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Neurovascular News

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Expanding the Endovascular Frontier of Neuro-Oncology

Jason Luo, Justin H. Granstein, MD, MPH, Philipp Taussky, MD, Christopher S. Ogilvy, MD

Introduction

Cancers associated with the head and brain have been known to be notoriously difficult to treat. Therapies carry numerous risks and complications; therefore, it is always the care team's responsibility to explore paths to alleviate risk while maximizing benefit to the patient. Developments in endovascular neurosurgery have grown exponentially in the 21st century, opening doors to new fields of therapeutic investigation such as endovascular neuro-oncology. Here at BIDMC, our team is involved at the forefront of this growing field. We are positioned to use neuro endovascular techniques for tumor diagnosis, complication management, and soon, new techniques of intervention.

Diagnostic and Decision Aiding Procedures

Pre-operative cerebral angiography is a useful tool used in cerebrovascular neurosurgery that allows surgeons to view the patient's vasculature and identify lesions. Similarly, in neuro-oncology, angiography aids in identifying the tumor's feeding vasculature and provides valuable decision making and risk management information. The endovascular surgeon can also, if necessary, selectively embolize arteries with high operative bleeding risk, allowing for improved tumor resection and postoperative outcomes.[1]

Another pre-resection technique in the endovascular surgeon's toolkit is the Balloon Test Occlusion (BTO). This technique describes inflating a balloon in a target blood vessel to temporarily occlude it and observing the awake patient's neurological status for changes or deficits. BTO is performed to identify vessels that are critical for cerebral perfusion, and those that have sufficient collateral support. By simulating vessel sacrifice under controlled conditions, BTO helps determine whether vessel occlusion during surgery can proceed safely and without neurological risk to the patient.[2] This can be accomplished for large vessels (carotid or vertebral artery) or smaller intracranial vessels.

Complication Management and Vessel Repair

Hemorrhages caused by cerebral tumors can occur when the lesion invades surrounding vasculature and tears thin immature vessels, or as an iatrogenic complication of surgery, radiotherapy, or immunotherapy. Carotid Blowout Syndrome (CBS) is a devastating hemorrhagic condition in which a branch of the carotid artery hemorrhages and causes life-threatening bleeding in cervical vessels. Studies have demonstrated that endoscopic approaches to treat skull base tumors put the dense internal carotid artery (ICA) vasculature at risk, and naso-/oropharyngeal tumors treated with radiotherapy have been associated with CBS of the external carotid artery.[3] In these instances, urgent repair of the damaged vessel is necessary and often done

endovascularly through the placement of a stent or flow diverter.
If vessel repair is not possible, embolization of the bleeding artery via coiling or embolic particles is performed. In the past twenty years, covered stents have become an alternative endovascular approach to traditional stenting due to its ability to reconstruct the affected artery while maintaining perfusion.[3] Techniques of endovascular repair and surgical control of hemorrhage are managed coordinating teamwork between ENT surgeons, Neurosurgeons and Neuroendovascular surgeons.

Blood-Brain Barrier (BBB) Disruption

Treating malignant tumors requires adequate delivery of chemotherapeutic drugs to the site of the tumor. This is particularly challenging in the brain due to the selective blood-brain barrier (BBB). The BBB is made up of endothelial tight junctions and acts as the brain's natural defense against toxins and infectious agents. However, it presents an obstacle against treating cerebral diseases like cancer since therapeutic agents cannot cross the BBB.
Recent techniques have emerged to temporarily open the BBB, disrupting its tight junctions long enough for drug delivery.

The earliest attempts at BBB disruption were done via manipulation of brain tissue osmolarity. By osmotically shrinking endothelial cells with high concentration of mannitol for example, the intercellular junctions widen, resulting in transient BBB opening. However, the BBB in primary brain tumors can already be partially disrupted and therefore, osmotic therapy has limitations and often has a more pronounced effect on normal tissue than on tumor tissue.

