MAYO CLINIC

NeurosciencesUpdate

Focus on Pediatric Neurosciences

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New Technology for the Treatment of Pediatric Epilepsy

Specialists at Mayo Clinic Children's Center in Rochester, Minnesota, can provide innovative treatments for children with epilepsy. Working closely with Mayo Clinic research teams, these specialists are able to offer cutting-edge options to eliminate or reduce seizures in children.

"Experts from various specialties come together to make decisions about medications and treatments. The research and clinical teams function seamlessly together," says Kai J. Miller, M.D., Ph.D., a neurosurgeon at Mayo Clinic Children's Center. "We're actively developing new technology so patients can receive the most novel therapies to treat seizures and preserve brain function."

Mayo Clinic Children's Center has a pediatric team dedicated to the care of children with epilepsy. All children undergo MRI using specialized protocols developed by Mayo Clinic's neuroradiology epilepsy experts. Some of these patients might be eligible for enrollment in clinical trials. In addition to medical treatments, the Mayo team can provide holistic care for the child and family, addressing the learning and behavioral challenges that often are seen.

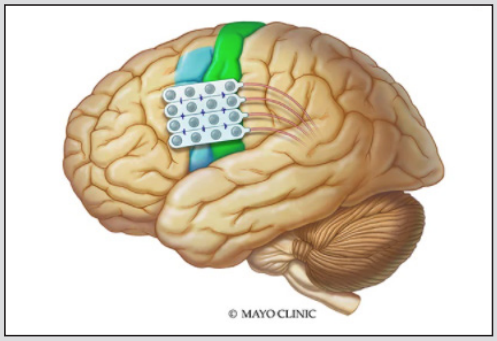

Figure 1. Chronic subthreshold cortical stimulation uses electrodes that are surgically implanted at the location of seizure onset. The electrodes are connected to a generator implanted in the chest.

After an initial evaluation, children and their parents can choose from a number of available options to reduce seizure frequency and severity. "For some children with drug-resistant epilepsy, surgery is an option. But for others, a unique type of medication or diet therapy can decrease seizure frequency and severity," says Elaine C. Wirrell, M.D., a pediatric epileptologist at Mayo Clinic Children's Center and co-founder of the Pediatric Epilepsy Research Consortium.

Surgical options

As a Level 4 comprehensive epilepsy center, the highest rating designated by the National Association of Epilepsy Centers, Mayo Clinic uses advanced surgical techniques, including robotic guidance during resective surgery. "With that guidance, surgeons can more precisely identify where seizures start — which allows us to target the seizures and stop them," Dr. Miller says.

Laser interstitial thermal therapy may be an option for some children. In this less invasive technique, MRI is used to guide the surgeon to place a probe through a small hole in the skull. A laser pinpoints and destroys a small portion of brain tissue.

"This therapy actually burns and destroys the place in the brain where the seizure originates, and does so without injuring the rest of the brain or requiring a large surgery," Dr. Miller says.

Other surgical options include:

- Corpus callosotomy. Used to treat children who experience frequent drop seizures leading to repeated and abrupt falls, corpus callosotomy severs the bundle of nerves connecting the right and left sides of the brain. Drop seizures are eliminated

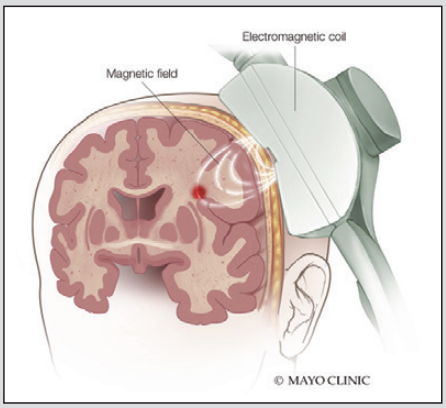

Figure 2. In transcranial magnetic stimulation, an electromagnetic coil placed against the scalp creates a magnetic field that stimulates certain areas of the brain.

Kai J. Miller, M.D., Ph.D.

Elaine C. Wirrell, M.D.

Katherine C. Nickels, M.D.

or markedly decreased for most children, preventing ongoing injury.

- Hemispherotomy. Children who experience seizures that originate from multiple sites in one hemisphere often require this surgery. It disconnects the abnormal, seizure-inducing hemisphere, allowing the other hemisphere to function normally and stopping the seizures.

