Oxford University Hospitals NHS
NHS Foundation Trust

NEUROPATHOLOGY

OXFORD UNIVERSITY HOSPITALS NHS

FOUNDATION TRUST

USER HANDBOOK

Internet www.ouh.nhs.uk/services/departments/neurosciences/neuropathology

Intranet http://ouh.oxnet.nhs.uk/Neuropathology

Contents

1. About us

The Department provides a diagnostic service for central and peripheral nervous (including ophthalmic) tissue to the clinicians of the Oxford University Hospitals NHS Foundation Trust and regional hospitals. The department also provides a national and international referral service as requested. Services can be summarised as follows:

d. Biopsy service:

- CNS biopsies including intra-operative consultations,
- Ophthalmic biopsies,
- Muscle biopsies,
- Peripheral nerve biopsies,
- CSF cytology service
- Skin biopsy service for small fibre neuropathies

e. Post-mortem service:

- 'Clinical interest' PMs of neurological conditions,
- Neuropathological Coroner's PMs

Medical interest' post-mortem examinations and post-mortems for 'brain tissue donation' are encouraged. Our department manages a considerable archive of tissues from a range of neurological diseases. This archive is a highly valuable resource for education and research.

2. Accreditation

Neuropathology is a UKAS accredited laboratory to ISO 15189:2012 (accreditation number 9642). The scope of our accreditation is listed on the UKAS website and a link to our scope can be found on our internet and intranet sites. Tests outside our scope of accreditation will be those still under development and those where research or expired reagents are required. Our users can be assured that the laboratory subjects these tests to identical quality assurance protocols to those that are UKAS accredited.

Current tests outside UKAS Scope of Accreditation

- Aquaporin 4 immunohistochemistry
- BCAT-1 immunohistochemistry
- Dysferlin immunohistochemistry
- GAB-1 immunohistochemistry
- H3K27M immunohistochemistry
- H3Lys27 immunohistochemistry
- Laminin B1 immunohistochemistry
- Laminin B2 immunohistochemistry
- MAP-2 immunohistochemistry
- Melan-A immunohistochemistry

- Olig-2 immunohistochemistry
- PIT-1 immunohistochemistry
- SF-1 immunohistochemistry
- TDP-43 immunohistochemistry
- T-PIT immunohistochemistry
- W6/32 immunohistochemistry
- YAP immunohistochemistry
- CD3 fresh frozen muscle immunohistochemistry
- CD20/L26 fresh frozen muscle immunohistochemistry
- CD79a fresh frozen muscle immunohistochemistry
- MIB-1 fresh frozen muscle immunohistochemistry
- NF-L fresh frozen muscle immunohistochemistry
- MHCII fresh frozen muscle immunohistochemistry
- Dysferlin fresh frozen muscle immunohistochemistry
- Laminin B1 fresh frozen muscle immunohistochemistry
- Laminin B2 fresh frozen muscle immunohistochemistry
- W6/32 fresh frozen muscle immunohistochemistry

SKIN BIOPSY SERVICE - this is an emerging service and all tests are currently outside the UKAS scope of accreditation. We will be working to bring it into our scope as soon as possible.

3. Our team

The department of Neuropathology comprises Consultant Neuropathologists and Specialty Registrar, Biomedical Scientists, laboratory, IT Project Manager and administrative staff.
The department is a diagnostic service within the Neuroscience Directorate and the NOTSS-CaN Division, and is aligned with Oxford University's Nuffield Department of Clinical Neurology and the Oxford Brain Bank.

4. Where to find us

Level 1 of the West Wing at the John Radcliffe Hospital.

Find us by using the Children's hospital lifts exiting at Level 1 - go through the double doors to the left and ring the intercom for entrance. You may also use the West Wing lifts/staircase – turn left out of the lifts and go through the doors marked Staff Only. Ring the intercom for entrance.

5. Opening Hours

From 8:30 am to 17:00 pm Mondays to Fridays but closed on public holidays.

a. Neurosurgical and ophthalmic samples

Samples should be received between **8:30 am** and **5 pm**, Monday to Friday (not bank holidays).

b. Muscle and skin biopsy samples

Samples should be sent before 4 pm, Monday to Friday (not bank holidays).
Due to the time required for preparation, operations should be arranged so that samples arrive in the laboratory by 4 pm.

c. CSF samples

Samples should be sent before 4 pm, Monday to Friday (not bank holidays).
Due to the time required for preparation, lumbar punctures should be arranged so that samples arrive in the laboratory by 4 pm.

d. Post mortem samples

Samples should be sent before 4 pm, Monday to Friday (not bank holidays).

