsy material by providing basic information (including a 3 page research summary and NIH biosketch) about their research project to the ADNI-NPC Tissue Committee (see below). The instructions and forms are web-based (www.alzheimer.wustl.edu/adrc2/ResourcesDB/Intro.asp) for easy access. Prospective investigators will be encouraged to consult with Drs. Morris and Cairns. Written reviews of the request from at least 2 members of the ADNI-NPC Tissue Committee, chaired by Dr. Cairns, or other experts recruited for a particular protocol will be provided for discussion and approval by email vote of the Tissue Committee conducted monthly or as requests dictate. The Tissue Committee will forward its recommendations to the ADNI Executive Committee (see below) for final approval. The criteria used by reviewers will be: scientific merit, feasibility, appropriateness of principal investigator qualifications, burden on ADNI samples, and appropriateness to ADNI goals/themes.

ADNI Neuropathology Core Tissue Committee

John Morris, Washington University School of Medicine
 Nigel Cairns, Washington University SOM
 Eileen Bigio, Northwestern University
 Dennis Dickson, Mayo Clinic, Jacksonville
 John Trojanowski, University of Pennsylvania

ADNI Executive Committee

Michael Weiner, UC San Francisco/SFVAMC
 Arthur Toga, UC Los Angeles
 Laurel Beckett, UC Davis
 William Jagust, UC Berkeley
 John Trojanowski, University of Pennsylvania
 Ron Thomas, UC San Diego
 Clifford Jack, Mayo Clinic
 Peter Snyder, Industry (Pfizer)
 Ron Petersen, Mayo Clinic

Case selection for approved tissue requests will be achieved through discussion with the requesting investigator, the ADNI-NPC staff, and the ADNI Coordinating Center. All samples leaving Washington University are de-identified by use of a code (generated for shipment only) and with the execution of a Limited Data Use Agreement (See Appendix). Upon shipment, a final list of samples shipped is shared with the ADNI Coordinating Center for purposes of reporting and tracking the transfer.

In return for the use of ADNI autopsy tissue, we ask the following of investigators: acknowledgment of the ADNI grant number in publications and presentations, productivity reports on publications or funding that were derived from the project, and no third-party sharing without notification. We do not charge for sharing materials/data unless the request requires effort beyond what can be subsumed under normal ADNI-NPC budgeted effort (as recommended by NIA). If the request justifies a charge, the cost is kept to a minimum and based on actual expenses (effort and materials).

Frequently Asked Questions

- 1. Who may give consent?** Order of Next-of-Kin: Durable Power of Attorney (DPOA), surviving spouse, any child, any parent, any brother or sister, any relative by marriage, and any friend, or according to state law. If one child (or other relative) is for autopsy and one is opposed, instruct them that all must come to agreement before we can proceed with autopsy.
- 2. Who will cover the transportation and brain removal costs for ADNI participants?** For ADNI sites that do not have established neuropathology services, transportation costs from point of death to the autopsy suite, costs of the autopsy procedure, and shipment of materials are covered by the ADNI-NPC so that the decedent's family and the individual ADNI site do not incur extra expense.
- 3. Who will cover the extra expenses incurred in my lab from the additional work required to fulfill the ADNI-NPC protocols?** Resources to defray the costs of sampling, tissue, processing, administration, and transport will be made available to each center already undertaking neuropathology. These resources are to facilitate the provision of the standard set of blocks for ADNI-NPC.
- 4. What if a participant expires in the middle of the night? When should the autopsy be performed?** While it is important that the brain be removed as soon as possible after death, for participants that expire outside of normal business hours the brain removal can be performed the following morning. For sites that currently undertake Neuropathology, please follow the established after hours procedures.
- 5. Whom should I contact if I need assistance at night or on the weekend?** The ADNI-NPC Coordinator is available by pager at +1-314-841-4738 should you need emergency assistance.

Appendix

Brain Removal Protocol for Sites
WITHOUT
Neuropathology Resources

Arranging Autopsy Service for Sites Without Neuropathology Resources

Please note, these procedures should be used to identify a person and location where a brain removal can be performed for ADNI sites that do not currently undertake neuropathology. These arrangements should be made in advance with the assistance of the ADNI-NPC Coordinator.