Another technique developed to disrupt the BBB is focused ultrasound (FUS). This approach involves intravascular injection of microbubbles before an extracranial ultrasound probe delivers ultrasonic waves at a precise location, often under MRI guidance. FUS mechanically opens the BBB through targeted ablation of microbubbles, which leads to stretching of the endothelial cells and temporary widening of junctions.[1]

Despite these advances, while studies show increased effectiveness of therapies when paired with BBB disruption, current evidence suggests that BBB disruption alone is not enough for effective drug delivery to the tumor.[4] Research has demonstrated that systemically administered drugs penetrate high-grade brain tumors in a highly heterogeneous manner, with substantial variability in drug concentrations even within BBB disrupted contrast-enhancing regions. These findings highlight that BBB disruption alone is insufficient to ensure adequate or uniform drug delivery, underscoring the need for targeted drug-delivery strategies that actively control regional perfusion and barrier penetration in neuro-oncology.[4]

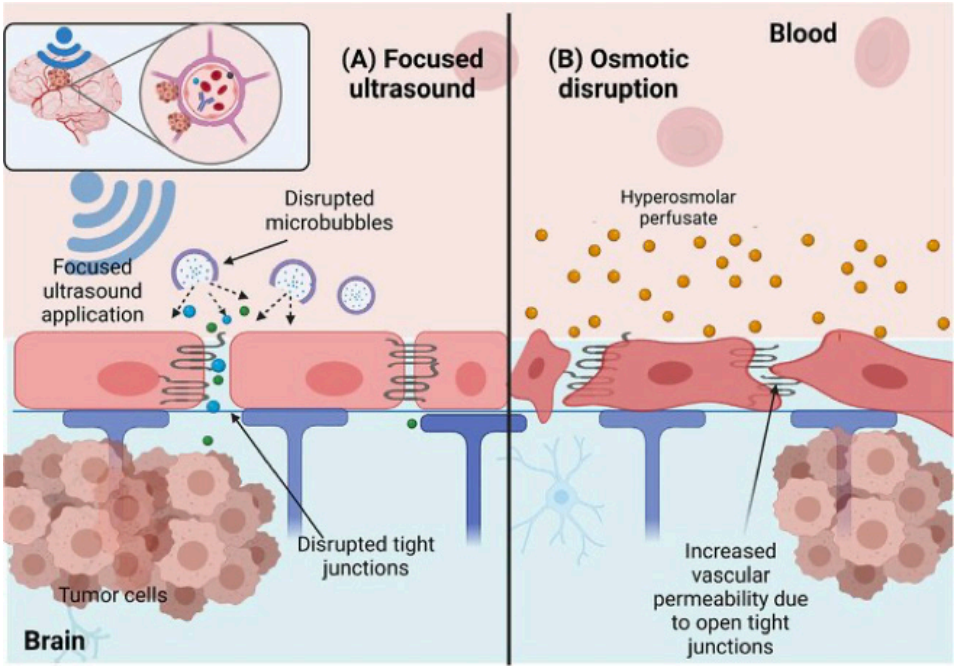

Fig 1: Rathi, Sneha et al. "The influence of the blood-brain barrier in the treatment of brain tumours." Journal of internal medicine vol. 292,1 (2022): 3-30. doi:10.1111/joim.13440

Intra Arterial Tumor Access

Intra-arterial tumor access represents a vascular-centric approach to drug delivery in neuro-oncology, designed to overcome the limitations of passive systemic therapy. Through microcatheters inserted at a distal artery like the femoral or radial artery, the endovascular physician can carefully access, navigate to, and deliver therapies directly to the intracranial vasculature. With modern advancements in endovascular devices, Endovascular Selective Intra-arterial Access (ESIA) is being explored in conjunction with highly specific BBB disruption to overcome the limitations of BBB disruption alone.[1] Currently, the results of Phase I clinical trials demonstrate BBB disruption + ESIA infusions of monoclonal antibodies such as bevacizumab and cetuximab to be well-tolerated in both adults with recurrent glioblastoma and children with high grade or diffuse pontine gliomas.[5,6] Studies testing for efficacy are warranted and underway.

In addition to antibodies, ESIA has been explored as a delivery strategy for radioembolic therapies such as yttrium-90 (Y-90) microspheres.[1] Y-90 radioembolization has been used extensively in hepatobiliary and gastrointestinal malignancies, including hepatocellular carcinoma, metastatic colorectal cancer, neuroendocrine tumors, and biliary cancers, where selective arterial delivery allows high local radiation doses while sparing surrounding tissue. Building on this experience, early feasibility studies are now evaluating super-selective intra-arterial delivery of Y-90 for intracranial tumors, including recurrent glioblastoma, with the goal of achieving focal tumor irradiation while minimizing toxicity to normal brain.