For children who have severe epilepsy or who cannot have surgery, neurostimulation treatments might be an option. These therapies apply electricity to the central nervous system with the goal of reducing seizure frequency and severity. Some neurostimulation treatments require surgical implantation of a device.

In a review published in the October 2019 issue of *Brain Sciences*, Mayo Clinic researchers found that neurostimulation is safe and effective, and proposed a methodology for selecting among available options for children with epilepsy. Those options include:

- Vagus nerve stimulation. This treatment sends regular, mild pulses of electrical energy to the brain via the vagus nerve in order to prevent seizures. A stimulator device is implanted under the skin in the chest, and a wire is wound around the vagus nerve in the neck.
- Responsive neurostimulation. This type of neurostimulation monitors brain waves and responds to electrical activity that looks like a seizure. This stops seizures before they cause clinical symptoms.
- Deep brain stimulation. Mayo Clinic is one of the leading sites in the United States for this therapy, which delivers controlled pulses to a target in the brain that is part of a circuit involved in seizures.
- Chronic subthreshold cortical stimulation (Figure 1, page 1). In some children, a responsive device might not detect abnormal electrical activity in time to prevent a seizure. Subthreshold cortical stimulation provides continuous electrical impulses to an area of seizure onset to suppress the generation of the abnormal seizure discharge and thus attenuate the seizure.
- Transcranial magnetic stimulation (Figure 2). An electromagnetic coil placed against the scalp delivers a magnetic pulse that stimulates nerve cells in the brain.
- Transcranial direct current stimulation. This technique applies a low-intensity current that manipulates neuronal activity and neuroplasticity.

Rare epilepsy syndromes

Mayo Clinic is researching innovative medications and participating in clinical trials for the treatment of rare but severe epilepsy syndromes, including Dravet syndrome and Lennox-Gastaut syndrome, as well as epilepsy syndromes with rare causes, such as CDKL5 deficiency disorder.

"As neurologists, we provide precision therapies through advanced understanding of etiologies and preferred treatments, such as potassium channel blockers for patients with potassium channel-related epilepsy encephalopathies and fenfluramine, stiripentol and cannabidiol for patients with Dravet syndrome," says Katherine C. Nickels, M.D., a pediatric epileptologist at Mayo Clinic Children's Center in Rochester, Minnesota. "While many therapies such as stiripentol are considered to be new in most institutions, they are the standard of care at Mayo Clinic."

Studies and trials that Mayo Clinic has led or participated in include:

- A clinical trial of a gene therapy known as STK-001 for the treatment of Dravet syndrome. "This therapy has the potential to prevent not only seizures but also the neurocognitive regression that these children have," Dr. Wirrell says.
- A clinical trial of the neurosteroid ganaxolone for children and young adults with CDKL5 deficiency disorder.
- Three clinical trials investigating the efficacy of cannabidiol therapy in children with Dravet syndrome, Lennox-Gastaut syndrome and tuberous sclerosis complex. "All of those trials found that cannabidiol provided greater benefits than placebo," Dr. Wirrell says.
- A study published in the January 2021 issue

of *Epilepsia* that found that the ketogenic diet was the most effective treatment studied for children with myoclonic atonic epilepsy.

"For many children with early-onset epilepsy, the prognosis using conventional therapies has been quite poor," Dr. Wirrell says. "We feel it's important to continue participating in clinical trials and other studies, as a precision medicine approach allows our patients to receive the best possible therapies."

For more information

Starnes K, et al. A review of neurostimulation for epilepsy in pediatrics. *Brain Sciences*. 2019;9:283.

Stoke Therapeutics Inc. An Open-Label Study To Investigate the Safety and Pharmacokinetics of Single Ascending Doses of Antisene Oligonucleotide STK-001 in Children and Adolescents With Dravet Syndrome. ClinicalTrials.gov.

Marinus Pharmaceuticals. Study of Adjunctive Ganaxolone Treatment in Children and Young Adults With CDKL5 Deficiency Disorder (Marigold) ClinicalTrials.gov.

Nickels K, et al. Epilepsy with myoclonic-atonic seizures (Doose syndrome): Clarification of diagnosis and treatment options through a large retrospective multicenter cohort. *Epilepsia.* 2021;62:120.

