Comparability of GFAP and UCH-L1 Measurements Using Handheld and Core Laboratory TBI Plasma Tests and Their Diagnostic Performance for Traumatic Intracranial Lesions

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Guest: Dr. Nathan Roberts is an Assistant Professor of Emergency Medicine at the Medical University of South Carolina, in Charleston, South Carolina.

Randye Kaye: Hello, and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I am your host, Randye Kaye.

Traumatic brain injury, TBI, is an injury to the brain caused by a sudden blow or jolt to the head or body, and it accounts for over 4.8 million emergency department visits in the United States. To improve triage and decrease the number of unnecessary computed tomography, CT, scans to assess these injuries, blood biomarkers can be used to rule out TBI before CT is performed.

Two biomarkers; glial fibrillary acidic protein, GFAP, sometimes known as GFAP, and ubiquitin carboxy-terminal hydrolase L1, UCHL1, have gained FDA approval for this use. These assays can be performed using platforms either at the point of care or using a large analyzer in a core laboratory.

Two such tests, the Abbott i-STAT TBI Plasma Test and the Abbott Alinity i TBI test, are examples of point-of-care and core laboratory tests, respectively. However, it is unknown if these tests are analytically consistent or clinically interchangeable. A direct comparison is needed to clarify how results vary across platforms and assess whether diagnostic accuracy and cutoff-based classification are consistent.

The November 2026 issue of *JALM* features an article comparing the analytic and diagnostic performance of these two tests. Today, we are joined by the article's first author, Dr. Nathan Roberts. Nathan B. Roberts, M.D., Ph.D., is an Assistant Professor of Emergency Medicine at the Medical University of South Carolina.

His research focuses on the use of blood-based biomarkers, particularly GFAP and UCHL1, to improve the emergency department evaluation and management of patients with traumatic brain injury. Welcome, Dr. Roberts. Why do we

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need blood-based biomarkers for traumatic brain injury in the emergency department?

Nathan Roberts: Let me first start off with my viewpoint. And I think sort of some necessary background is for this paper and for really all the work that I've had the opportunity to do in this area. It's been very much a multidisciplinary team. I'm an emergency physician, so I very much see everything through the lens of a clinician.

But I work with clinical chemists, statisticians, clinical psychologists. Everyone kind of brings their own perspective to the team. I say that because I'm certainly going to -- you'll hear as I talk about it, I very much bring the clinician's viewpoint to this.

So, if we're talking about why we need biomarkers in the emergency department, you have to first, in my mind, look at it from the perspective of the emergency department and how we actually evaluate head trauma. And most people think of head trauma as this severely injured patient that we're seeing in the trauma bay who has a very low Glasgow Coma Score, a GCS, and very obviously has a head injury. But the reality is that in the emergency department, we see across the U.S., millions of patients every year who are coming in for blunt head trauma, and the vast majority of those patients are minor head trauma. They are what we would call a GCS 13 and 15. They're walking, they're talking. Their exams may be completely normal.

They may have very little in terms of the history of the event, you know, what actually happened, whether it was a car crash, fall, that actually helps us tease out who has a serious injury. And the challenge from an ER clinician's perspective is that a lot of those patients, the vast majority of those patients we see, are minor head injuries, but a certain percentage of them are going to have very real injuries. And our role and our job in the emergency department is to figure out which patients actually have true injuries that may lead to decompensation and death.

You can exchange different phrasing for this. Traumatic intracranial lesions is one that we often use, or traumatic intracranial hemorrhage. The point is that they have a TBI, blunt head trauma, and something clinically significant going on within their brain. So the challenge is that we see millions of people in the ED every year for blunt head trauma. Most of them we see, we do an exam, we give them a history. And for the most part, those frankly aren't that helpful.

We worry about mechanisms, risk factors, things like that, but it really doesn't do a great job of risk stratifying who is more likely to have traumatic intracranial hemorrhage or

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traumatic intracranial lesion. Because of that, and because we don't want to miss an injury, we're worried about medicolegal concerns.

We're worried about making sure that patients have the answers that they want and need. We end up getting CAT scans on the vast majority of patients. Over 80% of the patients that we see with blunt head trauma that come into the ER end up getting a CAT scan.

Randye Kaye: 80%, that's a lot.

Nathan Roberts: It's a lot. The truth is that we scan the vast majority of these patients. The problem is over 90% of those are negative, but we keep doing it. This has been an ongoing issue in the field of emergency medicine. Critical decision rules have been developed, different tools that help guide and help risk stratify patients. The reality is that we continue just to scan all these patients.