Beyond radioembolization, intra-arterial access is increasingly recognized as a delivery platform rather than a single therapeutic modality. Oncolytic virotherapy represents one such application. Delta-24-RGD, a tumor-selective

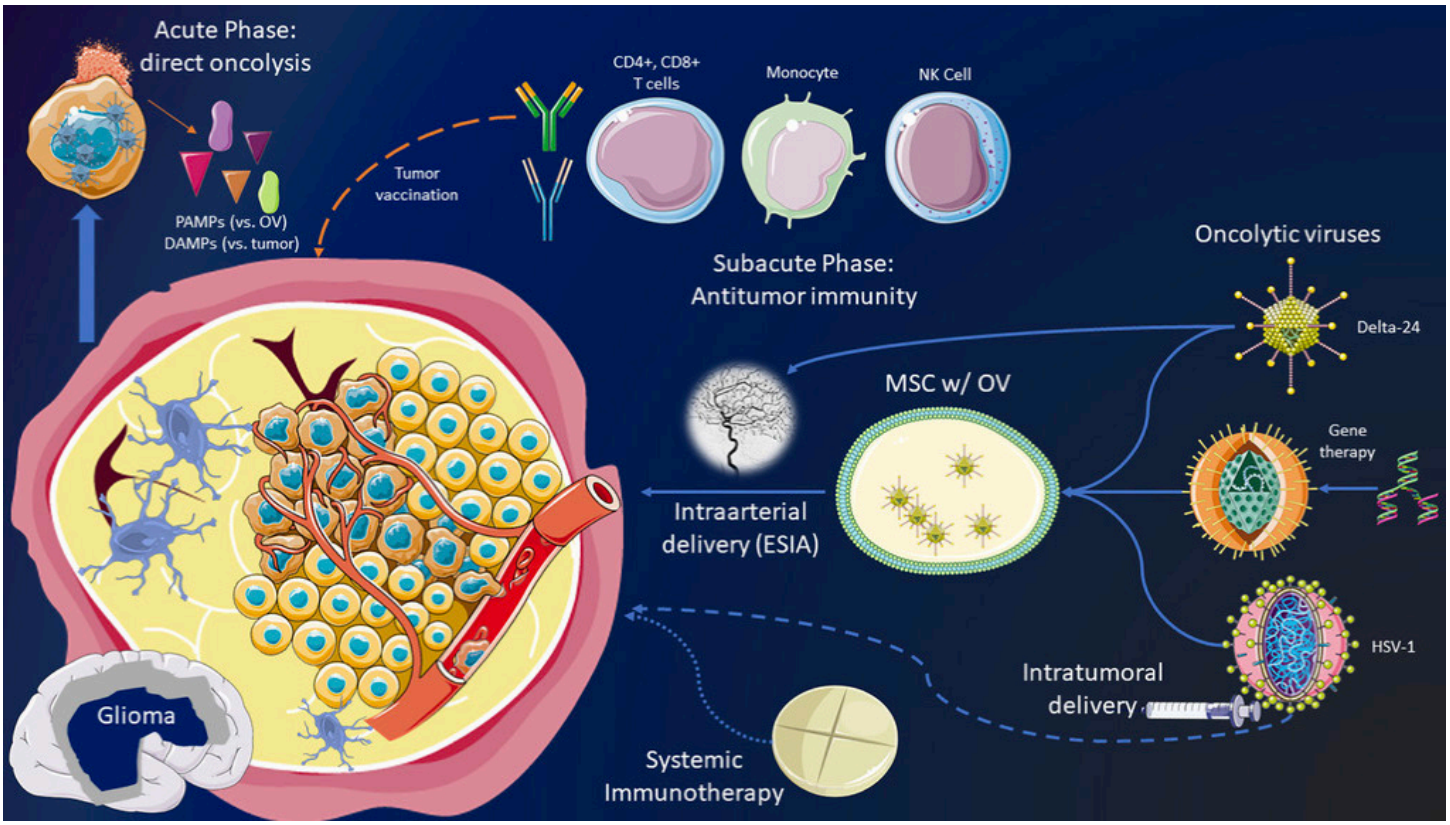

Fig 2: Srinivasan, Visish M., Frederick F. Lang, and Peter Kan. "Intraarterial Delivery of Virotherapy for Glioblastoma." Neurosurgical Focus, vol. 50, no. 2, 2021, p. E7, https://doi.org/10.3171/2020.11.FOCUS20845.

oncolytic adenovirus, has demonstrated the ability to replicate within glioma cells, induce direct oncolysis, and stimulate downstream immune responses.[1] To overcome the limitations of intratumoral injection, investigators have developed intra-arterial delivery strategies using mesenchymal stem cells as carrier vehicles, leveraging their tumor-tropic properties to transport and release the virus within tumor tissue following endovascular infusion. Early-phase clinical trials have demonstrated the safety and feasibility of this approach, with ongoing studies evaluating its therapeutic potential.

