# LRI Children's Hospital

## Muscle and/or Skin Biopsy in children

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| Staff relevant to: | Medical & Nursing staff working within UHL Children's Hospital |
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| Written by:<br>Reviewed by: | N Hussain<br>Usama Abdulrazak and Dhinesh Baskaran |
| Trust Ref: | C39/2016 |

### 1. Introduction and Who Guideline applies to

A muscle biopsy is a procedure carried out to acquire a small muscle specimen for studies including histology, histochemistry, electron microscopy, biochemistry and genetic studies, to diagnose muscle disorders. The need for muscle biopsy has declined recently due to availability of advancement in genetics testing such as whole exome/genome sequencing.

Open muscle biopsy, a preferred method at LRI, is carried out by the Paediatric Surgical team. Organisation of muscle biopsy, preparing relevant paper work, handling of samples and their transport to local, regional and national centres needs co-ordination among several disciplines.

After acquisition, the muscle samples are sent to the pathology and special biochemistry departments along with the relevant paperwork. If the specimens are required to be sent to National Commissioning Group (NCG) centres for further evaluation, these need to be accompanied by appropriately filled relevant NCG pre-referral forms, which can be downloaded from the links given below

This guideline is intended for use by the Medical, Nursing and Laboratory staff working within UHL Children's Hospital.

## 2. Guideline Standards and Procedures

NHS National Commissioning Group (NCG) has designated central funding for a "Diagnostic and Advisory Service for Rare Neuromuscular Diseases" for patients in England and four groups of diseases are currently covered:

Mitochondrial Disorders Service Newcastle Upon Tyne
Limb Girdle Muscular Dystrophies in Newcastle upon Tyne
Congenital Muscular Dystrophies at GOSH in London
Ion Channel Disorders at the National Hospital/Institute of Neurology in London
Congenital Myasthenic Syndromes in Oxford

**Indications:**

- Neuromuscular disorders
- Mitochondrial disorders

**Clues to mitochondrial disease:**

- Elevated Serum lactate
- Features of both neuropathy and myopathy
- When there is a family history of similar phenotype, death during the neonatal period or childhood, deafness, diabetes, cardiac involvement, visual impairment, and developmental delay.
- If there is **unexplained** multisystem involvement affecting heart, brain, retina, and / or skeletal muscle.
- If the clinical presentation is during the stressful periods, such as serious illness, surgery, and anaesthesia, or when, episodes of rhabdomyolysis are disproportionate to the amount of stress.

**Arranging muscle biopsy and paper work:**

Obtain verbal consent at the time of offering biopsy. The Paediatric Surgery team will take formal written consent before performing the procedure.

Arrange before biopsy: arrange for CK, lactate and echocardiography

Refer to paediatric surgical team for a muscle requesting two small samples (the optimal sample size is a cylinder of tissue 1cm long and 0.5cm diameter, with the long axis parallel to the muscle fibres) for histology and mitochondrial studies.

Once an appointment for biopsy has been confirmed by the Paediatric Surgery Secretary, the biopsy requesting team MUST contact one of the Clinical Scientists within the Special Biochemistry laboratory to give advance notice as soon as practicably possible and ideally at least one week beforehand through email or phone Special biochemistry team:

- Helen Jerina, Senior Clinical Scientist (helen.jerina@uhl-tr.nhs.uk)
- Dr Lee (virgina.lee@uhl-tr.nhs.uk), or
- Dr Maddocks (lorna.maddocks@uhl-tr.nhs.uk) on 16553/ 16560/17589

and Histopathology Team:

- Peter Wells-Jordan (peter.wells-jordan@uhl-tr.nhs.uk) on 16590 to inform about the patient details & date, time, and location of the procedure. If Peter Wells-Jordan is not available, use the listed extension numbers to contact team members to notify of biopsy request.

On the morning of the procedure**,** please telephone the laboratory (x16553, 16560 or 17589) to confirm the procedure is still going ahead and phone again just before attendance is required. A member of the laboratory team will then attend the procedure.

In the event of cancellation, the aforementioned teams should be updated.

The muscle biopsy requesting team will complete the relevant paperwork.
Yellow Histopathology form for histochemistry/electron microscopy;
NCG forms for Congenital Muscular Dystrophies, Limb Girdle Muscular Dystrophies, and Mitochondrial studies can be accessed through links below.
Please include as much relevant clinical information as possible on the request form (Pattern of muscle weakness, developmental delay, growth failure, cardiac involvement, hearing impairment, optic atrophy, & retinopathy etc.). Also, state the site of biopsy and the muscle biopsied. Handover the paper work to the Surgery Day Care ward clerk to place in the patient notes.