Prenatal Repair Can Improve Hindbrain Herniation

Mayo Clinic has demonstrated that *in utero* repair of myelomeningocele can improve hindbrain herniation prenatally. As a result, complications associated with myelomeningocele at birth, such as Chiari malformation and hydrocephalus, can often be avoided.

"We're finding that about 90% of the prenatal myelomeningocele repairs that we perform result in reversal of brain malformation before birth. This is a big breakthrough for children with spina bifida," says Edward S. Ahn, M.D., a neurosurgeon at Mayo Clinic Children's Center in Rochester, Minnesota.

Prenatal myelomeningocele repair is performed by a multidisciplinary team led by Dr. Ahn and a Maternal and Fetal Medicine specialist. The team also includes pediatric and adult anesthesiologists, pediatric cardiologists to continuously monitor fetal cardiography, and specialized nursing support. All patients have ultrasound and MRI performed by neuroradiologists with specialized training.

"Without surgical intervention, the natural course for these babies is a severe congenital spinal defect that can cause motor weakness and bladder problems," Dr. Ahn says.

Cerebrospinal fluid that leaks through the meningocele can cause Chiari malformation, which in turn can lead to hydrocephalus requiring ventriculoperitoneal shunt placement after birth. Prenatal repair also prevents the spinal cord's exposure to amniotic fluid, which may be toxic to the spinal cord.

Myelomeningocele is generally diagnosed through routine fetal ultrasound during the second trimester of pregnancy. Surgical repair can be performed between 19 and 26 weeks of gestation. When possible, Mayo Clinic specialists prefer to perform surgery at around 24 or 25 weeks of gestation, when the fetus is slightly larger.

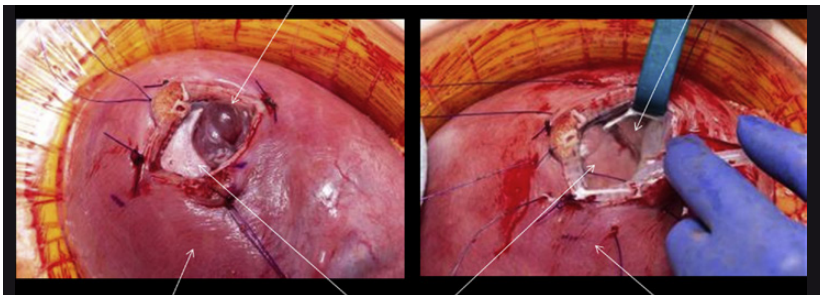

Figure. Photographs show *in utero* open repair of fetal myelomeningocele at 25 weeks of gestation. Myelomeningocele is apparent (top white arrow). The spinal defect has been closed (top white arrow).

In addition to their expertise with open surgical repair, Mayo Clinic surgeons have experience performing myelomeningocele repair fetoscopically. That minimally invasive approach lessens the risk of preterm birth and allows the mother to have a vaginal delivery during that pregnancy and in subsequent pregnancies.

Edward S. Ahn, M.D.

Elucidating prenatal benefits

Using MRI, Mayo Clinic researchers have documented improvement in hindbrain herniation as soon as six weeks after prenatal myelomeningocele repair. A study published in the April 2020 issue of *Mayo Clinic Proceedings* reports three consecutive fetuses with prenatally diagnosed myelomeningocele that had *in utero* repair between 24 and 25 weeks of gestation (Figure). All three fetuses had lumbosacral defects with evidence of hindbrain herniation.

MRI performed six weeks after prenatal open surgical repair showed improvement in hindbrain herniation in all three fetuses. Deliveries occurred at 37 weeks' gestation via cesarean section without notable complications. Postnatal follow-up examinations were generally unremarkable,

with one baby having mild ventriculomegaly at 3 months of age.

"We would expect to see the same degree of improvement when myelomeningocele repair is performed fetoscopically," Dr. Ahn says.

In utero myelomeningocele repair is part of Mayo Clinic's broader prenatal regenerative therapy program. Through that program, Mayo Clinic seeks to provide specific fetal interventions with the potential to promote regrowth and redevelopment of malformed organs. "The idea is to restore normal development before birth," Dr. Ahn says.