A longstanding concern surrounding intra-arterial therapies has been the potential risk of cerebral ischemia or stroke resulting from arterial catheterization, flow disruption, or embolic complications. However, advances in endovascular technique, microcatheter design, and procedural imaging have substantially mitigated these risks. Contemporary intra-arterial approaches rely on atraumatic, flow-directed microcatheters, super-selective distal access, and controlled infusion protocols that preserve physiologic blood flow during therapy delivery. Across early-phase clinical trials evaluating intra-arterial chemotherapy, monoclonal antibodies, and cell-based therapies, rates of ischemic stroke have been low.[7] These findings suggest that, when performed with modern endovascular tools and careful patient selection, intra-arterial tumor access can be achieved safely without introducing unacceptable cerebrovascular risk.

In addition to therapeutic delivery, endovascular approaches are being investigated as a novel diagnostic tool. Early work has demonstrated that vascular material can be retrieved endovascularly without direct penetration of brain parenchyma, such as in studies that collected endothelial cells from cerebral aneurysms via catheter sampling and analyzed them for gene expression profiles. This strategy offers a minimally invasive and potentially repeatable means of molecular profiling, potentially for tumors that are deep, diffuse, or not amenable to surgical biopsy. While still investigational, intra-arterial biopsy highlights the expanding role of endovascular platforms not only in treatment, but also in the diagnosis and longitudinal monitoring of brain tumors.

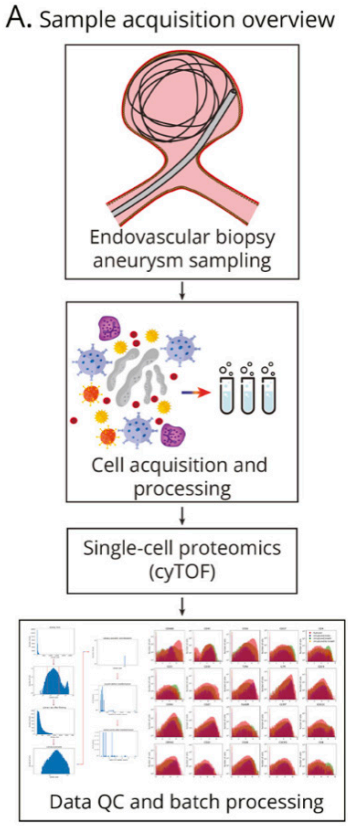

Fig 3: Antonios, Joseph et al. "Immune Characterization of Intracranial Aneurysms Using Noninvasive Endoluminal Biopsy With High-Dimensional Single-Cell Phenotyping." Neurology vol. 105,8 (2025): e214185. doi:10.1212/WNL.0000000000214185

Endovascular Intrathecal Approaches

Endovascular innovation in neuro-oncology extends beyond tumor-directed therapies to the management of tumor-associated neurological conditions, including hydrocephalus. Hydrocephalus is characterized by pathological accumulation of cerebrospinal fluid (CSF) within the cerebral ventricles due to impaired CSF flow or absorption. Traditional treatment relies on ventriculoperitoneal (VP) shunt placement, a procedure that diverts CSF from the ventricles to the peritoneal cavity through surgically implanted hardware.
While effective, VP shunts are associated with high complication and failure rates, with many requiring revision within two years due to infection, obstruction, or mechanical failure.[8]

The eShunt® (Cere Vasc Inc.) represents a novel endovascular, biomimetic approach to hydrocephalus management that seeks to restore physiologic CSF absorption rather than bypass it. Under normal conditions, CSF is absorbed from the subarachnoid space into the venous circulation through arachnoid granulations. The eShunt is designed to recreate this pathway by providing a controlled conduit for CSF to drain from the subarachnoid space into the venous system, typically via the inferior petrosal sinus and internal jugular vein. By leveraging existing venous anatomy and pressure gradients, this approach aims to normalize ventricular size without the need for intracranial catheters or long subcutaneous tubing.

