



Pascal Jabbour, MD, and Carol Shields, MD.  
Photo by Roger Barone

# Saving Eyes, Saving Vision

A Neurosurgeon and an Oncologist Join Forces  
to Treat a Childhood Eye Cancer

By Sari Harrar

## STORY SUMMARY

- Physicians from Jefferson's Department of Neurological Surgery and Wills Eye Hospital's Ocular Oncology Service are collaborating to treat retinoblastoma, the most common childhood cancer of the eye, with chemotherapy delivered directly to the retina through the ophthalmic artery.
- Intra-arterial chemotherapy (IAC) sidesteps the systemic side effects of traditional chemotherapy, allowing targeted delivery of higher-dose anti-cancer drugs. It reduces the need for enucleation (removal of the eye) in 36-100 percent of cases with moderate to advanced retinoblastoma. Many children also find that some vision is restored.
- Jefferson and Wills physicians are at the forefront of international research on the outcomes and side effects of IAC and are leading proponents of IAC as a first-line (primary) treatment for moderate and advanced retinoblastoma.

"Would you look at my baby's eyes, too?"

New mom Leanne Davis, a high-school English teacher from Warren, Mich., made the off-hand request at her eye exam in 2011. "I had retinoblastoma as a child, and maybe it was on my mind," she explains. "I'm glad I asked." At 4 months, her son Cole had early signs of this rare and potentially lethal childhood cancer, too.

Cole's cancer was stubborn. It re-appeared despite 21 rounds of chemotherapy, laser photocoagulation, radiation and cryotherapy in various combinations. But the Davis family and their doctors in Detroit and Philadelphia were even more persistent. When a new tumor the size of a blueberry was discovered in the boy's right eye in October 2014, a breakthrough therapy called intra-arterial chemotherapy — delivered by Jefferson neurosurgeon Pascal Jabbour, MD, working in collaboration with Wills Eye Hospital ocular oncologist Carol Shields, MD — saved not only Cole's life, but also his eye and returned his vision as well.

"Cole's playing with his trucks, watching his favorite *Mighty Machines* TV show and doesn't have to lean forward to see the pictures when I read to him anymore," says dad Clint Davis, a high-school chemistry teacher, on the morning of Cole's final round of intra-arterial chemotherapy at the Jefferson Hospital for Neuroscience in January 2015. "The yellowish glint we saw in his eyes sometimes is gone, too."

Intra-arterial chemotherapy — IAC for short — relies on a unique partnership between physicians with finely honed, yet very different skill sets. An oncologist must carefully assess the cancer's progress in each tiny patient to identify the right candidates. A neurosurgeon must thread a microcatheter through fragile, whisper-thin arteries from a child's groin to eye, then deliver

a high-dose chemotherapeutic agent in carefully timed puffs.

At Jefferson, the second U.S. medical center (and one of few in the world) to offer IAC, the collaboration is making history. "In the recent past, many children lost their eyes to this disease," says Jabbour, associate professor of neurological surgery and chief of the Division of Neurovascular and Endovascular Neurosurgery. "We are saving 62-72 percent of eyes with advanced retinoblastoma thanks to IAC at Jefferson — and 100 percent in earlier stages of the cancer."

It's also saving eyesight — a benefit that surprised and delighted the team.

"IAC is probably one of the biggest breakthroughs in eye cancer of the past two decades," notes Shields, co-director of the Ocular Oncology Service at Wills and professor of ophthalmology at SKMC. "We've doubled the number of eyes we can save, compared to other treatments. And we're seeing early evidence that it can restore peripheral and even central vision in some patients. I hear from happy parents all the time. Their kids were on the brink of blindness. Now they're stacking blocks, doing puzzles, playing T-ball. It's so exciting."