**Sample handling:**

The muscle sample for mitochondrial studies is collected in cryogenic propylene tube (supplied by chemical pathology) to be snap frozen by lab staff in liquid nitrogen and transported to laboratory by the laboratory staff.

The sample for histochemistry and electron microscopy must be wrapped in saline dampened gauze. Please do not over-soak the gauze as this causes saline artefact. The sample should not be too dry either, as this can affect the tissue quality as well.

The Special Biochemistry staff can deliver the samples to histopathology laboratory if they are coming for sample collection for mitochondrial studies. Otherwise, the biopsy requesting team will collect and hand-deliver the muscle sample to the Histopathology team in Sandringham building within 20 minutes.

**Processing/Analysis centres:**

For Histology/histochemistry – LRI/QMC
For Mitochondrial tests/respiratory chain enzymes – Newcastle
For Limb-girdle-muscular-dystrophy – Newcastle
For Congenital muscular dystrophy/Congenital myopathies – GOSH

## SKIN BIOSPY

Skin biopsy is a procedure carried out to collect a small piece of skin for fibroblast culture for enzyme assays or cytogenetic studies, and for histological studies.

## Indications of Skin Biopsy

Enzyme assays:

- Fatty Acid Oxidation defects
- Pyruvate Dehydrogenase deficiency
- Pyruvate Carboxylase deficiency
- Histological studies for Lafora-body disease, Neuronal Ceroid Lipofuscinosis, Neurocutaneous syndromes such as Hypomelanosis of Ito

## Arranging Skin biopsy and paper work:

If patient requires both skin and muscle biopsy, this should be carried out under the same procedure by the surgical team

If skin biopsy only required (e.g. for fat oxidation disorders), this can be carried out by the metabolic medical team under local anaesthetic.

Obtain an informed verbal consent when offering biopsy. The Paediatric Surgery team will take formal written consent before performing the procedure. Specific written consent is required prior to skin biopsy for fibroblast culture (3 levels of consent which can be facilitated by the metabolic team) before sending sample to Simon Olpin @ metabolic lab Sheffield Children's Hospital. The consent form is available in the childrensneurology (X) drive on computer as Sheffield CH Skin Biopsy Consent form.
Referral to Paediatric Surgery Team for arranging a skin biopsy and requesting for a 0.5 cm x 0.5cm skin sample (from axillary skin for Lafora biopsy, from the site of muscle biopsy for enzyme studies, and from a skin lesion for neurocutaneous syndromes).

Once an appointment for biopsy has been confirmed by the Paediatric Surgery Secretary, the biopsy requesting team MUST contact one of the Clinical Scientists within the Special Biochemistry laboratory to give advance notice as soon as practicably possible and ideally at least one week beforehand through email or phone Special biochemistry team:

- Helen Jerina, Senior Clinical Scientist (helen.jerina@uhl-tr.nhs.uk)
- Dr Lee (virgina.lee@uhl-tr.nhs.uk), or
- Dr Maddocks (lorna.maddocks@uhl-tr.nhs.uk) on ext 16553/ 16560/17589

And
Histopathology Team:

- Peter Wells-Jordan (peter.wells-jordan@uhl-tr.nhs.uk) on ext 16590 and
- Cytogenetic team on ext 15637 to inform about the patient details & date, time, and location of the biopsy and ask for request HAMS medium for Fibroblast culture, but not for histology.

The skin biopsy requesting team should complete the relevant paperwork.

- Clinical Chemistry form for Sheffield Metabolic lab (print out from the link given below) for fibroblast culture for enzyme assays,
- White Cytogenetic form (LRI) for fibroblast culture for cytogenetic studies, and
- Yellow Histology form (LRI) for histological studies.

Please include as much relevant clinical information as possible on the request form. Also, state the site of biopsy. Handover the paper work to the Surgery Daycare ward clerk to place in the patient notes
On the morning of the procedure please telephone the laboratory (x16553, 16560 or 17589) to confirm the procedure is still going ahead and phone again just before attendance is required. A member of the laboratory team will then attend the procedure.