1. Contact Participant or informant/collateral source to clarify autopsy procedure. Obtain information about the closest hospital and the funeral home they plan to use at the time of death.
2. Contact the closest hospital and request to speak to Pathology (autopsy). Inquire with the Pathology Department staff, the availability of a pathologist to perform brain removal. If they do not have one on staff, inquire as to whom they utilize when autopsies are needed.
 - If there is a local ADC/ADRC, contact their autopsy coordinator to make arrangements for autopsy.
 - If you remain unable to find someone, contact the funeral home for any suggestions they may have.
 - Look up neurologists in the area in the Membership Directories of the American Academy of Neurology or the American Association of Neuropathologists and ask them for suggestions.
 - Contact the local Alzheimer's Association for any recommendations they may have regarding local autopsy services.
 - Consider other hospitals, medical schools, and the local coroner or medical examiner.
3. Once a named pathologist is identified, contact the participant's funeral home and make preliminary arrangements for transportation to the autopsy location at time of death. Obtain a preliminary cost for these services. Discuss any atypical cost with the ADC/ADRC/ADNI-NPC Director or Co-Director.
4. Fax, mail, and/or email a copy of the Autopsy Brain Protocol to the out-of-town Pathologist. Answer any questions they may have or refer them to Dr. Cairns at ADNI-NPC.
5. Inquire as to the cost for the Pathologist's services. Remind them we are a research study and have limited funds.
6. Place the name and contact information in the Pathologist List for future reference (optional).

Please contact the ADNI-NPC Coordinator should you need assistance in arranging for autopsy/brain removal for ADNI participants.

Autopsy Procedures (to be carried out by site ADNI coordinator at time of death)

1. Notify the ADNI-NPC Core of the death of the ADNI participant.
2. Contact family or informant/collateral source to clarify autopsy procedure. Obtain information about the funeral home they plan to use.
3. Contact the pathologist or technician who has agreed to perform the brain removal. These arrangements should be made in advance with the assistance of the ADNI-NPC Coordinator. If arrangements have not been made in advance or you are unaware of the arrangements, contact the ADNI-NPC Coordinator.
4. Ensure that the pathologist or person performing the brain removal has a copy of the ADNI-NPC Brain Removal Protocol. This should also be supplied in advance; however, copies are available in the document repository on the ADNI website (<https://adni.ucsd.edu/dav/>) for download.
5. Schedule the brain removal in accordance with the pathologist's schedule. While it is important that the brain removal take place as soon as possible after death, participants that expire outside of normal business hours (i.e. overnight) can have the brain removed the following morning.
6. Once the pathologist and brain removal location have been identified, contact the participant's funeral home and make arrangements for transportation to and from the autopsy location. Obtain a preliminary cost for these procedures. Discuss any atypical costs with the ADC/ADRC/ADNI-NPC Director or Co-Director.
7. After brain removal, the pathologist should ship the fixed and frozen brain tissue to the ADNI-NPC following the Brain Removal Protocol (see below).
8. The ADNI-NPC Coordinator will follow up with the pathologist to ensure that the tissue is shipped and received at the ADNI-NPC lab.
9. The ADNI-NPC will send letters of thanks to the participant's family and the pathologist after the brain removal is completed.
10. Final Neuropathology reports will be available from the Neuropathology Core in 3 to 6 months after the brain removal. It is left to the ADNI Clinician's discretion to obtain the Neuropathology reports and share the findings with the participant's family/DPOA.

ADNI Neuropathology Core Brain Removal and Shipping Protocol

Thank you for helping with the donation of this brain. Your contribution will help us to find the causes, and more effective treatment, of neurodegenerative diseases.

1. Weigh the brain fresh with the dura removed. Record the weight and the time interval between death and removal of the brain and freezing of brain specimens.
2. Separate the cerebrum from the brainstem and cerebellum by a cut through the midbrain. Separate the two cerebral hemispheres and brainstem by midline cuts. Place the **RIGHT** hemisphere (medial surface face down) on aluminum foil on a pre-cooled metal plate/tray (e.g. brass, aluminum), on dry ice, if available. If no dry ice is available, freeze hemisphere by placing on foil on a tray or plate in freezer (at below -20°C, -70°C is better). The right half brainstem and cerebellum should be frozen with the medial (cut) surface flat to the plate. Once frozen, remove aluminum foil and place: (1) the right hemibrain and (2) the right brainstem and cerebellum in labeled zip-lock plastic bags. Ship frozen tissue in container with dry ice.
3. Place the **LEFT** half-brain, -brainstem and -cerebellum in 10% neutral buffered formalin for at least two weeks prior to shipping to St. Louis. For shipping, wrap brain in tissues/cloth soaked in formalin to provide physical support in transit. Place in sealed plastic bag. Place in rigid watertight container and in a rigid outer container for transport. **DO NOT TRANSPORT FROZEN AND FIXED BRAIN IN THE SAME CONTAINER**, use separate containers for frozen and fixed material.