Beyond its role in CSF diversion, the eShunt also introduces a novel opportunity for endovascular drug delivery to the central nervous system. By providing controlled access to CSF pathways via the venous system, this approach may enable repeat, minimally invasive delivery of therapeutic agents into the subarachnoid space without the need for ventricular catheters or intrathecal injections. Traditional routes for intrathecal therapy like lumbar puncture, Ommaya reservoirs, and intraventricular catheters are limited by uneven drug distribution, infection risk, and procedural morbidity. In contrast, an endovascular CSF access platform could allow therapies to be administered in a controlled, image-guided manner while leveraging natural CSF circulation for broader CNS distribution.

Preclinical studies have demonstrated the feasibility of endovascular cisternal access for delivery of biologics, viral vectors, and gene therapies, achieving widespread parenchymal distribution without direct penetration of brain tissue.[9] When combined with advances in targeted intra-arterial delivery and BBB modulation, the eShunt device highlights a future in which endovascular systems serve not only to manage hydrocephalus, but also as physiologic conduits for CNS drug delivery. While clinical validation is ongoing, this dual functionality underscores the broader potential of endovascular neuro-oncology to integrate treatment of both tumor burden and therapy delivery within a single minimally invasive framework.

Looking Forward

Advances in endovascular diagnostic capabilities, intra-arterial tumor access, and targeted drug delivery highlight the emergence of endovascular neuro-oncology as a distinct and rapidly evolving subspecialty. By shifting therapeutic paradigms from passive systemic exposure to precise vascular targeting and physiologic restoration, these approaches offer new opportunities to improve outcomes while minimizing morbidity. Continued collaboration between neuro-oncology, neurosurgery, and endovascular specialists will be essential as feasibility studies mature into efficacy trials and these techniques move closer to broader clinical adoption. Given our recently established collaborations with the Dana Farber Cancer Institute, the BIDMC Brain Aneurysm Institute is uniquely positioned for advances in these collaborations.

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Carotid artery stenting with medical management provides significant stroke reduction compared to medical management alone: A brief overview of the CREST-2 results.

Suroop Marwah, Syed Sarmad Bukhari, MD, Justin H. Granstein, MD, MPH, Philipp Taussky, MD, Christopher S. Ogilvy, MD.

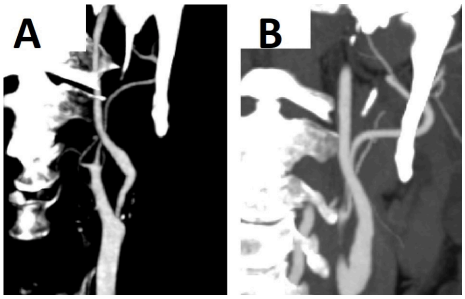

Figure 1. CT angiogram demonstrating severe carotid artery stenosis before plaque removal (A) and restoration of arterial patency after endarterectomy (B). The procedure removes atherosclerotic plaque directly from the artery to improve blood flow and reduce future stroke risk

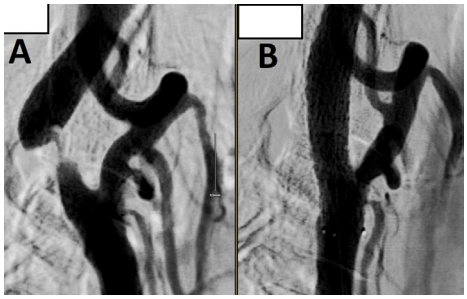

Figure 2. Diagnostic angiogram showing high-grade internal carotid artery stenosis before intervention (A) and improvement of stenosis following endovascular stent placement (Panel B). The stent expands the narrowed segment, improving cerebral blood flow and reducing long-term stroke risk

Introduction

Asymptomatic carotid artery stenosis is defined as severe narrowing of the internal carotid artery without a prior stroke or transient ischemic attack and is commonly detected in older adults. It is often found incidentally during imaging or during evaluation of a carotid bruit. For many years, patients with severe (≥70%) narrowing have been recommended to undergo surgery (carotid endarterectomy) to reduce future stroke risk.

Randomized trials from the 1990s and early 2000s showed that carotid endarterectomy reduced stroke risk compared with the best medical therapy available at that time. However, cardiovascular prevention has improved dramatically since then. High-intensity statins, tighter blood pressure control, modern diabetes therapies, smoking cessation strategies, and advanced lipid-lowering agents have all contributed to lower overall stroke rates.

This progress led to an important clinical question: when patients are already receiving intensive modern medical therapy, does carotid revascularization add meaningful reduction in stroke risk? The CREST-2 trial was designed to answer this question.

