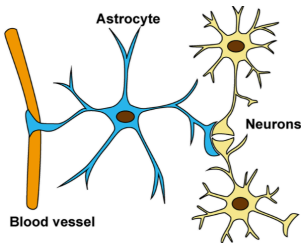
University of Michigan Guidelines for Using GFAP and UCH-L1 in Brain CT Imaging Decision-Making for Traumatic Brain Injury Evaluation

When assessing patients with traumatic brain injury (TBI), a combination of two blood tests, GFAP and UCH-L1, can help determine whether a head CT scan is necessary to identify acute traumatic intracranial injuries seen on CT but not isolated skull fractures. Here's a simple overview of how these tests work:

What is GFAP? Glial Fibrillary Acidic Protein is a structural protein in astrocytes. Astrocytes intimately surround cerebral blood vessels with the endfoot processes. When these blood vessels are injured, astrocytes are often damaged as well. Injury or death of astrocytes leads to the release of GFAP into the bloodstream, much like the release of troponin when cardiac myocytes are injured. GFAP levels are elevated within an hour following injury and start to decline after 24 hours.[1]



Summary

GFAP and UCH-L1 tests are FDA approved to help clinicians decide whether a suspected TBI patient needs a brain CT, just like D-DIMER for CT PE. A negative result (GFAP < 65 pg/mL and UCH-L1 < 360 pg/mL) suggests a CT scan is not needed.

They should be used in low-risk patients who are being evaluated for the necessity of CT imaging. However, they should not be used in injuries > 24 hours, patients on anticoagulants, patients in whom brain CT imaging can't be avoided, or patients getting a brain CT for reasons other than TBI.

What is UCH-L1?
(Ubiquitin-Carboxy Terminal Hydrolase L1) is an enzyme found in neurons. It is released when neurons are damaged or die, appearing slightly earlier than GFAP. However, the levels start to decline within 8 hours of injury.[1]

Approximately 30% of patients with negative brain CT scans show traumatic intracranial lesions on MRI.[2] GFAP and UCH-L1 quantitatively correlate with brain injury severity. They are elevated in CT-negative patients who have positive MRI findings compared to those who are negative on both CT and MRI.[3] Although most GCS≥13 TBI have a favorable recovery, elevated biomarker levels on the day of injury are associated with incomplete recovery at 6 months.[4] Therefore, patients with significant elevations and a negative CT need a referral to the TBI clinic at discharge (see flow diagram on next page).

Performance of the Abbott iSTAT GFAP and UCH-L1 tests for brain CT Decision-Making in TBI

The Abbott iSTAT test measures levels of GFAP and UCH-L1 in *whole blood*, delivering results in 15 minutes.

Interpreting Results:

Negative Test: If GFAP is less than 65 pg/mL **and** UCH-L1 is less than 360 pg/mL, the test result is considered negative, and CT imaging may not be needed.

Positive Test: If GFAP is equal to or above 65 pg/mL **or** UCH-L1 is equal to or above 360 pg/mL, the test result is considered positive, and a CT scan may be warranted.

Evidence Behind These Tests

The FDA has approved using these biomarkers in combination, based on research demonstrating their diagnostic accuracy. These tests have shown promise in supporting decision-making by helping to identify patients at lower risk, potentially reducing the need for unnecessary CT scans.[5–9]

Major studies examining the diagnostic accuracy of GFAP and/or UCH-L1 for traumatic intracranial hemorrhage

1st Author	Assay	AUC	N	Sensitivity	Specificity
Bazarian[4]	Banyan GFAP and UCH-L1	N/A	1977	97.6%	36.4%
Bazarian[5]	iSTAT GFAP and UCH-L1	N/A	1936	95.8%	40.4%
Okonkwo[6]	iSTAT GFAP and UCH-L1	0.85	1359	96.4%	30.3%
Papa[7]	Banyan GFAP only. Samples were obtained within 1 hour of injury.	0.88	804	98.1%	34.4%
Czeiter[8]	SIMOA GFAP and UCH-L1	0.89	2867	No cut-offs examined.	