As a multispecialty center, Mayo Clinic has expertise in both maternal and fetal care. "We have specialists taking care of the mother and the fetus, and then the neonate, all under one roof. Maternal and Fetal Medicine specialists are involved from the very beginning," Dr. Ahn says. "We convene regularly to review our procedures and to innovate and improve those procedures." In addition, the Spina Bifida Clinic on the Rochester campus of Mayo Clinic coordinates care for children and teenagers with the condition.

"It's a privilege for us at Mayo Clinic to care for these children from before they're born to the time they're growing up and reaping the benefits of this prenatal intervention," Dr. Ahn says.

For more information

Ruano R, et al. *In utero* restoration of hindbrain herniation in fetal myelomeningocele as part of prenatal regenerative therapy program at Mayo Clinic. *Mayo Clinic Proceedings*. 2020;95:738.

Retinoblastoma: Specialized Neuroradiology for Optimal Care

Victoria (Michelle) M. Silvera, M.D.

Julie B. Guerin, M.D.

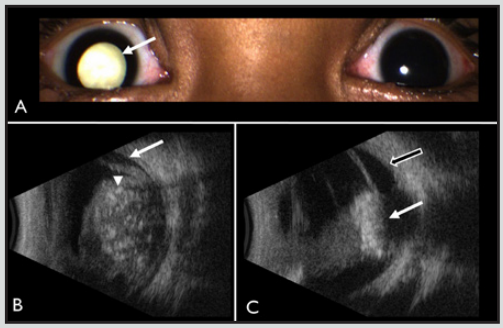

Figure 1. Images illustrate the treatment of a 2-year-old child with group E retinoblastoma at Mayo Clinic. A. Photograph shows leukocoria (white arrow) in the child's right eye. B. Ultrasonography shows a large, round, hyperechoic retinal mass within the right globe, with tumor calcifications seen as foci of high reflectivity (white arrowhead) with posterior acoustic shadowing and serous detachment of the retina (white arrow). C. Following three cycles of intra-arterial and intravitreal chemotherapy, the follow-up ultrasound image shows shrinkage of the tumor to a calcified hyperechoic scar (white arrow). Minor serous retinal detachment persisted (black-and-white arrow). Images reprinted with permission from *American Journal of Neuroradiology.* In press.

Although retinoblastoma is the most common malignant eye tumor in children, it is a very rare cancer. State-of-the-art imaging performed by experienced pediatric neuroradiologists is the key to maximizing patient outcomes.

"Our goal is preservation of the child's life, eye and sight. That requires a multidisciplinary and highly specialized approach to accurately stage the cancer," says Victoria (Michelle) M. Silvera, M.D., chief pediatric neuroradiologist at Mayo Clinic in Rochester, Minnesota.

If the tumor is contained within the globe of the eye, eye-preserving therapy is often an option. A tumor that stretches back along the optic nerve generally requires enucleation. Rarely, retinoblastoma spreads to the intracranial space.

"So much hinges on whether the tumor is in the optic nerve. Highly detailed imaging is critical for appropriate diagnostic staging and for survival," says Julie B. Guerin, M.D., a pediatric neuroradiologist at Mayo Clinic's campus in Rochester, Minnesota. "Both high-resolution and contrast-enhanced MRI are important for identifying key features that impact treatment decisions."

At Mayo Clinic, treatment is individualized for each patient. "The treatment can be complex. It is critical to have a multidisciplinary team well versed in retinoblastoma care," says Lauren A. Dalvin, M.D., an ocular oncologist at Mayo Clinic's campus in Rochester, Minnesota, who leads the retinoblastoma care team.

Interventional neuroradiology also plays a key role. For patients with advanced disease in one eye, Mayo Clinic routinely uses intra-arterial rather than intravenous chemotherapy. "Intra-arterial chemotherapy delivers a very high dose directly to the tumor, which increases the efficacy of therapy while also minimizing side effects," says Waleed Brinjikji, M.D., a neurointerventionalist at the Rochester campus of Mayo Clinic. "There is a pretty steep learning curve with this procedure, so it's very important to have an interventional neuroradiologist with experience in treating young children."

Multidisciplinary diagnosis and treatment

Typically, retinoblastoma is first noticed by a parent or pediatrician who sees a "white pupil" (leukocoria) in a child's eye (Figure 1). "That

reflection of light, which normally passes through to the retina, is very concerning for tumor," Dr. Silvera says.