## Where Oncology and Neurosurgery Intersect

Retinoblastoma grows in the eye's light-sensing retina. In the United States, just 300 children develop this malignancy annually; more than half are treated at

## A Tradition of Collaboration

In 1972, Wills Eye Hospital affiliated with Jefferson Medical College (now Sidney Kimmel Medical College). As Jefferson's Department of Ophthalmology, it's the place where all SKMC students receive basic eye instruction and training. And it's just one example of a close collaboration that's advancing eye care, prevention and research. Others include:

- **The Wills Vision Research Center at Jefferson.** Established in 2011, the Center draws on more than 15 scientific disciplines to improve the diagnosis, treatment and prevention of visual diseases. Recent collaborative studies have examined connections between low vision and depression; the power of community education to increase yearly eye screenings among people with diabetes; and the genetics of glaucoma, says Center co-director Julia Haller, MD, ophthalmologist-in-chief at Wills.
- **The Wills Eye Emergency Department at Jefferson.** Close collaboration between Wills and Jefferson's Comprehensive Traumatic Injury Program gives patients access to one of only three emergency rooms in the nation specializing in eye care. Open 24 hours a day, 365 days a year.
- **The Jefferson Comprehensive Concussion Center.** A partnership between Jefferson, the Rothman Institute and Wills Eye, the JCCC opened at the Philadelphia Navy Yard in 2013. It provides clinical care in areas such as neuro-ophthalmology, neuroradiology, psychiatry and complex rehabilitation at one facility.

Wills. Early detection and better treatments have boosted the survival rate to 97 percent — but at a steep price. Until recently, about 40-50 percent of kids with advanced retinoblastoma lost one eye, and around 10 percent lost both eyes despite aggressive therapies; the rate was higher for those with the most severe disease. Among them is Cole's mom, Leanne, whose cancer was cured in the early 1980s with laser photocoagulation and enucleation — the removal of her right eye — when she was 9 months old. She wears a nearly impossible-to-detect prosthesis in her right eye and has good vision in the left.

"Retinoblastoma is rarely fatal in the United States, but the therapies left something to be desired," Shields explains. "Enucleation prevents recurrence and spread. But when a child loses one or both eyes, it obviously changes their life forever. We were also concerned about the side effects of conventional treatments such as systemic chemotherapy and external-beam radiation. When we heard about IAC for retinoblastoma from a visiting Japanese researcher in 2008, I was intrigued but also cautious. Injuring the ophthalmic artery, which feeds the retina, could cause blindness."

Shields contacted Robert H. Rosenwasser, MD, the Jewell L. Osterholm Professor and Chair of the Department of Neurological Surgery at Jefferson. "I was enthusiastic," he says. "At Jefferson, we were already performing vascular neurosurgery on newborns, placing catheters in very small arteries in the brain similar in

size or smaller than those involved with IAC. So I knew it was possible. This has been a game-changer internationally for the treatment of retinoblastoma. And historically, it's huge for neurosurgeons. It's a whole new concept for us."

Rosenwasser performed the first IAC procedures at Jefferson in 2008, then taught the procedure to Jabbour, who was finishing his fellowship in interventional neurosurgery. Both surgeons contributed to refinements that protect the ophthalmic artery by stopping the catheter just short of this high-stakes blood vessel.

But reaching this destination requires careful navigation of a network of twisting arteries, done while consulting fluoroscopic X-ray images on two large screens hung above the operating-room table and "listening to your fingers," as Jabbour describes it. "The femoral artery at the groin, where we insert the sheath, is just two millimeters wide — one-fourth the size of an adult's. The ophthalmic artery is less than a half-millimeter in diameter," he says. "Too much force could rupture a blood vessel, too little means you're moving too slowly."

With the catheter "parked" at the right spot, the chemotherapy drug melphalan (and sometimes a second agent) is pulsed through the catheter in rhythm with the child's heartbeat. "It's like a puff of smoke that gets carried into the retina," he says. Jabbour delivers 1 cc of the drug per minute during the half-hour procedure.