If you have any queries with this protocol please contact:

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ADNI-NPC Neuropathology Protocols

ADNI-NPC Tissue Harvesting from Centers that DO NOT Perform Neuropathology

For those centers that DO NOT currently undertake neuropathology, and do not plan to do so during the period of this project, ADNI-NPC will assist in arrangements in consultation with the local center to harvest the brain and to ship tissue to ADNI-NPC where a systematic neuropathological evaluation will be performed which will include the following:

Tissue Processing

Routine sampling for histology includes taking blocks from the LEFT brain hemisphere which are fixed in neutral buffered (10%) formalin (NBF), or similar. All remaining tissue is preserved until the neuropathological assessment is complete and a report has been issued. The ADNI Neuropathology Core currently samples multiple sites for neuropathologic diagnosis and research needs: olfactory bulbs, middle frontal gyrus, orbitofrontal cortex, olfactory cortex, anterior cingulate gyrus, caudate nucleus and putamen at the level of the nucleus accumbens, anterior commissure and nucleus basalis of Meynert, lentiform nucleus (globus pallidus, putamen), superior and middle temporal gyri, inferior temporal gyrus, amygdala, hippocampus pes to include entorhinal cortex, hippocampus at level of lateral geniculate nucleus, hypothalamus, thalamus and subthalamic nucleus, precentral gyrus, postcentral gyrus, inferior parietal lobe (angular gyrus), posterior cingulate gyrus and precuneus, occipital lobe (calcarine sulcus), posterior inferior frontal gyrus (Broca's area), posterior superior temporal gyrus (Wernicke's area), midbrain, pons, medulla oblongata, cerebellum with dentate nucleus, vermis, and spinal cord from all dementia cases and cervical, thoracic, lumbar and sacral spinal cord from all FTLD and movement disorder cases, when possible. Any additional pathology or abnormality is also sampled. In addition, thick blocks (~7mm) are taken from the frontal lobe, temporal lobe, hippocampus, striatum, and pons, and fixed in formalin for tissue microarray experiments. The RIGHT hemibrain is stored at -80°C for biochemistry and use by the Biomarkers Core.

Histology

In all cases, the following histology is performed on the blocks indicated above, or as requested by the neuropathologist: hematoxylin and eosin and a modified Bielschowsky silver impregnation. Routine immunohistochemistry will be performed using the following antibodies: ubiquitin (Dako), tau (PHF1 and/or AT8), β -amyloid (4G8 and/or 10D5), and α -synuclein (LB509). In cases with ubiquitin-positive inclusions, the following additional IHC will be performed: TDP-43, and α -internexin or phosphorylated neurofilament (SMI31). Prion immunohistochemistry will be performed where indicated.

Histology Review

Dr. Cairns reviews the histological slides in a systematic manner. The data are entered into the NACC Neuropathology Data Form and transmitted by Dr. Grant (Biostatistics Core) to the ADNI Coordinating Center. The final neuropathologic diagnosis and

neuropathologic report will be forwarded to ADNI for entry into the central database and to the center that made available the tissue.

Neuropathologic Assessment and Diagnostic Criteria

The operational criteria for the classification of AD and other pathologies defined by NACC will be applied to all ADNI-NPC cases (and are currently applied to all WU ADRC cases). The neuropathological diagnosis will be determined by Dr. Cairns and Dr Robert Schmidt (Division of Neuropathology, WUSTL) using consensus neuropathologic criteria for AD, and for non-AD disorders. The NACC Neuropathology Form includes an entry for the diagnosis of AD by each of the 3 sets of criteria: CERAD, NIA-Reagan, and Khachaturian. ADNI-NPC cases thus will be diagnosed in accordance with each of these criteria, as no consensus currently exists in favor of one set in relation to the others (particularly for the incipient stages of AD addressed by the ADNI study). This will allow investigators maximal utility in applying the neuropathological diagnoses most appropriate to their research aims.

Sample Forms and Letters

Acknowledgement of Autopsy Authorization Letter-Participant Copy

Date:

Name and Address

Re: Research participant's name

Dear:

Thank you for your continued support of the Alzheimer's Disease Neuroimaging Initiative (ADNI). We very much appreciate your cooperation regarding our brain donation program because it is an extremely important component of our research.

Please share your wishes about brain donation and the details with your family and/or persons who will be taking care of those arrangements. Enclosed are several copies of this letter as well as wallet-sized cards with instructions about how to contact us at the time of death for your/their convenience.

At the time of death our office should be called at **XXX-XXX-XXXX**. If the office is closed, a recorded message instructs the caller to **(Please fill in your site-specific after hours autopsy procedures here)**.

The Alzheimer's Disease Neuroimaging Initiative (ADNI) Coordinator will arrange for the autopsy and transportation of the body to **(insert autopsy location)** where the autopsy takes place. A complete report of the brain autopsy findings will be sent to your Power of Attorney, next of kin, or person you have designated.

Thank you again for participating in our project. If you have additional questions, please feel free to contact the autopsy coordinator at the ADNI office. Please notify us of any changes in your address, telephone number or other contact information.