Traditional treatments

Carotid endarterectomy is an open surgical procedure that removes plaque directly from the artery. It has long been considered the standard of care for severe carotid stenosis. However, it requires a neck incision and temporary clamping of the artery. Even in experienced centers, the 30-day risk of stroke or death is generally between 1% and 3%, and there is also a risk of myocardial infarction and cranial nerve injury.

Carotid artery stenting is a minimally invasive catheter-based procedure. A stent is placed within the artery to improve blood flow, avoiding open surgery. Although earlier trials suggested a slightly higher early stroke risk compared with surgery in some populations, procedural techniques and operator experience have improved substantially over time.

All patients in CREST-2 received aggressive medical therapy. Blood pressure targets were below 130 mm Hg, LDL cholesterol was targeted to below 70 mg/dL, and patients received antiplatelet therapy, diabetes management, smoking cessation counseling, and lifestyle support. This level of structured prevention reflects current best practices in primary care.

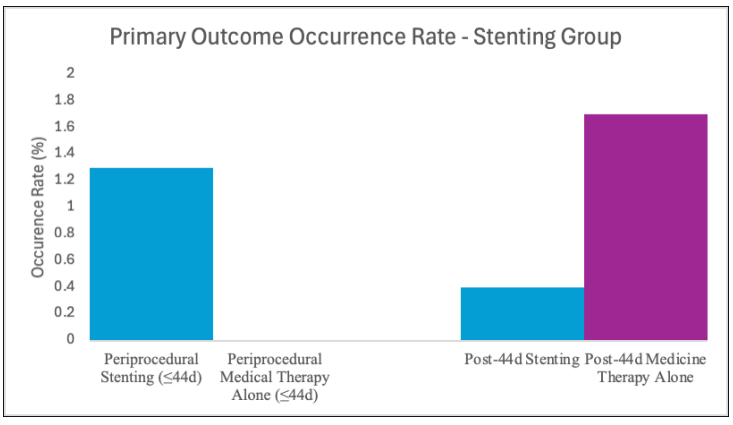

Figure 3. Comparison of peri-procedural (≤44 days) and post–44 day primary outcome rates in patients randomized to carotid artery stenting plus intensive medical therapy versus intensive medical therapy alone. Although stenting was associated with a small early procedural risk (1.3%), long-term post–44-day event rates were substantially lower than with medical therapy alone, resulting in a significant overall reduction in 4-year stroke risk.

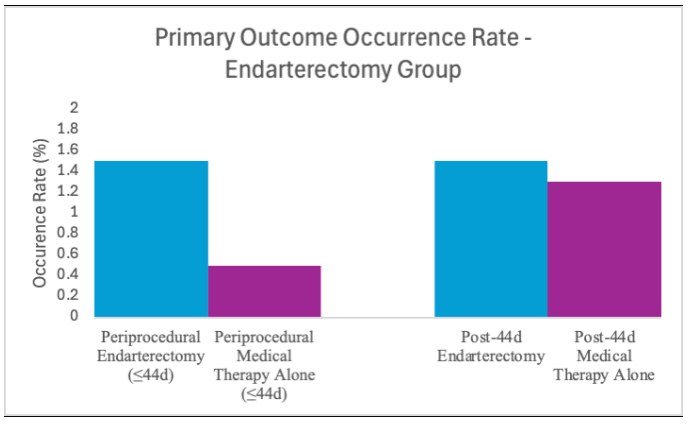

Figure 4. Bar graph comparing peri-procedural (≤44 days) and post–44-day primary outcome rates in patients randomized to carotid endarterectomy plus intensive medical therapy versus intensive medical therapy alone. Surgery was associated with a modest early procedural risk and did not demonstrate a statistically significant reduction in the composite 4-year primary outcome compared with medical therapy alone.