Afterward, instead of asking a resident or surgery fellow to take out the groin sheath — the plastic tube used



Retinoblastoma can sometimes be detected via flash-enhanced photographs; a white haze or glare in a child's pupil can be an early sign of the cancer.

Credit: National Cancer Institute/Getty Images





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—Pascal Jabbour, MD

to guide insertion of the catheter during the procedure — Jabbour removes it himself. He then applies gentle pressure — “just a little more than you’d use to take your pulse” — to the site with two fingers for the next 30 minutes. “There are no child-sized plugs to close the wound,” he says. “A baby has just one-tenth the blood volume of an adult. Even a little bleeding could be disastrous. Too little pressure can allow bleeding, but too much pressure on the femoral artery could cut off blood to a leg. From the beginning, I couldn’t imagine anyone else doing any part of the procedure. It’s me, from beginning to end, from skin to skin.”

Most children who receive IAC for retinoblastoma are between 3 months and 5 years old, but the team has treated a 30-year-old with late-onset disease. Most receive three to four sessions, with four to 10 weeks in between. IAC is most often used in intermediate to advanced cancers, grades B through E — though Shields adds that more advanced cases with cancer in eye tissue beyond the

Jabbour spends time with patient Cole Davis and his stuffed otter, Sparky, just before Davis’ final intra-arterial chemotherapy treatment.

Photo by Roger Barone

retina may need more than one type of treatment. “IAC can help about 80 percent of American kids with retinoblastoma, because their disease hasn’t moved beyond the retina yet. If it moves into other tissues in the eye that aren’t fed by the ophthalmic artery, we add other approaches. If the tumor has grown outside the eye, we enucleate because the child is at high risk for metastasis and death. Saving life is

always the first priority, followed by saving the eye and then saving vision.”

### “Time Will Tell”

In one of her first papers on IAC, published in the May 2010 issue of *Clinical and Experimental Ophthalmology*, Shields and her husband, Jerry A. Shields, MD (the couple co-direct Wills’ Ocular Oncology Service), wrote: “Despite its allure,

intra-arterial chemotherapy should be used with caution...Time will tell.”

Four years later, a July 2014 report in the journal *Ophthalmology* co-authored by Shields, Jabbour, Rosenwasser and others outlined the outcomes of Jefferson’s first 70 eyes treated with IAC. The results were worth celebrating: 100 percent of eyes with intermediate-stage retinoblastoma (grades B and C) were saved, as were 94 percent of those with more advanced grade D cancer and 36 percent with grade E, the most advanced. Up to 95 percent of microscopic cancers, called seeds, were obliterated.

The most common complications — eyelid swelling and drooping (5 percent rates for each) and increased blood flow (hyperemia) to the forehead (2 percent) — were temporary. Another 2 percent had some traces of blood within the eye. “There was no patient with stroke, seizure, neurologic impairment...or death,” the team noted.

The group took a new step, suggesting IAC will become a safe, effective primary treatment for many stages of retinoblastoma — instead of the back-up plan when all else fails. “This is controversial, and some other centers don’t agree with it,” Jabbour notes. “We think it’s the future.”

By January 2015, Jabbour and Shields had used IAC to treat more than 150 cases of retinoblastoma from across the nation and around the world. And they host a steady stream of visitors from medical centers around the world who’d like to offer IAC closer to home. “We get sent a lot of big tumors,” Shields says. “We’ve had kids come with one eye gone and cancer in the other. I want to have a victory for every child and Pascal feels the same way. Is it because we’re both parents? [Shields has seven children, Jabbour has two.] That might be part of it.” ■

**To learn more about retinoblastoma or to support this program at Jefferson, contact Joseph Lynch, Associate Director of Development, Jefferson Hospital for Neuroscience, at 215-955-8342 or [joseph.w.lynch@jefferson.edu](mailto:joseph.w.lynch@jefferson.edu).**



Cole Davis with his parents, Leanne and Clint, and their dogs at the family’s home in Michigan. Photo by Aaron Fortin