An ophthalmologist generally makes the initial diagnosis of retinoblastoma, which can be heritable (Figure 2) or sporadic. Diagnosis of the heritable type typically occurs before age 1 and diagnosis of the sporadic type by age 2. Tumor size can range from very small to large enough to engulf the entire eye, although in the United States the disease is generally found before then.

Mayo Clinic's ophthalmological exam includes color fundus photography, ultrasonography, fluorescein angiography and optical coherence tomography.

To confirm an initial diagnosis and to stage the tumor, Mayo Clinic's pediatric neuroradiologists obtain detailed images using 3-tesla MRI with a high-performance multichannel head coil.

A pediatric anesthesiologist administers general anesthesia before the imaging procedure. "Any motion by the child would degrade the image," Dr. Silvera says. "Achieving the highest-quality imaging possible is essential to identifying tumor, particularly within the optic nerve, and sparing the child a second round of general anesthesia and imaging."

Detailed imaging is necessary to check for intracranial disease, which has a poor prognosis. "The contralateral eye is also carefully assessed on imaging, particularly in children with heritable retinoblastoma," Dr. Silvera says. "Great care is needed because any contralateral tumor is typically much smaller than the tumor in the eye that presents with symptoms."

If eye-sparing treatment is an option, Mayo Clinic's ocular oncologists can administer intravitreal chemotherapy, laser therapy, cryotherapy or thermal therapy with the patient under general anesthesia. If intra-arterial chemotherapy is required, it can be administered directly afterward, while the patient is still under the same anesthesia.

The intra-arterial procedure involves threading a catheter from the femoral artery up to the ophthalmic artery. "The vast majority of these patients are under the age of 3 years, so their blood vessels are very small and fragile. It's critical to have an interventional neuroradiologist who can safely perform procedures on these very delicate children," Dr. Brinjikji says. At Mayo Clinic, patients are generally able to return home on the day of the procedure.

Brachytherapy is another treatment option for retinoblastoma that does not respond well to chemotherapy. To prevent side effects Mayo Clinic generally avoids external beam radiotherapy for children with retinoblastoma.

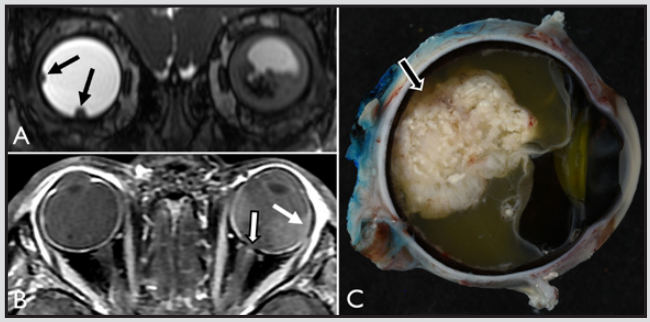

Figure 2. Images illustrate the treatment of a 21-month-old child with hereditary retinoblastoma, with Group B retinoblastoma of the right eye and Group E retinoblastoma of the left eye. A. Coronal 3D fast imaging employing steady-state acquisition (FIESTA) shows two small retinoblastoma tumors (black arrows) in the right globe. A hypointense mass with serous retinal detachment is visible in the left globe. B. T1-weighted post-gadolinium image with fat saturation shows interruption of the normally enhancing chorioretinal interface (white arrow), which could represent subtle choroidal invasion. MRI does not show tumor extending into the left optic nerve (black and white arrow). Tiny foci of enhancement surround the left optic nerve cuff, representing normal small vessels. The left globe was larger than the right, consistent with buphthalmos. Enucleation of the left eye was performed due to the buphthalmos and persistent eye redness and discomfort. C. Gross pathology specimen of the enucleated left eye demonstrated the large retinoblastoma posteriorly within the globe (arrow). Histopathology (not shown) demonstrated a moderately differentiated retinoblastoma with tumor involving the optic nerve head and no post-laminar tumor extension, as accurately diagnosed on the preoperative MRI. Images reprinted with permission from *American Journal of Neuroradiology*. In press.

Patients who require enucleation can have the procedure at Mayo Clinic and then be fitted with a prosthesis. "The prostheses nowadays are very good and natural appearing," Dr. Silvera says.

Follow-up imaging is another important aspect of care. "We're looking for recurrence of tumor in the affected orbit but also in the contralateral globe if the child has the genetic form of retinoblastoma, and for tumor in the brain," Dr. Silvera says.

