



POLICY UPDATE NOTIFICATION

TITLE: Tissue submission requirements for fresh tissue that will not be processed to inactivate infectious microorganisms (i.e. SARS-CoV-2): skeletal muscle biopsy.
DATE: October 28, 2020

In an effort to ensure the safety of our faculty and staff, while maintaining service excellence for our clients and mutual patients, Michigan Medicine Laboratories (MLabs) has updated our tissue submission requirements. Complete evaluation of skeletal muscle requires submission of fresh, frozen tissue, which will be handled without fixation and remain frozen. Fresh, frozen tissue represents an infectious risk (SARS-CoV-2) to laboratory personnel who perform aerosolizing procedures in order to prepare the fresh, frozen tissue.

To submit patient skeletal muscle biopsy tissue to Michigan Medicine Laboratories, this policy requires:

- Patients undergoing skeletal muscle biopsy that will be referred to MLabs must have a pre-procedure test for SARS-CoV-2 (COVID19).
- As with all other COVID tests, the patient must be instructed to isolate as much as possible following the specimen collection, after the test result and prior to their procedure.
- The specimen collection must occur within **96 hours prior to the procedure.**
- The pre-procedure test must be a high sensitivity PCR assay to detect viral nucleic acids.
- **SARS-CoV-2 antigen tests are not acceptable** for pre-procedure tests as they are insufficiently sensitive to detect virus in asymptomatic patients.
- **SARS-CoV-2 antibody testing (IgM/IgG) are also not acceptable** for pre-procedure tests as they measure immune response to SARS-CoV-2 and not the presence/absence of virus.
- The patient test result must be **NEGATIVE (NO VIRAL RNA DETECTED)**.
- A copy of the COVID test result must accompany the specimen requisition.
- Michigan Medicine Laboratories cannot accept fresh, frozen tissue that will remain unfixed (not placed in formalin or glutaraldehyde) from COVID19 POSITIVE, COVID19 EQUIVOCAL, or UNTESTED patients.
- If the pre-procedure COVID test is positive or equivocal, the biopsy procedure should be rescheduled and the patient re-tested within 96 hours prior to the procedure.



FROZEN MUSCLE



MUSCLE BIOPSY REQUISITION



NEGATIVE COVID REPORT



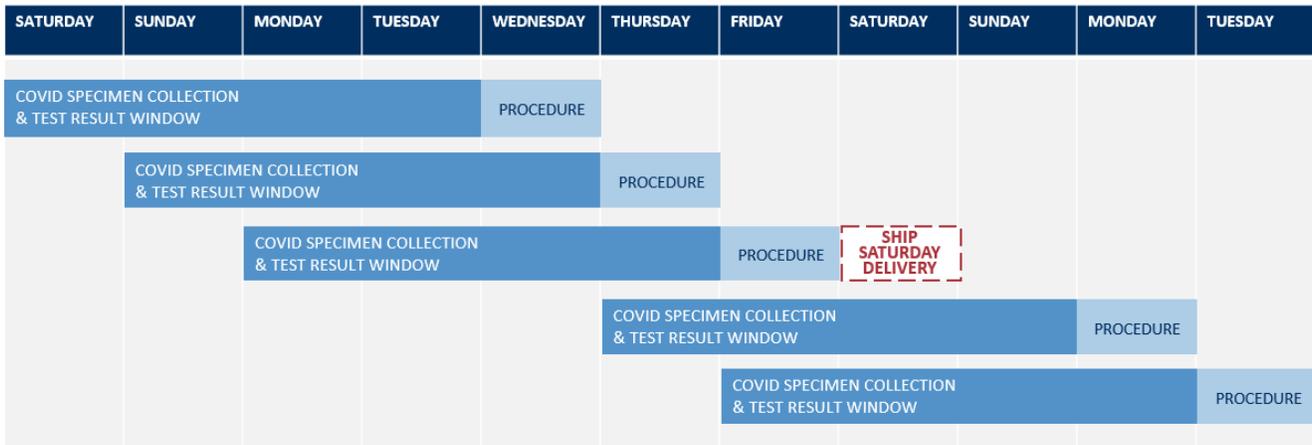


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SCHEDULING SKELETAL MUSCLE BIOPSY PROCEDURE AND PRE-PROCEDURE TESTING

The below graphic depicts the acceptable pre-procedure COVID test specimen collection time windows:

SKELETAL MUSCLE BIOPSY: Pre-procedure COVID Testing + Procedure + Shipping



Skeletal muscle biopsies for some inflammatory, degenerative disorders and storage diseases, benefit from evaluation by specially trained neuropathologists, like those at Michigan Medicine Laboratories. Scheduling surgery for a morning to mid-day procedure is essential to ensure same day shipping, specimen integrity and timely evaluation for the patient.