6. Out of Hours Service

Neuropathology consultants do not provide a routine out of hours (24 hours/7days) on-call service. In exceptional circumstances an out of hours intraoperative consultation can be requested in advance; however availability cannot be guaranteed as this service is not funded. If out-of-hours biopsies are required it is essential to discuss the possibility of a required intraoperative consultation with the consultant on duty as soon as possible. All intraoperative requests must be accompanied with an intraoperative request form.

7. Our testing policies

A. General requirements for all specimens

1. All specimens must be received with an EPR label (Histo Neuro or Neuro CSF). The only exceptions are cases from other (non-OUH) hospitals.

2. Minimum identification:
   a. Three identifiers, including at least one unique identifier (MRN/NHS number).
   b. Tissue description
   c. Details of requestor (name and contact number)
   d. Location for report
   e. Date and time of tissue collection

   Specimens that do not conform to these requirements may not be accepted by the laboratory and be returned.

3. Specimen labels must match exactly that on the EPR request. A mismatch will lead to rejection of the specimen and it will be returned.

4. Consent:
   a. Consent information relating to use of tissue and data for research must be transcribed from the patient's procedure consent form onto the Neuropathology EPR request or request form.
   b. Consent must be accurately transcribed in order to comply with the Human Tissue Act (2004).
   c. Consent for neuropathological post mortem (PM) report must be given by the person of highest qualifying relationship.
   d. Post mortem samples will be rejected and returned if there is inadequate consent information. The exception is tissue sent under the jurisdiction of the Coroner.
   e. Coroner's offices are required to request consent from persons of qualifying relationships regarding the use and disposal of the post mortem tissue.

5. Risk of Infection
   a. It is the responsibility of the requesting clinician to inform the laboratory of all known infection risks.
   b. Biohazard tape/labels should be attached to the specimen container as appropriate.

B. Neurosurgical and ophthalmic samples

1. All neurosurgical and ophthalmic samples should be requested via EPR. The request must include information in all fields, including whether an intraoperative smear is required.

2. Samples taken during opening hours should be sent fresh as soon as possible after removal. Samples taken outside these hours should be fixed in formalin and sent to the laboratory the following day.

3 If a patient has consented for samples of the biopsy to be used for specific research projects, a signed copy of the consent must be provided to the laboratory before the tissue is released.

4. The laboratory should be informed of any intraoperative smears by calling the main extension number (34417) in advance. All requests for an intraoperative smears must be made using a "Smear request form". Cases received without these forms will be managed by our routine pathway.

C. Muscle biopsy samples

N.B. samples received in formalin or formal saline will not be suitable for diagnosis.

1. Muscle biopsies should be booked at least 24 hours in advance by contacting the laboratory (x34417, ask for muscle bench). Complex cases should be discussed with the neuropathology consultant team in advance to provide maximum clinical information. This could be done via e-mail (oxford.neuropath@nhs.net, our team would pass the message to the relevant consultant).

2. Muscle biopsy request forms, which can be downloaded from the Neuropathology intranet site or requested from the laboratory, must accompany the biopsy. The samples must be requested via EPR.

3. Muscle biopsy samples should be received by the laboratory no later than 4 pm.

4. Muscle biopsy samples should be at least 1 cm^3 and be placed into a dry universal container and delivered to the department immediately.

D. Nerve biopsies

1. The laboratory should be contacted in advance to inform the team of an upcoming nerve biopsy.

2. The department requires at least a 3 cm length of nerve, placed into a dry universal container.

3. The sample should be delivered to the department immediately with a completed EPR request.

4. The sample should be received by the laboratory no later than 4 pm.

E. Cytology samples (CSF/vitreous fluid)

1. If requested via EPR:
   a. The specimen must be labelled with an EPR label
   b. The EPR request must be completed in full, including the consent information and location for report.

2. If requested using Neuropathology request card:
   a. There must be at least 3 patient identifiers on the specimen label and request card.
   b. Consent, infection risk and requesting clinician information must be completed.