And then some ER clinicians will say, okay, so what? A CT scan is part of our toolset, why not use it? But if anyone's been in the ED recently, you know that the wait time is incredibly long. Patients are in the ER for an incredible amount of time. You add in CT scans, that's one major factor, but CT scans contribute to increasing health care costs, increasing length of stay in the department, and it's a lot of radiation for our patients, especially when over 90% of those scans that we're getting are negative.

So TBI biomarkers introduce a new tool because they actually provide a blood-based objective marker of CNS injury. And that's something that we previously haven't had for TBI, if that makes sense.

Randye Kaye: Yeah, it absolutely makes sense. So how are the GFAP and UCHL1—how are they currently used in the evaluation of patients with head trauma?

Nathan Roberts: These two biomarkers are used in tandem as a single test. We're just recently moving this to the bedside. It's been used in, well, around the world more commonly than before here, but it's certainly gaining traction and growing throughout hospital systems in the US.

But at this point, we have a wealth of data, over a decade of clinical trials looking at the research behind different TBI biomarkers. And I should say that a number of different biomarkers have been identified, but at this point in 2026, two have very clearly risen to the forefront, especially for acute TBI evaluation, which is GFAP and UCHL1. Now they're used in tandem because they have complementary kinetics.

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So what I mean by that is UCHL1 is thought to spike more quickly after injury, so it's detectable in peripheral blood much faster, much sooner after injury. But it's going to decrease and it's going to go down towards this baseline much faster, really, over the first 12, 24 hours, whereas GFAP may take a few more hours to rise after injury, but it's going to stay elevated for a long time, at least a few days. So the idea is that if you're evaluating someone in the first 12, 24 hours of injury, one of these biomarkers, or both, should be elevated if they have any clinically significant injury.

If I take a step back from that, GFAP, or "GFAP" as some people will call it, and UCHL1, so these are glial and neuronal proteins. So they're enriched in the CNS and we know that if there is injury to the CNS and particularly to those cells, that they release these proteins and you can detect them in peripheral blood. We also know that the biomarker level that is detectable in peripheral blood correlates with the degree of injury.

So why that matters is you may have a patient who has clinically signed symptoms of a concussion, but they don't have any findings on a CT or an MRI, which is more sensitive than a CT, but you'll see a little increase in these biomarkers compared to someone who's not injured versus someone who you're seeing in the trauma bay and has a very significant head injury. And very obviously, as TBI with a CT scan to match, they're going to have a much higher level of biomarkers. So we see through a lot of studies, what we see in clinical practice is that the biomarker levels correlate with the degree of injury.

The opportunity there is that if you have a patient that you're evaluating for blunt head trauma, you can send these biomarkers and they come back quickly. It's a blood test, so we can get into the different assays in a bit, but there's either a portable bedside test or there's also a core lab test that you can send, but they come back certainly faster than you can get a CT in most situations. And if the biomarkers are not elevated beyond a certain threshold, then you can say the likelihood that a patient has a clinically meaningful injury on a CT or clinically meaningful intracranial hemorrhage or anything like that is low. It allows you to rule out clinically traumatic intracranial hemorrhage, things like that.

Randye Kaye: Okay, thank you. Are these tests, this is a separate question, are they less expensive than a CT?

Nathan Roberts: Yes. Without getting into the individual numbers, they are less expensive, certainly to the patient and to the hospital as well. The numbers are one aspect, but the harder to quantify aspect is the time, right?

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How do you -- I mean, certainly we can look at minutes, hours that patients are spending in the department, but I think when you talk about the potential savings from this test, certainly there is the pure monetary aspect of how much money can we save a hospital system or how much money can we save our patients, which gets into the complications of insurance and so on.

But what is also just as exciting, perhaps more exciting from my clinician standpoint is that we were getting patients out of the hospital and out of the ER much faster when we we're able to use these blood tests. And what that really means is that we have patients in the waiting room. Obviously, I'm not in ER right now, but I can imagine there are people waiting in our waiting room and they will be there when I go into my shift later. Those patients aren't being fully cared for yet, right? They're not being cared for until they can get back to a room.

There's some nuance and caveat to that. It's not like we're ignoring them, but we want them back into our ER room so that we can actually appropriately assess them and care for them rather than out in our waiting room. So every minute that we can save by sending a blood test to get a patient out of the room or out of the ER safely is another minute that we can spend bringing one of those patients back from the waiting room and then assessing them faster so that they're no longer waiting.

So I think there's certainly the monetary aspect, but I think what's more exciting from my standpoint is the amount of time we can save and how much more efficiently we can move patients through the department. So that really gets us to our next patient safely much faster.