SKELETAL MUSCLE BIOPSY: Pre-procedure COVID Testing + Procedure + Shipping

	SURGERY DAY Procedure Complete Time to Ship Specimen		PRE-PROCEDURE SPECIMEN Collection Days		SHIPMENT Special Instructions
MONDAY	14:00	➔	Thursday - Sunday	➔	FIRST DELIVERY
TUESDAY	14:00	➔	Friday - Monday	➔	FIRST DELIVERY
WEDNESDAY	14:00	➔	Saturday - Tuesday	➔	FIRST DELIVERY
THURSDAY	14:00	➔	Sunday - Wednesday	➔	FIRST DELIVERY
FRIDAY	14:00	➔	Monday - Thursday	➔	SATURDAY DELIVERY

MLabs recommends NOT scheduling skeletal muscle biopsies on Saturday or Sunday as storage of frozen skeletal muscle at -20C may be limited and shipping to MLabs is not available over the weekends.



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If COVID test results within 96 hours of collection is challenging within your facility/setting; please contact MLabs. MLabs offers COVID testing and may be able to assist you.

HOW MLABS HANDLES VARIANCES:

NO COVID TEST REPORT RECEIVED WITH SPECIMEN

Skeletal muscle biopsies that are submitted without an accompanying COVID test result will be HELD until the MLabs Client Services team can secure a copy of the COVID NEGATIVE test result. The specimen will be accessioned to allow tracking within the Laboratory Information System; however, no tissue will be processed until a copy of the COVID test result is provided. This may cause significant delays in patient evaluation and care.



NO COVID TEST REPORT RECEIVED WITH SPECIMEN



MLABS CLIENT SERVICES CALLS SUBMITTING PHYSICIAN



COVID TEST RESULT FAXED TO: 734-936-0755



DELAY IN EVALUATION

NO COVID TEST PERFORMED PRIOR TO PROCEDURE

If NO COVID test was performed, the fresh, frozen tissue will NOT be evaluated. Only evaluation of the formalin fixed, paraffin embedded tissue and/or tissue for electron microscopy will be performed. **This could result in an incomplete evaluation and diagnosis for the patient. This may result in a future repeat procedure for the patient.**