F. Skin biopsy samples for the evaluation of IENFD

1. The laboratory should be informed in advance of any biopsies. Service level agreements will be prepared for work carried out for any non-OUH Trust

2. Biopsies taken in the OUH should arrive in PLP fixative, no later than 4:00 pm

3. Biopsies from other centres are fixed in PLP and then sent to us in cryoprotectant (sucrose).

G. Post mortem tissue

1. Consultant Neuropathologists and the laboratory should be informed of any PM tissue that is likely to be sent for a neuropathological assessment.

2. Consent is required for all post mortem requests, other than those from the Coroner or for tissue under PACE.

3. Minimum criteria:
   a. Name
   b. Date of birth
   c. Place of examination
   d. Location for report

8. Specimen transport

a. Internal transfers

i. Porters (Bouygues and theatres) and the internal pod system.
ii. Neuropathology pod number 858

b. Between OUH hospitals

i. Shuttle van

c. External transfers

i. Couriers (TNT, FedEx)
ii. Hospital transport companies

9. Infection control

It is the responsibility of the sender to be aware of the risks and to inform the lab

Due to the risk to lab staff, whenever there is a suspicion of infection, it is preferable to handle formalin fixed tissue. If such cases need a smear or frozen section, it is a mandatory requirement that the specimen be placed in a suitable, sealed container and adequately labeled as an “infectious risk”.

Biopsies involving potential high-risk infective tissue such as CJD should be discussed well in advance with consultants. We will treat all biopsies from patients with an unclear (non-neoplastic, neurodegenerative) neurological syndrome as potentially infected with the TSE (transmissible spongiform encephalopathy) agent.

Separate samples for microbiological investigations should be sent directly to the Microbiology Department at the John Radcliffe site.

10.Turnaround times

The department follows the recommendations of the Royal College of Pathologists turnaround time guidelines with minor modifications as dictated by local factors and agreed with the clinical teams. The turnaround times given are in calendar days from the date the sample is taken.

Specimen type	Target turnaround time (calendar days *except PMs*)	Notes
Neurosurgical sample	7	Except where decalcification is required or further fixation (for larger specimens)
Pituitary biopsy	14	
CSF sample	2	
Ophthalmic sample	11	
Muscle biopsy	14	Except consult cases (21 days)
Nerve biopsy	21	
Skin biopsy	4 months	
Post mortem (brain)	10 weeks	From date of receipt
Post mortem consult	5 weeks	

11.Clinical testing and requirements

Name	Specimen/container requirements	Other
Brain biopsy – tumour biopsy for intraoperative	Fresh sample (no formalin or saline) in EPR-labelled container. The sample must be delivered immediately to the lab.	EPR request must contain theatre number and contact tel./bleep number.
Brain biopsy – tumour sample for processing	Fresh sample (no formalin or saline) in EPR-labelled container. The sample must be delivered immediately to the lab.	Consent must be accurately transcribed to request. Additional consent relating to specific research projects must accompany the samples.
CSF sample for cytology (only)	At least 0.5 ml in an EPR-labelled, sterile container. The sample must be delivered straight to Neuropathology. Samples must arrive in the lab before 4 pm.	Flow cytometry is carried out by the Haematology Department, JRH and a minimum of 1.0 ml should be sent directly for investigation. Contact Person: Kevin Leyden (BMS), ext. (5)72827 and the service is provided Monday to Friday.
CSF sample for 14.3.3 testing	If you consider this test for suspected cases of prion disease, you must contact the CJD Surveillance Unit in Edinburgh. Tel: 0131 5373075 (Dr Alison Green). They will discuss requirements with you. If the decision is made to perform this test, we may store the sample for you while waiting for Edinburgh to arrange transport. Please keep us informed on X 34417.	