From July 2021 to April 2023, we studied 1960 patients at the University of Michigan Emergency Department who had both a CBC and head CT scan for suspected TBI. Using residual CBC samples, here's what we found regarding the accuracy of these biomarkers in guiding head CT decisions:

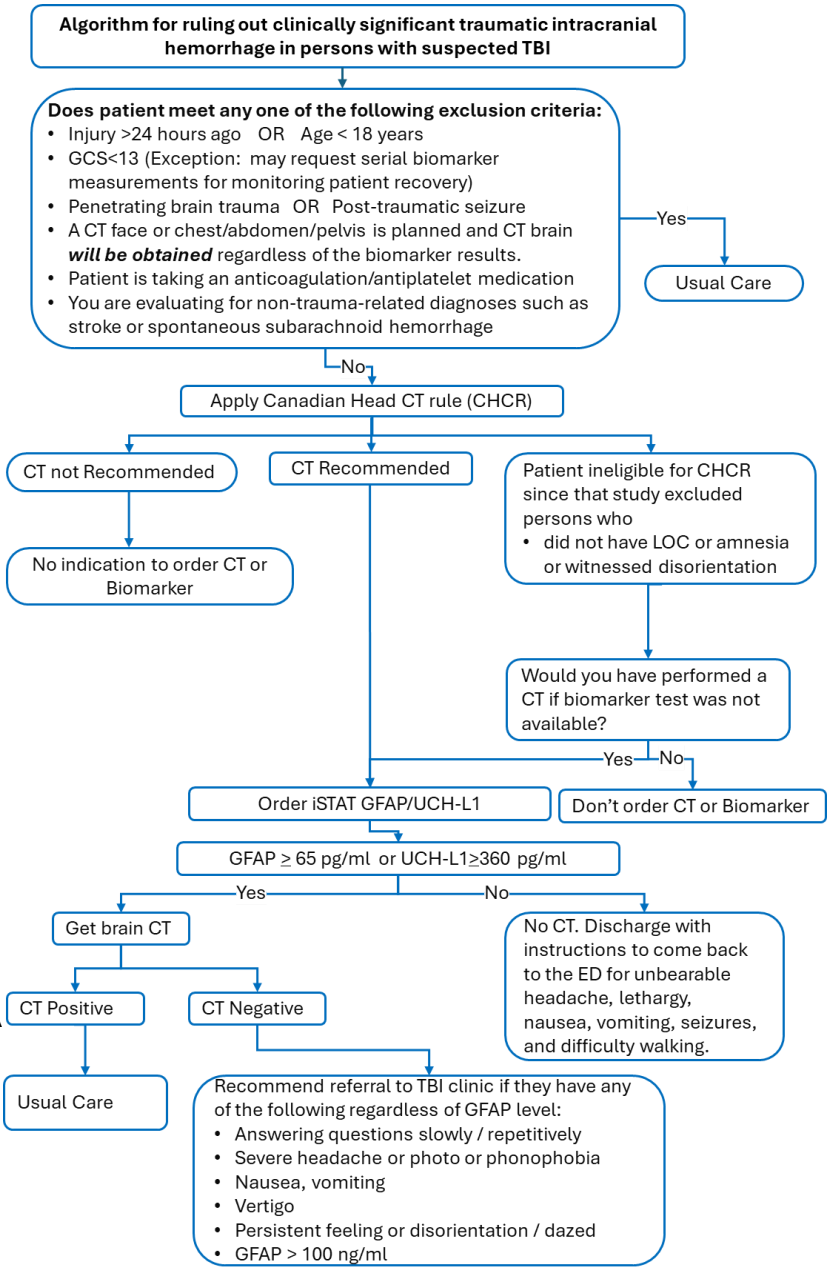
- When **GFAP and UCH-L1** were used together, the sensitivity was 97% with a specificity of 30%.

- Two patients with a clinically significant CT were missed: (1) Patient post-MVC who takes Plavix; (2) Patient with h/o cirrhosis and hepatocellular carcinoma and an INR=1.3 who had multiple falls.

When to Use This Test: Use this test for individuals who either meet the Canadian Head CT criteria for needing a head CT or who were not included in the Canadian Head CT study population (e.g., no loss of consciousness, amnesia, or disorientation) but still seem to be low-risk for a positive CT. This test is helpful when you're on the fence about ordering a CT but want additional information to make a safer decision.

When to Avoid This Test:

- **Timing**: Only use this test if evaluating injury occurring within 24 hours of blood draw.
- **Specific Scenarios**: Avoid this test in patients already set to undergo a pan-CT (chest, abdomen, pelvis) or maxillofacial CT if you plan to CT the brain regardless of the biomarker results, those with a Glasgow Coma Scale (GCS) score below 13, or those who had a seizure after the injury (higher risk for a positive CT). It is okay to use the test in intoxicated patients.
- **Non-Traumatic Cases**: This test is not recommended for cases where CT is ordered for non-traumatic reasons, such as ruling out a spontaneous subarachnoid hemorrhage.
- **Medication Restrictions**: This test should not be used for patients on oral anticoagulation/antiplatelets (coumadin, Non-vitamin K oral anticoagulants (NOACs), plavix, full dose but not baby aspirin) since we do not have sufficient data for this group.



References

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