Children with retinoblastoma are at risk of developing retinoblastoma-like tumor in deep portions of the brain, specifically in the pineal and parasellar regions. Tumor in these regions is called trilateral or quadrilateral retinoblastoma, depending on the extent of tumor. "We look carefully for this on follow-up MRI, as this complication needs to be managed promptly. It carries a poor prognosis," Dr. Guerin says.

Initially, most patients are seen once a month, with appointments often coordinated with cycles of chemotherapy. Over time, if the cancer has completely regressed, the time between visits might be slowly extended.

"Most recurrences happen within the first three years, so we keep close tabs on these children during that period," Dr. Dalvin says. "After that, the interval between visits might be extended to six to 12 months."

Lauren A. Dalvin, M.D.

Waleed Brinjikji, M.D.

In developed countries, the survival rate for retinoblastoma is over 98%. Globe salvage rates have improved with the introduction of intra-arterial chemotherapy. For children with Group E disease — the most advanced stage — salvage rates are about 50%."For Group D eyes, we can save nearly 80%,"Dr. Dalvin says."The globe salvage for less advanced Groups A, B and C is over 90%."

Mayo Clinic organizes retinoblastoma care to make it as efficient and effective as possible for the child and the family."Retinoblastoma is a complex disease,"Dr. Silvera says."It requires an expert, multidisciplinary team and a long-term commitment to the patient and family."

Pediatric Brain Tumors: Rapid and Focused Care

Jonathan D. Schwartz, D.O., M.P.H.

Pediatric brain tumors require specialized treatment that differs from the regimens used in adults. Mayo Clinic's Pediatric Brain Tumor Clinic uses a multidisciplinary approach focused on the particular needs of children while drawing on the broad resources of a major tertiary center.

Part of Mayo Clinic Children's Center, the Pediatric Brain Tumor Clinic brings together pediatric specialists in Neuro-Oncology, Neurology, Neurosurgery, Neuroradiology, Radiation Oncology and Neuropathology. Patients referred to Mayo for pediatric brain tumors can often be seen the next day.

"Our multidisciplinary team can be put into place very quickly,"says Jonathan D. Schwartz, D.O., M.P.H., a pediatric neuro-oncologist at Mayo Clinic Children's Center in Rochester, Minnesota. "We communicate with one another so everyone is on the same page, and families can quickly get a detailed diagnosis and a treatment plan."

State-of-the-art imaging, such as 7-tesla MRI, facilitates the planning of surgical and radiation procedures. For complex tumor resections, Mayo's pediatric neurosurgeons collaborate with colleagues in Neurosurgery, Otolaryngology (ENT)/Head and Neck Surgery, and Neuro-Ophthalmology.

"Depending on the case, we might work, for example, with skull base or peripheral nerve surgeons who are recognized as leaders in their fields,"says David J. Daniels, M.D., Ph.D., a pediatric neurosurgeon at Mayo's campus in Rochester, Minnesota."This collaboration allows us to manage cases that can't be easily done elsewhere."

To safeguard the developing pediatric brain, Mayo Clinic uses proton beam therapy to deliver more-targeted radiation."Children who get proton treatment have fewer side effects in terms of IQ changes, cognitive development, growth, and endocrine development and hormonal problems than children who have traditional radiotherapy,"says Nadia N. Laack, M.D., chair of Radiation Oncology at Mayo Clinic Children's Center in Rochester, Minnesota.

As a large-volume center, Mayo Clinic is also committed to clinical trials and research aimed at providing more-targeted treatments. "Right now, the number of treatment options for pediatric brain tumors is limited. It's critical that we develop novel therapeutics and treatment options to maximize treatment and minimize long-term consequences for children,"Dr. Schwartz says.

Precision targeting of tumors

Pediatric brain tumors pose unique challenges and require highly specialized expertise."The entire resources of Mayo Clinic's strong Neuro-Oncology program are available to our pediatric patients,"Dr. Laack says.

In addition to investigating 7-tesla MRI, Mayo is studying the nuclear medicine marker known as fluorine F 18 fluorodopa-positron emission tomography to delineate precise targets for radiation treatment. Diffusion tensor imaging (DTI) tractography may be used to guide tumor resection.

"DTI allows us to really understand the relationship between the tumor and eloquent areas of the brain and corticospinal tract,"Dr. Daniels says.