Name	Specimen/container requirements	Other
Muscle biopsy (adult)	At least 1 cm^3 of muscle in a sterile universal container with no formalin or saline. More tissue may be required, depending on the investigations required. EPR label must be on the container. The sample must be delivered immediately to the laboratory.	Notify the laboratory at least 24 hours before the planned procedure. Complete the muscle biopsy request form (see Document Library)
Muscle biopsy (paediatric / neonatal)	At least 1 cm^3 of muscle in a sterile universal container with no formalin or saline. More tissue may be required, depending on the investigations required. EPR label must be on the container. The sample must be collected immediately from theatres by a Neuropathology Biomedical Scientist. Samples must be prepared and frozen within 30 minutes of being taken.	Notify the laboratory at least 24 hours before the planned procedure. Complete the muscle biopsy request form (see Document Library) Inform the laboratory if you also plan to take a skin sample for fibroblast culture (you will need to complete a separate Cytogenetics form).
Nerve biopsy	At least 3 cm length of nerve in a sterile universal container with no formalin or saline. EPR label must be on the container. The sample must be delivered directly to Neuropathology.	Notify the laboratory at least 24 hours before the planned procedure.
Ophthalmic biopsy	Samples must be placed in sterile universal containers and be clearly labelled with an EPR label.	Conjunctival biopsies for immuno-fluorescence are currently sent, via Neuropathology, to St John's Institute of Ophthalmology, London.

Name	Specimen/container requirements	Other
Skin biopsy for IENFD	A 3 mm punch biopsy is required. Samples from OUH must be placed into a universal container containing PLP fixative and then delivered directly to the laboratory. EPR label must be on the container. Samples from outside the OUH should be placed into a universal container containing PLP fixative overnight (at 4°C) and then transferred to cryoprotectant (sucrose solution). At this point they should be delivered to the laboratory (must be within 48 hours of transfer to the sucrose.	N.B. Fixation delay may impair results. Fixation in PLP should not exceed 24 hours.
Post mortem (Coroner)	Please liaise with the laboratory prior to sending tissue and include a referral letter/ clinical information as appropriate. For routine cases (e.g. ?SUDEP) a referral letter from the pathologist who performed the initial post-mortem may suffice. However, any cases which either require a neuropathologist to be present at post-mortem or more complex input should be discussed with duty neuropathologist first.	Samples should be fixed in 10% neutral buffered formalin (unless plans are made to transfer fresh samples immediately to the lab) for at least 1 week, prior to delivering to the laboratory.
Post mortem (Hospital)	If a 'medical interest' / 'brain-tissue-donation' post-mortem examination has been agreed upon, the Neuropathology department (tel. 01865 234904) as well as the mortuary should be notified (mortuary tel.: 01865 220495). Neuropathology consultants are always happy to discuss the case and possible management issues with a member of the clinical team prior to the post-mortem.	It is important that an up to date post mortem consent form, completed and signed, accompanies the body to the mortuary. Samples should be fixed in 10% neutral buffered formalin (unless plans are made to transfer fresh samples immediately to the lab) for at least 1 week, prior to delivering to the laboratory.
Temporal artery biopsy	1 cm is the minimum length for histological assessment. The biopsy needs to be performed within 72 hours of commencing the patient on steroids. If the patient is already on steroids this should be stated on request form with the duration of treatment specified. EPR label must be on the container.	

Name	Specimen/container requirements	Other
Vitreous fluid	Clinicians should contact the laboratory in advance to seek advice. The laboratory requires at least 1ml of fluid in a sterile container.	

12.Results

Neurosurgical, ophthalmic and neurology samples	**Results are available electronically (EPR). No paper copy sent to OUH clinicians unless requested.**
CSF results	Directly onto EPR – no paper copy sent (unless external).
Post mortem results	Reports sent to referring service.

13.External factors affecting performance

Factor	Consequence
Tissue samples – Fixation delay	Degradation of tissue, which may affect the quality of results
Tissue samples – Container too small for samples	Artefact – sample will take on the shape of the container. Poor fixation, due to insufficient formalin for sample size
Samples – labelling errors	Delay to sampling – cannot be processed with insufficient labels
CSF fluid – processing delay (e.g. incorrectly sent to Cell Path)	Autolytic change from delayed processing may affect the quality of results.
Muscle biopsies placed into formalin or saline	Unable to complete full testing for diagnosis.
Skin biopsies placed into formalin or saline	Unable to complete full testing for diagnosis.

14.Measurement uncertainty

The laboratory has considered measurement uncertainty for all measurements undertaken by the laboratory as part of any diagnostic test. This information is available to users on request.