Randye Kaye: Right. I understand. So regarding this study, what clinical question did it seek to answer and how does that fit within the existing TBI biomarker and literature?

Nathan Roberts: No, great question. So, I think it's also important to give a little necessary background, which is we now have a number of FDA cleared platforms, right? So we have what this paper looks at, the i-STAT TBI plasma test, which is the electrochemical immunoassay, and that's from the i-STAT instrument. So that's a portable instrument versus the Alinity i TBI test, which is your core lab chemiluminescent immunoassay. At this point, when this paper came out, or when we were doing this work, I should say, there were these two FDA cleared assays. Now we have another one.

We have a whole blood test that can be run at bedside. But there were these two assays and independently, they had been studied in different cohorts. You know, we had -- we

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meaning other research in this area -- had defined and shown the diagnostic accuracy for traumatic intracranial lesions. And they looked very similar.

There really wasn't a lot of data out there comparing the two head-to-head. Now, if you take sort of a bigger step back and you say, from a clinician standpoint or a hospital standpoint, or, you know, a clinical chemist standpoint, which lab are you, which assay are you going to choose? Is it more based on, you know, operational aspects or are there differences in diagnostic accuracy that you need to bring into consideration?

Because, you know, at least from my standpoint, you know, we can talk about turnaround time, costs, all those things, but if one test doesn't have the same diagnostic accuracy as the other one, well, then that's, that's going to be a major issue. And we should pick the one that has the, you know, the highest sensitivity. So there's that question, which is from the diagnostic accuracy standpoint, if we truly compare these head-to-head, how do they compare?

But there's also the question of what do we do with all of these studies? Where in one cohort, they're using the Alinity i TBI test, the core lab test. And in another study, they're using the i-STAT TBI plasma test. Can we compare that data? Can we look at quantitative numbers? Can you take a value from one assay? Can you compare it to the other assay? And how can we actually potentially combine the results from different studies?

And related to that question, in real world practice, as these tests continue to gain traction and continue to be used throughout the U.S., different institutions are using different versions of the test, right? So we are using the Alinity i TBI test, which is the core lab test on the Alinity i system. And let's say a hospital that we may receive patients from is using the i-STAT version of the test. Can we actually compare those?

If we were to look at serial measurements of the biomarkers or something along those lines, how do the numbers actually compare? Those are some of the questions that we were trying to answer, is that if we actually compare these two tests head-to-head, how do they really compare in terms of diagnostic accuracy? And how do the concentrations actually compare?

Randye Kaye: Okay, so how comparable were they? And what do these findings mean for hospitals choosing between point of care and core laboratory TBI testing?

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Nathan Roberts: I think the biggest takeaway for me is that they both maintain a very high sensitivity. So, in our cohort, we had 32 clinically significant injuries. So, looking at the diagnostic accuracy for these two assays, they both captured all of those, which for me is step one, right?

If one is missing injuries, then I would say that, you know, obviously there's more that goes into this, but that would make me pause. If one test wasn't capturing something and the sensitivity is lower than say, well, I would prefer the test that has a higher sensitivity.

So both assays captured all clinically significant injuries, all 32 in our cohort. And then if you look at the individual classification, meaning the Alinity i, if it's positive, is the i-STAT also positive? We saw that the classification, so the positive negative agreement was roughly 92%, which is good. You can also, you know, from the converse say, okay, what about the other roughly 8% that they disagree on?

So we dove into that a little bit. What we saw is that, especially for GFAP, or "GFAP," we see that when there was discordance, when there was a disagreement, a lot of times it's not that there's a wildly different GFAP result. It's that on one assay, it's below the cutoff threshold, but on the next one, it's just slightly above.

And it's one of those false positive results where one assay is just slightly above. And it was also bidirectional, meaning that it wasn't like one assay had more false positive results than the other didn't. I guess you could say misclassified, but they both had false positive results just slightly on one end of the other for roughly a similar number of examples.

We saw slightly different results with UCHL1. What I mean by that is UCHL1 false positive results seem to trend more towards the, or didn't trend more towards the Alinity i. And we saw that the specificity was a little bit lower, meaning there were more false positives on the Alinity i test.

Personally, I think that's also an area for future research. And that gets into some of the limitations of this study, which is that the Alinity I system in other cohorts, we've also seen that it has a very similar specificity overall. And granted, these are not head-to-head comparisons, but a similar specificity compared to the i-STAT test.

So different platforms, different assays have shown similar specificity. When we were comparing head-to-head in this cohort, we did see a small decrease in specificity on the Alinity i system. I think that is something that is worth looking at again.