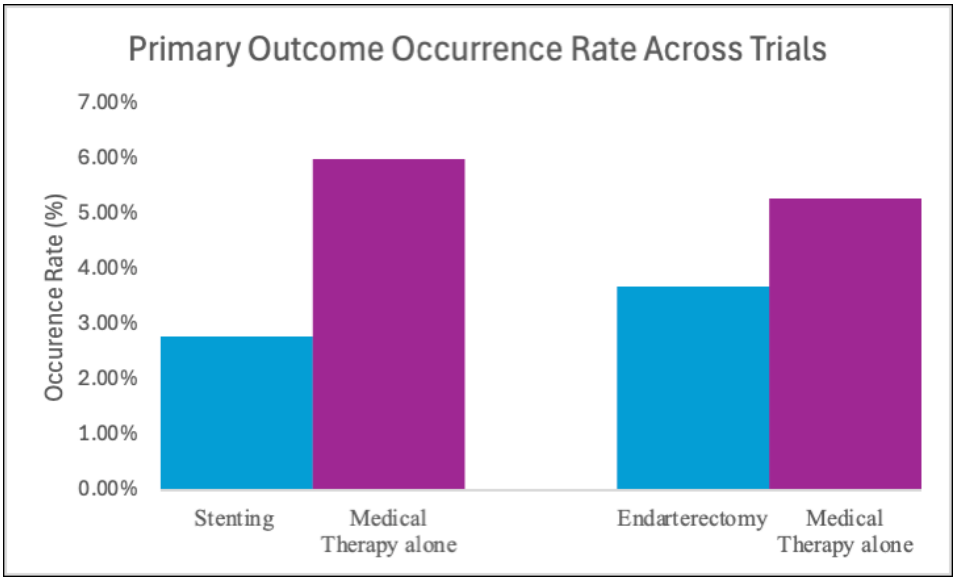

Figure 5. 4-year composite primary outcome rates (stroke or death within 44 days or ipsilateral stroke through 4 years) among patients receiving carotid stenting plus intensive medical therapy, carotid endarterectomy plus intensive medical therapy, and intensive medical therapy alone. Stenting showed a statistically significant reduction in 4-year event rates compared with medical therapy alone, whereas for endarterectomy, this difference did not reach clinical significance.

CREST-2 trial

CREST-2 consisted of two parallel randomized trials. One compared stenting plus intensive medical therapy with medical therapy alone. The other compared endarterectomy plus intensive medical therapy versus medical therapy alone. Patients were at least 35 years old, had at least 70% asymptomatic carotid stenosis, and had not experienced a stroke or TIA within the prior six months.

The primary outcome combined early stroke or death within 44 days of randomization with ipsilateral ischemic stroke over four years of follow-up. This design allowed investigators to capture both the short-term procedural risk and the long-term stroke prevention benefit.

Results

One of the most important findings was how well modern medical therapy performed. At 4 years, the primary event rate in the medical-therapy group was 6.0% in the stenting trial and 5.3% in the endarterectomy trial. This corresponds to an annual stroke risk of roughly 1.4–1.6%, which is substantially lower than rates reported in older studies.

In the stenting trial, the four-year event rate had an absolute risk reduction of 3.2% and is statistically significant. In practical terms, stenting reduced stroke risk by nearly half over a period of four years.

There was an early procedural risk to consider. Within the first 44 days, stroke or death occurred in 1.3% of patients undergoing stenting, compared with none in the medical-therapy group. However, after this early period, the annual ipsilateral stroke rate was substantially lower in the stenting group, at 0.4% per year, compared with 1.7% per year in the medical-therapy group. This suggests that once patients have passed the short-term procedural risk period, long-term stroke protection improved with stenting.

CREST-2 demonstrates that modern medical therapy alone is highly effective and substantially lowers stroke risk in asymptomatic carotid stenosis. However, it also shows that carotid stenting provides an additional, statistically significant reduction in long-term stroke risk.

While both procedures carry a small early stroke risk of approximately 1–1.5%, stenting achieved meaningful long-term stroke reduction using a minimally invasive approach and avoided open surgery. In contrast, endarterectomy did not demonstrate a statistically significant benefit over medical therapy in this trial.

Major takeaway

Modern intensive medical therapy is essential and effective for all patients with asymptomatic severe carotid stenosis. However, **carotid stenting provides an additional reduction in four-year stroke risk and represents a reasonable, evidence-supported option for selected patients.** Endarterectomy did not demonstrate clear statistical superiority over medical therapy in CREST-2. Decisions should be individualized, with careful discussion of both early procedural risk and long-term stroke-prevention benefits.

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Time is Brain

Jason Luo, Evan McNeil, Justin H. Granstein, MD, MPH, Philipp Taussky, MD, Christopher S. Ogilvy, MD

Acute ischemic stroke remains a leading cause of morbidity and mortality, and timely restoration of cerebral blood flow is a central determinant of neurological outcome, with the probability of favorable functional recovery dropping steeply (from 75% to 40%) once the 2-hour mark is exceeded.[1] Mechanical thrombectomy has transformed the management of large vessel occlusions, allowing for efficient systems of care that can reliably achieve high-quality reperfusion within early treatment windows. At BIDMC, continued efforts between Neurosurgery and the Stroke Neurology Team have been made to streamline stroke workflows and minimize treatment delays, all while upholding our standard of delivering excellent clinical care.