Tumor resection is further enhanced by Mayo's routine collaboration among surgical specialists. Dr. Daniels cites a recent case in which a pediatric patient's tumor extended from the brain through one eye to the face. The surgical team included a pediatric neurosurgeon, an ENT surgeon and an eye surgeon."None of us could have done that case alone,"Dr. Daniels says.

Radiation therapy is directed at maximizing tumor treatment while minimizing damage to surrounding tissue. Gamma Knife radiosurgery is used in select pediatric patients with benign brain tumors as well as metastatic disease. For primary brain cancer, Mayo Clinic has used proton beam therapy for about five years.

"There are increasing numbers of reports with long-term follow-up data demonstrating that children receiving proton radiation for brain tumors, such as medulloblastoma, show minimal declines in their cognitive development,"Dr. Laack says."That contrasts with traditional radiotherapy, where we generally see a steady decline in development after treatment."

That reduced toxicity can be achieved without compromising tumor outcomes. As

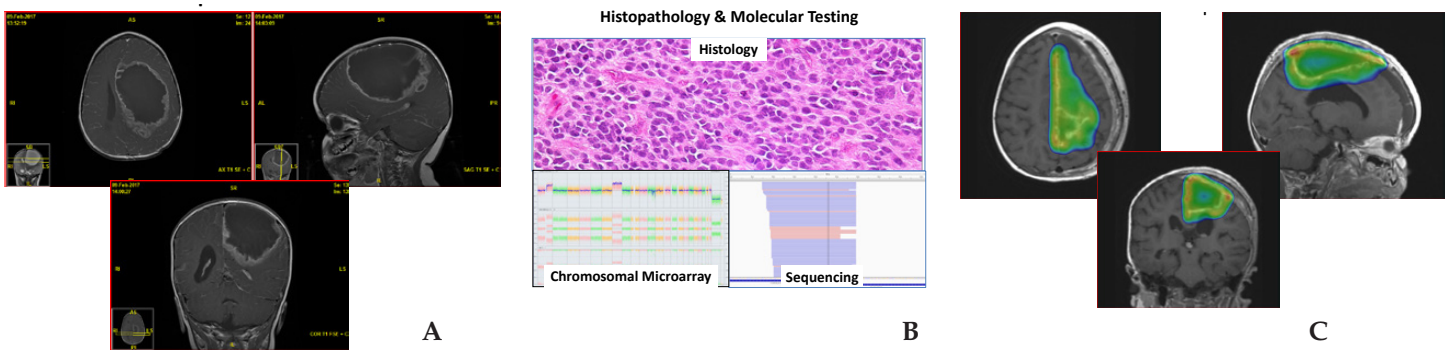

Figure. Images of a pediatric brain tumor illustrate Mayo Clinic's multifaceted approach. A. Preoperative MRI shows a high-grade ependymoma in an 18-month-old patient. B. Histopathology shows an anaplastic ependymoma, with subsequent sequencing and chromosomal microarray demonstrating RELA fusion-positive tumor — indicating an aggressive tumor and underlining the desirability of radiation therapy. C. To avoid toxicity in surrounding brain tissue, Mayo used proton beam therapy. The proton dose cloud, shown in color, demonstrates the close conformity of proton therapy to the child's tumor.

described in the September issue of the *International Journal of Radiation Oncology, Biology, Physics*, the two-year survival rate for children with brain tumors treated with pencil beam scanning therapy at Mayo Clinic is 93%.

Recommendations concerning the optimal approach to an individual's disease are made at weekly meetings of Mayo's multidisciplinary pediatric brain tumor board. "We discuss our own patients' cases, as well as outside cases, to determine if there is an approach that might help," Dr. Laack says. "Our model of care ensures that each patient has a thorough case review and potentially access to new radiation studies or techniques or new surgical options."

The tumor board also incorporates Mayo's expertise in neuropathology. The integration of comprehensive genetic testing, such as neuro-oncology-specific next-generation sequencing and chromosomal microarray analysis, can provide more-detailed information about an individual child's brain tumor (Figure). "That's especially helpful for tailoring therapy directly to the patient if a tumor has a risk of recurrence," Dr. Schwartz says.