In the event of cancellation, the aforementioned teams should be updated.

**Sample handling:**

- Special biochemistry team will collect samples for fibroblast culture to be sent to Dr. Simon Olpin, Consultant Clinical Scientist, at Sheffield metabolic lab who will subsequently arrange for enzyme studies.
- The sample for histology and electron microscopy must be wrapped in saline dampened gauze. Please do not over soak the gauze as this causes saline artefact. The sample should not be too dry either, as this can affect the tissue quality as well.
- If the Special Biochemistry team are not coming, the biopsy requesting team will collect and hand-deliver to the Histopathology team in Sandringham building, or Cytogenetic team within 20 minutes for cytogenetic studies.

**Processing/Analysis Centre:**

Histological studies arranged through Histopathology, LRI
Fibroblast culture is carried out at Sheffield Metabolic lab (Dr Simon Olpin)
Once fibroblasts are cultured by the Sheffield metabolic lab, the enzymes studies will be carried out by:
- Fatty Acid Oxidation defects and Pyruvate Carboxylase deficiency studies at Metabolic Lab, Sheffield Children's Hospital
- For Pyruvate Dehydrogenase deficiency Dr Simon Olpin sends the culture fibroblasts to - Gary Brown, Dept. of Biochemistry, University of Oxford
Use the following link to print out forms:

NCG form for congenital muscular dystrophies https://www.gosh.nhs.uk/medical-information/clinical-specialties/neuromuscular-information-parents-and-visitors/refer-patient-neuromuscular-department

NCG form for Limb Girdle Muscular Dystrophies
http://www.ucl.ac.uk/neuromuscular/clinicalservices/ppform

Skin biopsy for enzyme assay form for Sheffield
Laboratory Medicine - Sheffield Children's NHS Foundation Trust (sheffieldchildrens.nhs.uk) . ***Choose Clinical Chemistry request form***.

## 3. Education and Training

No training required to implement this guideline

## 4. Monitoring Compliance

None identified at present

## 5. Supporting References

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## 6. Key Words

Biopsy, Muscle, Samples, Skin

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

| CONTACT AND REVIEW DETAILS | |
|---|---|
| Guideline Lead (Name and Title)<br>Dhinesh Baskaran - Consultant<br>Dr Usama Abdulrazak - SHO Paediatric Neurology | Executive Lead<br>Chief Medical Officer |
| Details of Changes made during review:<br>Relevance of muscle biopsy in diagnosis.<br>Staff to contact where kept up to date<br>Links for biopsy request forms updated.<br>Removed reference to GGH transportation as services no longer based at GGH site | |

**Appendix 1:**
**Procedure to Ensure Viability of Muscle & Skin Biopsy acquisition on PICU and CICU. (Simon Chiles & Dr Elaine Maddocks)**

## CICU-LRI site.

Storage facilities for samples and access to liquid nitrogen is available within the trust at the LRI site through specialist biochemistry and the procedure for transporting the biopsies is facilitated by the specialist biochemistry staff.

Arrange with General Paediatric Surgical Team Registrar to arrange theatre slot and anaesthetics.

Inform Specialist Biochemistry Team (Lead Dr Elaine Maddocks) 0116 258 6553 on the 4th floor of the Sandringham building at the LRI.

Liaise between both teams to ensure compliancy, if necessary the process may be performed on PICU - LRI.

The specialist biochemistry team will facilitate the collection, storage and transfer. They will organise liquid nitrogen for the flash freezing as well as the flash freezing container for muscle biopsy, they will also supply the correct medium for the skin biopsy, dependant on test required, usually HAMS solution that is sent to Sheffield for mitochondrial disorders.

The bio chemistry team will organise the human tissue use consent forms and the surgeons will organise the consent for the procedure.

Once a decision made to perform and muscle and skin biopsy it is imperative to **contact Specialist Biochemistry Team (Lead Dr Elaine Maddocks) 0116 258 6553 on 4th floor of the Sandringham building, LRI.** The muscle biopsy needs to be transferred to Newcastle and the skin biopsy to Sheffield dependant on the required tests, **the transfer is once a week on a Wednesday and requires the sample to be in the laboratory by 1600hrs on the Tuesday.**

The patient details need to be provided to the laboratory for them to supply the containers with appropriate labelling, and to send by email the requisite human tissue use consent forms for the appropriate consent from the parents/guardians, the surgeons will organise the procedural consent.