In our recent 2025 institutional review, BIDMC achieved a 93.75% rate of successful reperfusion (TICI 2b/3) within 120 minutes, surpassing both the Massachusetts state average (78.0%) and the national average (76.0%) (Figure 1). These findings reflect a coordinated performance across the stroke care team, including rapid emergency department triage, timely neurointerventional team activation, and efficient intraprocedural technique.

BIDMC's performance highlights the effectiveness of its integrated stroke system and supports its role as a high-performing center for advanced endovascular stroke care.

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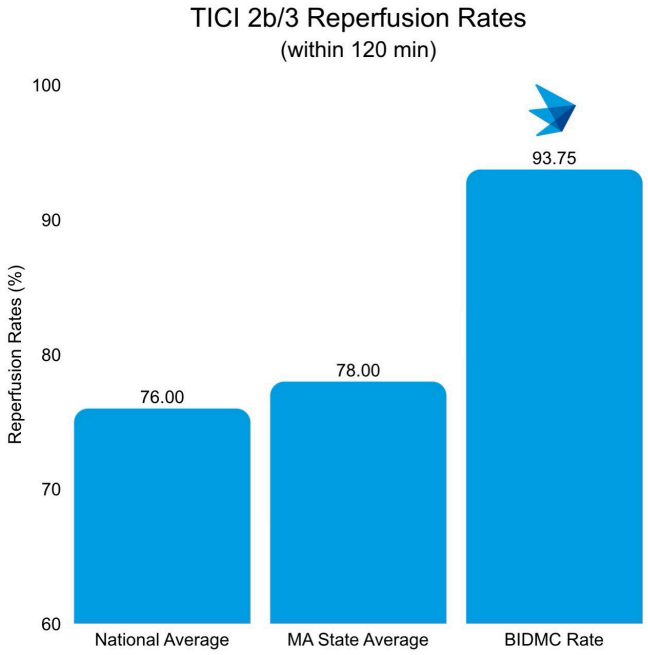

Fig 1: Comparison of national, Massachusetts (MA), and BIDMC TICI 2b/3 reperfusion rates within 120 minutes.

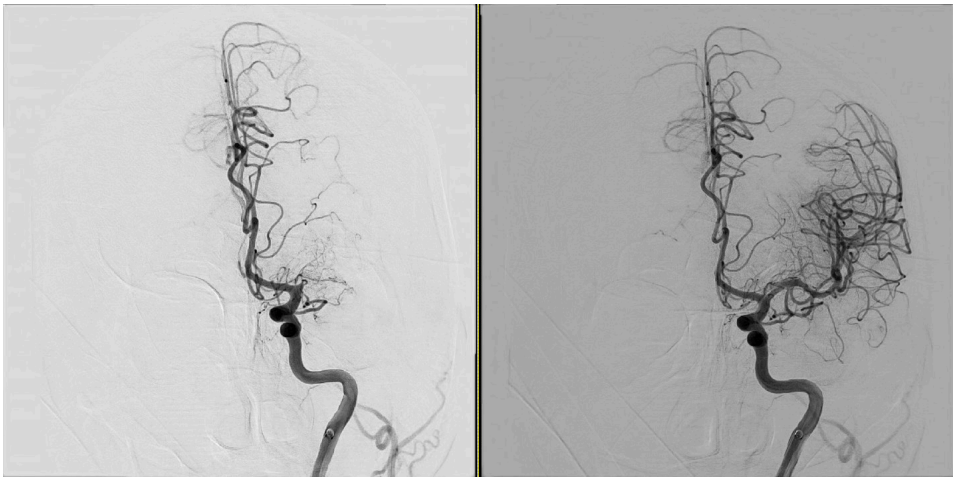

Fig 2: Recent left M1 occlusion with TICI3 recanalization after one pass with the FreeClimb 070® aspiration catheter delivered with the Tenzing 7® catheter delivery device (trademark: Route92 Medical). The time from groin puncture to reperfusion was 7 minutes.

Fig 3: The multidisciplinary BIDMC Stroke Neurology and Neurosurgery team driving advances in timely endovascular stroke reperfusion.

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