Advancing personalized care through research

As a member of consortia including the Children's Oncology Group and the National Comprehensive Cancer Network, Mayo Clinic strives to give select pediatric patients access to clinical trials. "Our tumor board evaluates if a particular clinical trial might benefit children and if we can safely advocate to open that trial to younger ages," Dr. Laack says.

Mayo is also active in developing its own clinical studies. One current investigation is a detailed look at how radiation affects children's cognitive functioning. Specifically, the researchers are evaluating how tumor location and radiation dose correlate with subsequent problems with memory, attention, vision, motor skills, and spatial and executive functioning.

"We're trying to understand each child's individual strengths and weaknesses and adjust our radiation dosing based on that," Dr. Laack says.

A separate pilot clinical study is evaluating the feasibility of using memantine to reduce cognitive impairment in children who receive radiation therapy. Mayo investigators previously conducted a similar successful study in adults.

In addition to testing existing medications, Mayo is working to develop new therapies. The Experimental Drug and Therapeutics for Pediatric Brain Tumor Laboratory, led by Dr. Daniels, studies the physical properties of various medications and how they might be used against pediatric brain tumor. Dr. Daniels hopes eventually to test some of these medications in the setting of convention-enhanced delivery.

"Delivering a drug directly to the brain tumor bypasses the blood-brain barrier," he says. "We are keenly interested in trying to understand which drugs might be optimal for treating tumors in this way."

One potential disease target is diffuse intrinsic pontine glioma (DIPG), a rare tumor that typically occurs in young children and is fatal within a year. "In our lab studies, we've found that alisertib — a selective Aurora A Kinase inhibitor — is quite effective on these tumors," Dr. Daniels says. "In addition, we've shown that alisertib enhances the activity of radiation, which is the only therapy that has ever been found to benefit kids with DIPG."

In both research and treatment, Mayo's goal is a personalized medicine approach. The key is greater insight into individual tumor makeup.

"With that knowledge, we'll better understand the consequences and side effects of treatment. We will be much more precise about how

David J. Daniels, M.D., Ph.D.

Nadia N. Laack, M.D.

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Clinical trials, CME, Grand Rounds, scientific videos and online referrals

an individual's tumor should be approached," Dr. Laack says. "We are working toward a future where each individual child has fewer side effects and the best chance of cure."

For more information

Rongthong W, et al. Effect of prospective use of radiobiologic effect (RBE) modeling in treatment planning on magnetic resonance imaging (MRI) radiation related changes (RRC) in pediatric patients with brain tumors treated with pencil beam scanning proton therapy (PBS). *International Journal of Radiation Oncology, Biology, Physics*. 2019;105(suppl):E628.

The Experimental Drug and Therapeutics for Pediatric Brain Tumor Laboratory. Mayo Clinic. *https://www.mayo.edu/research/labs/experimental-drug-therapeutics-pediatric-brain-tumor.*

Education 2021 Neurology and Neurologic Surgery Continuing Medical Education Programs

May

7th Annual Neuro and Intensive Care: Review, Workshops and Controversies 2021 — LIVESTREAM

May 6-8, 2021
This course is designed for medical providers who care for patients with neurological and neurosurgical emergencies, acute stroke and brain hemorrhage, acute brain injury, coma, and disorders that require hospital, emergency department and intensive care unit (ICU) evaluation and management.

October

Mayo Clinic Conference on Brain Health and Dementia 2021

Oct. 29, 2021
Mayo Civic Center, Rochester, Minn., or LIVESTREAM
This conference, the first conference under this name, replaces the long-standing Meeting of the Minds conference. Attendees will have the choice to attend in person if circumstances allow, or at one of a dozen host sites in Minnesota to be identified by May 1. The event will also be livestreamed for viewing on personal devices.

Information and registration

Mayo Clinic in Rochester, Minnesota
Phone: 800-323-2688 (toll-free) or 507-284-2509
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Website: *https://ce.mayo.edu/neurology-and-neurologic-surgery*

Expedited Patient Referrals to Mayo Clinic Departments of Neurology and Neurologic Surgery

While Mayo Clinic welcomes appointment requests for all neurologic and neurosurgical conditions, patients with the following conditions are offered expedited appointments:

1. Cerebral aneurysms
2. Cerebral or spinal arteriovenous malformations
3. Brain, spinal cord or peripheral nerve tumors
4. Epilepsy with indications for surgery
5. Carotid disease

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