Sincerely,

(Include signature for Site ADNI Director and/or Autopsy Coordinator with contact information)

Acknowledgement of Autopsy Authorization- Nursing Home Copy

Date:

Attn: Administration
(address)

RE: Subject Name

Dear Administrator:

One of your residents, **Subject Name**, is a participant in the research study program of the Alzheimer's Disease Neuroimaging Initiative (ADNI) at **(insert site location)**. He/She has given consent for a brain autopsy at the time of death.

We greatly appreciate your assistance in the collection of this valuable human tissue to be used in advancing our knowledge about Alzheimer's disease. We have enclosed instructions for this. Please place these instructions in the resident's chart. We are also enclosing a sticker to be placed on the face sheet in order to alert the staff to the family's wishes.

At the time of death, we ask that you fax a copy of the following medical record to our office at **(insert site fax number)**: most recent physician progress note, last two weeks of nursing notes, and the current medication record.

Thank you for your cooperation and interest. Should you have any questions concerning this protocol, please do not hesitate to contact us at **(insert site ADNI coordinator contact number)**.

Sincerely,

(Insert ADNI coordinator signature)

(Place Participant's Name Here)

PROTOCOL FOR PREPARATION FOR BRAIN DONATION

At the time of death, the following steps should be taken after notifying the family members and personal physician of the deceased patient:

1. Contact the Alzheimer's Disease Neuroimaging Initiative (ADNI) Coordinator's office during working hours (**XXX-XXX-XXXX**). If after 5:00 PM or on weekends, (***insert site specific after hours autopsy protocol here***)
2. As soon as possible following death, fill plastic bags with ice and pack them around the head of deceased (to cool it and retard the post-mortem loss of biochemical substances).
3. The Alzheimer's Disease Neuroimaging Initiative (ADNI) Coordinator will arrange for transportation of the body to (***insert autopsy location***) where autopsy will be performed.
4. **IMPORTANT**: If at all possible, the body should reach the mortuary within six hours of death, sooner if possible.

Acknowledgement of Autopsy Authorization Letter- Funeral Home Copy

Date

Funeral home
(address)

Ladies and Gentlemen:

(insert participant's name), a resident at ***(insert location)***, is a participant in the Alzheimer's Disease Neuroimaging Initiative (ADNI) at ***(insert site name/location)***. Consent for a brain autopsy at the time of his/her death has been granted by ***(insert person granting consent)***. Plans have been made to have the autopsy performed by ***(insert pathologist)*** at ***(insert location)***.

(Insert participant's name) family has made the decision to use your funeral home when his/her mother's death occurs. Should you have any questions, do not hesitate to contact me at the ADNI Coordinator's office at ***(XXX-XXX-XXXX)***.

Thank you for your time and consideration of this matter.

Sincerely,

(Insert ADNI Coordinator's signature)

Acknowledgment of Autopsy Authorization Letter- Personal Physician Copy

Date:

Address

RE: Subject Name

Dear Dr.:

We have been informed by ***(insert participant's name)*** that he/she is under your medical care. ***(Insert participant's name)*** is a participant in the Alzheimer's Disease Neuroimaging Initiative and consent for a brain autopsy at the time of his/her death has been granted by ***(insert person granting consent)***. Plans have been made to have the autopsy performed by ***(insert pathologist)*** at ***(insert location)***.

We realize that your awareness of this information will aid in the success of this endeavor. Should you have any questions, please do not hesitate to call. Our number is ***(XXX-XXX-XXXX)***.

Sincerely,

(Insert ADNI Coordinator signature)

Wallet-sized cards, front and back, given to participants when consent signed:

<p>The undersigned has registered intent for BRAIN DONATION upon death, for purpose of research, with the Alzheimer's Disease Neuroimaging Initiative (ADNI), <i>(Insert ADNI site location)</i></p> <p>Name _____ Date _____</p> <p>Signature _____</p>	<p>AT TIME OF DEATH: Contact the Alzheimer's Disease Neuroimaging Initiative</p> <p>(XXX-XXX-XXXX): Monday-Friday, 8 a.m - 5 p.m. (XXX-XXX-XXXX): Weekends or evenings</p> <p>As soon as practicable after death, the body of the deceased should be moved to a place of cold storage.</p>
<p>The undersigned has registered intent for BRAIN DONATION upon death, for purpose of research, with the Alzheimer's Disease Neuroimaging Initiative (ADNI), <i>(Insert ADNI site location)</i></p> <p>Name _____ Date _____</p> <p>Signature _____</p>	<p>AT TIME OF DEATH: Contact the Alzheimer's Disease Neuroimaging Initiative</p> <p>(XXX-XXX-XXXX): Monday-Friday, 8 a.m.- 5 p.m. (XXX-XXX-XXXX): Weekends or evenings</p> <p>As soon as practicable after death, the body of the deceased should be moved to a place of cold storage.</p>
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