15.Referral service

Some cases or tissue preparations may be referred to other sites for a second opinion or specialist analysis. Routine referral sites include:

- Muscle tissue (congenital myopathies) to NCG reference centre, Dubowitz Neuromuscular Centre, Institute of Neurology, London.
- Muscle tissue for Respiratory Chain Studies to Clinical Biochemistry Dept., Queen Square National Hospital for Neurology and Neurosurgery, London.
- Muscle tissue for DNA studies to Oxford Medical Genetics Laboratories, Churchill Hospital, Oxford.
- Muscle tissue (muscular dystrophies) to NCG reference centre Newcastle.
- Glioblastomas for MGMT promoter methylation testing to Dept. of Neuropathology, Queen Square National Hospital for Neurology and Neurosurgery, London (at the request and cost of the clinical team); routine testing in patients with glioblastoma
- Selected brain tumours for genetic testing of certain mutations, which have clinical implications (e.g. IDH, Histone H3F3, BRAF, KRAS, ALK) to the Department of Neuropathology at Queen Square, London or the Oxford Molecular Diagnostics Centre (mostly at the request and cost of the clinical team)
- Some soft tissue and bone tumours to Dr Zsolt Orosz, Nuffield Orthopaedic Centre, Oxford.
- Molecular tests to Central and South Genomics Service at Birmingham Women and Children's Hospital.
- Lymphomas and suspected lymphoid malignancies to Haematopathology (Dr Daniel Royston, Dr Gareth Turner, Dr Gabrielle Rees and Professor Francesco Pezzella at Cellular Pathology, John Radcliffe Hospital).
- Routine immunohistochemical staining and ER/PR and HER2 scoring to Cellular Pathology laboratory, John Radcliffe Hospital.
- Choroidal malignant melanomas for FISH analysis to Prof Sarah Coupland, Royal Liverpool University Hospital.
- Rare orbital or intra-ocular neoplasms to Prof Phil Luthert / Dr Caroline Thaung, Institute of Ophthalmology, London
- Ophthalmology reporting - interim support for the reporting of some ophthalmic samples from Moorfield's Hospital. London.

16.Governance

- See the Neuropathology Quality policy
- The laboratory is UKAS accredited to ISO 15189:2012 Medical laboratories – requirements for quality and competence (lab number 9462).
- The laboratory holds licences to practice as accredited by the Human Tissue Authority (licence number 12052).
- The department and its staff adhere to the Trust’s, national and international confidentiality and freedom of information policies. All staff are required to undertake training annually.
- External quality assurance
  - UK NEQAS Cellular Pathology technique
  - UK NEQAS CPT for muscle
  - UK NEQAS for immunocytochemistry
  - Slide evaluation scheme with Neuropathology laboratories at Southmead Hospital in Bristol and Derriford Hospital in Plymouth.
  - CSF preparation comparison with the Cytology service in Cellular Pathology, OUH.

- Internal quality assurance
- Integrity of patient sample and sample details
- Individual slide check and approval
- Regular audits of pre-examination, examination and post-examination procedures, equipment and processes.
- User satisfaction surveys
- Key performance indicators

17.Contact us

Neuropathology
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For general enquiries • Telephone 01865 234904 • Email oxford.neuropath@nhs.net
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Neuropathology Laboratory & Quality Manager, Chief BMS Hannah Keyser 01865 231537 Hannah.keyser@ouh.nhs.uk
Administrator Jody Morgan 01865 234904 jody.morgan@ouh.nhs.uk **IT Project Manager** Samantha J. Cragg Samantha.cragg@ouh.nhs.uk 01865 234932
Main laboratory 01865 234417 Oxford.neuropath@nhs.net Louise Young – Deputy Lab Manager and BMS Lead for neuromuscular service Jessica Ward – Human Tissue Lead and HTA Person Designated
Specimen reception 01865 231695
Complaints/concerns Please contact Hannah Keyser (Laboratory Manager) or Dr Clara Limbaeck (Clinical Lead) or the Trust's Patient Advice Liaison Service (01865 221473).

- For specialist advice/guidance, please use the above contacts. Ensure you do not use the patient name in the subject line.
- Please use the department's nhs.net account for all additional testing requests.

18.Document library

Documents used to prepare this user handbook are listed here. These documents can be made available to our users if required. Contact Hannah Keyser (Hannah.keyser@ouh.nhs.uk)

Document title	Unique identifier
Neuropathology Quality Manual	MNPP 377
Neuropathology Quality Performance Indicators	MQUA 803
Neuropathology Specimen Transport Policy	LSPEC 14
Neuropathology intraoperative smear procedure	LSPEC 131