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But I think the big takeaway from my standpoint is that they both captured all of the clinically significant injuries and the overall agreement was high, which was reassuring. And what that really tells me is that the diagnostic accuracy really shouldn't be the driving question behind which platform you choose in your hospital. You really should be looking at things that make more sense operationally.

Obviously, we're always hoping for more and more data, but this fits in with the growing literature saying that these tests have similar excellent diagnostic accuracy and are great rollout tests for traumatic intracranial hemorrhage, one traumatic intracranial hemorrhage. So you can really make a decision based on what's best for your hospital system or your ER rather than looking at the individual diagnostic accuracy or any differences in that.

Randye Kaye: Okay, thank you. So question, are these ready for routine clinical use in the ED?

Nathan Roberts: They are, and they're growing in popularity. My old institution, which most of the authors on this paper were at the University of Michigan. I've now moved on -- so the University of Michigan is using this test and they're having great success. We have been using the Alinity i TBI test, the core lab test at MUSC where I am now since the summer. And frankly, it's been fantastic.

And it's really exciting for a clinician scientist. We're always talking about bench to bedside. And I think it's a lot of fun to see the decades of research that have gone into these tests and developing to understand these biomarkers. And it's hard to describe how exciting it is to actually see that for the first time in true clinical practice. I just have a grainy picture on my phone. So I was taking a picture of a computer screen. But with the first patient where we send the test is negative, we save them a CT scan.

So they are finally at the point where they are ready for clinical use. And it's a fantastic rule out test. And we're learning a lot of lessons. And it's still early here at our institution because we've been running this really since June. Faculty love it. The clinicians love it. Patients love it. They love having that objective biomarker test, especially the ones that they come in and you really don't want to get them a CT. And you try to reassure them that this is unlikely to show anything.

They still want to test, right? They want something other than just a reassurance and being able to show them something objective, saying, look, these are markers of CNS injury. And because of this, you don't need a CT. It's really been a lot of fun to see. So the short answer is yes, they are ready for

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clinical use. They're FDA cleared. We have multiple FDA cleared assays. And we are continuing to see more EDs adopt this around the country and really around the world, but certainly throughout the US.

Randye Kaye: Wonderful. So just one follow up question here. My final question, where do these TBI biomarkers go next beyond simply deciding who needs a head CT?

Nathan Roberts: This could be an entire conversation in itself. And I'll try not to go off on too many tangents because I think this is one of the more exciting aspects of biomarker research. Especially GFAP, UCHL1. I really think this is the tip of the iceberg, what we're doing now, which is really re-stratifying and deciding who needs a CT and deciding who can be safe for -- basically CT triage right now. I think that's the tip of the iceberg because when you get back into that data, looking at how biomarkers correlate with the degree of injury, I think we're going to move beyond CT triage to also prognosis, recovery, looking at things like serial biomarkers, things like pediatric head injury. Right now it's just adults.

So I think there's a lot of interesting next steps that people are working on, but I think we are also going to see where biomarkers are going to be used to actually define TBI for individual patients. What I mean by that is right now, a lot of what we use is GCS, which is a coma score. And frankly, it doesn't really capture the heterogeneity of TBI.

You can have patients that have two scores that have wildly different injuries. And if anyone's not familiar with it, you lose points on your GCS score for not opening your eyes, not to bash the GCS. We certainly use it clinically and it has important roles, but the point is that it doesn't capture the heterogeneity of TBI.

But now there's a major NIH, NINDS initiative, CBI-M, where they're trying to use more of a multifaceted, personalized definition of TBI for individuals. And that's bringing in factors like clinical factors, imaging factors, but it's also introducing biomarkers. So it is bringing in the objective data that biomarkers give you.

So if you have a patient with a GFAP of 50 versus a GFAP of 300, it gives you some objective and quantitative information about CNS injury. So I think one of the important next steps and where biomarkers are going is that we are going to see them not just used for CT triage, but also to provide more quantitative data to help define individual injuries for patients so that you have more of an individualized, personalized definition of your individual TBI. So, I think those are some of the most exciting next steps where we'll see these biomarkers next.

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Randye Kaye: Okay. Thank you. So very interesting. Thank you so much for joining us today.

Nathan Roberts: Thank you so much for chatting.

Randye Kaye: That was Dr. Nathan Roberts discussing the *JALM* article, "Comparability of GFAP and UCH-L1 Measurements Using Handheld and Core Laboratory TBI Plasma Tests and Their Diagnostic Performance for Traumatic Intracranial Lesions." Thanks for tuning in to this episode of *JALM* Talk. See you next time and don't forget to submit something for us to talk about.

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