NO COVID TEST PERFORMED PRIOR TO PROCEDURE



MLABS M.D. OR NEUROPATHOLOGY CONTACTS REFERRING PHYSICIAN

PARTIAL EVAL

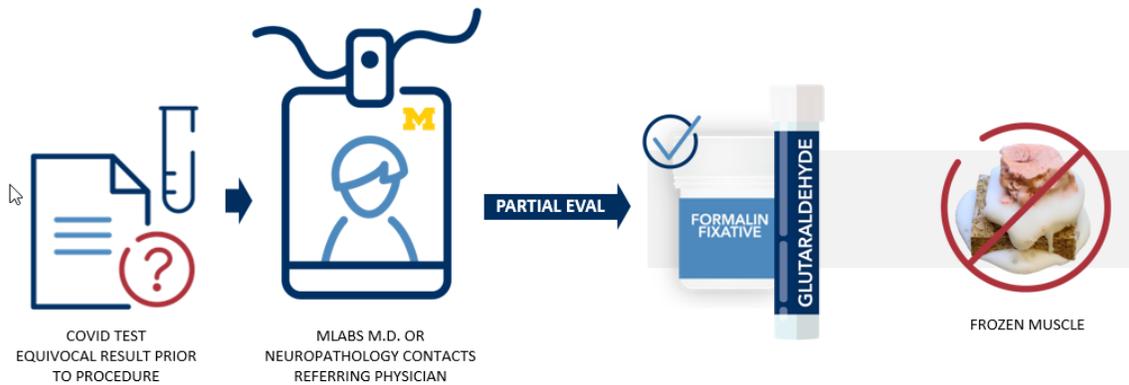


FROZEN MUSCLE

POLICY UPDATE NOTIFICATION

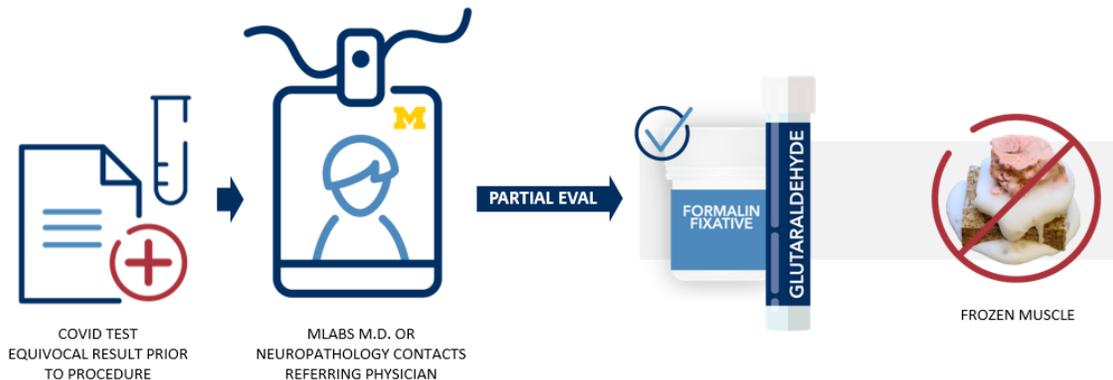
PRE-PROCEDURE COVID TEST RESULT EQUIVOCAL

If the COVID test result is **EQUIVOCAL**, the fresh, frozen tissue will **NOT** be **evaluated**. Only evaluation of the formalin fixed, paraffin embedded tissue and/or tissue for electron microscopy will be performed. This could result in an incomplete evaluation and diagnosis for the patient. This may result in a future repeat procedure for the patient.



PRE-PROCEDURE COVID TEST RESULT POSITIVE

If the COVID test result is **POSITIVE**, the fresh, frozen tissue will **NOT** be **evaluated**. Only evaluation of the formalin fixed, paraffin embedded tissue and/or tissue for electron microscopy will be performed. This could result in an incomplete evaluation and diagnosis for the patient. This may result in a future repeat procedure for the patient.





POLICY UPDATE NOTIFICATION

BACKGROUND

Skeletal muscle biopsy evaluation is a complex procedure that requires submission of skeletal muscle in three (3) different states in order to perform complete evaluation.

- 1) Unfixed, frozen skeletal muscle tissue is evaluated using frozen section microscopic preparations with enzyme and other histochemistry that is only able to be performed on fresh, frozen tissue. These special tests are vital to the evaluation of many inflammatory and degenerative conditions affecting skeletal muscle. Tissue that is frozen at -20C does NOT inactivate/kill many infectious microorganisms, including SARS-CoV-2. The tissue sectioning process also creates risk of aerosolization of viral particles, if present within the skeletal muscle. The possibility of live, aerosolized virus is a significant health risk to laboratory personnel. Skeletal muscle biopsies for COVID-positive patients should be delayed until the patient has recovered and is no longer COVID-positive.
- 2) Formalin fixed skeletal muscle tissue. Skeletal muscle removed from the patient is immediately fixed in a solution of neutral buffered formalin. This provides for routine histologic processing. Formalin fixation DOES inactivate/kill many infectious microorganisms (including SARS-CoV-2). Evaluation of skeletal muscle with formalin-fixed, paraffin embedded tissue does not confer the same degree of infectious risk.
- 3) Glutaraldehyde fixed skeletal muscle tissue. Skeletal muscle removed from the patient is immediately fixed in glutaraldehyde solution. Glutaraldehyde fixation DOES inactivate/kill many infectious microorganisms (including SARS-CoV-2). Glutaraldehyde fixed, embedded tissue for electron microscopy does not confer the same degree of infectious risk.

While SARS-CoV-2 is a significant cause of respiratory illness, SARS-CoV-2 virus has been detected in tissues other than lung. Autopsy studies have detected SARS-CoV-2 viral particles in oropharynx, lung, heart, kidney, spleen, gastrointestinal tract and skeletal muscle [Citations and ATS publication in press].

All other specimen acceptance policies continue to apply. Specimens must be submitted (1) in the appropriate specimen collection device/container, (2) with two patient identifiers on the specimen label, (3) accompanied by a completed requisition with the same patient identifiers, (4) ordering physician information, including critical value call back telephone number and (5) transported at the required specimen preservation temperature.

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REFERENCES:

Ferrandi, PJ, Always SE and Mohamed JS. The interaction between SARS-CoV-2 and ACE2 may have consequences for skeletal muscle viral susceptibility and myopathies. *J Appl Physiol* 129:864-867, 2020 (July 16, 2020).