Study Title	Cranioplasty Before or After 30 Days Following Decompressive Craniectomy for Traumatic Brain Injury (CP-TIMING)
Funding I/C	Department of War (DOW)
Study Description	CP-TIMING is a prospective, multicenter, adaptive, dual-stratum randomized controlled trial designed to determine the optimal timing of cranioplasty (CP) following decompressive craniectomy (DC) for traumatic brain injury (TBI). The trial evaluates whether biologically guided earlier CP, based on an objective CT assessment of cerebral swelling resolution, reduces CP-related treatment burden compared with standard delayed reconstruction. By incorporating an imaging-based assessment of biological readiness into treatment allocation, CP-TIMING aims to generate the first Level I evidence to guide CP timing after DC.
Study Design	Adult patients (≥18 years) undergoing unilateral DC for TBI will undergo a standardized non-contrast head CT at Day 30 (±7 days) and be stratified according to biological readiness using the Visual CP Scale. Patients demonstrating adequate swelling resolution (Visual CP Scale ≥4) will be randomized 1:1 to ultra-early CP at Day 30 (±7 days) or standard CP at Day 90 (±7 days). Patients with persistent swelling (Visual CP Scale <4) will be randomized 1:1 to intermediate CP at Day 60 (±7 days) or standard CP at Day 90 (±7 days). The primary endpoint is CP-related treatment burden at 6 months (i.e., post-traumatic hydrocephalus, infection, wound complications, etc.), with neurological recovery measured by the Glasgow Outcome Scale–Extended (GOSE) as a key secondary outcome. Randomization will be stratified according to surgeon's choice of implant.
IRB	TBD
Coordinating Center	JHU
Study Length	Study total 60 months (5 years), Duration for participants is 12 months
Study Enrollment #	N~400
Eligibility Criteria	**Inclusion Criteria** - Age >= 18 years. - Patient treated with unilateral decompressive hemicraniectomy. - Patient's eligible for surgery within 14 days after decompressive hemicraniectomy as determined by the treatment team - Legally authorized representative or patient able to provide informed consent. **Exclusion Criteria** - Active systemic or local infection/contamination at time of randomization. - CSF diversion in place before TBI requiring decompressive craniectomy. - Bilateral craniectomy. - Life expectancy 3 months due to comorbid conditions present before TBI.
Total # of Sites	30-35
Site Requirements	Study sites will need to have the following at their site to be considered: • American of College Surgeons (ACS)-verified Level I or Level II trauma center (or equivalent high-volume neurotraumta center) with an active neurosurgical program that perofrms hemicraniectomies and cranioplasties • Established multidisciplinary traumatic brain injury (TBI) care, including neurosurgery, neurocritical care, trauma and rehabilitiation services • Infrastructure to perform longitudinal follow-up and outcome assessments through 12 months following procedure
Site Invesitgator Qualifications	Site Invesitigators should have the following: • Board certified neurosurgeon • Experience managing patients undergoing hemicraniectomies and cranioplasties
Investigator Therapeutic Area	Neurosurgery

Key Timeline Dates:	<u>The following dates are projections and subject to change:</u> **Site Selection Decisions: July 2027** **Site Selection Notifications: August 2027** **Enrollment Begins: January 2028** **Last Patient/Last Visit: June 2032** ***(6-month follow-up after final enrollment)*** **Study Closure: December 2032**