

Parents Face Painful Choice In Treating Childhood Cancer --- New Brain-Tumor Protocol Highlights Growing Tradeoff Between Survival, Side Effects

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A NEW TREATMENT for a common childhood brain tumor is posing a wrenching choice for families and underscores an emerging issue for **cancer** patients: possibly reducing the chances of survival in hopes of minimizing the devastating side effects of treatment.

One of the most agonizing realities of today's improved **cancer** therapies is that a cure often comes at the expense of the patients' long-term health. Radiation and chemotherapy can ravage organs, weaken bones and damage memory and cognitive ability. The neurological effects are particularly devastating in children, whose brains still are developing.

Now, as survival rates have improved, researchers increasingly are focusing on improving the quality of life. The challenge has been to find ways to make treatments less toxic without sacrificing effectiveness. Nowhere is this challenge more vivid than in a new treatment for medulloblastoma, the most common malignant childhood brain tumor.

The traditional way to treat medulloblastoma is with surgery, followed by radiation and chemotherapy. One of the worst side effects of this treatment is that children who live can wind up with permanent damage, including learning disabilities, a loss of motor control and, in some children, even mental retardation. This is mainly because of the high doses of radiation to the brain.

Now, some families are doing something different. They are using a lower dose of radiation combined with an extra round of chemotherapy to treat their children, in the hopes it still will kill the tumor but with less neurological destruction.

In choosing this route, the parents must accept the fact that their child's odds of surviving may be reduced as much as 10%, according to doctors who are offering this therapy. Survival rates generally are high: For children with a tumor that hasn't spread to other organs and can be removed by surgery, cure rates are currently 75%-80%. So some parents are willing to take lower but still-good odds of survival in exchange for the potential of a much better quality of life if their child does survive.

This tradeoff of survival versus quality of life is emerging in a number of diseases, including breast and prostate cancers. The debate is sharpest in childhood cancers because children have so much to lose -- and they cannot choose for themselves. Thanks to more aggressive treatments and new drugs, an estimated one in 250 adults under 40 will be survivors of childhood **cancer** by the year 2010, according to an American Academy of Pediatrics publication. But "at what cost are these children surviving?" says Paul G. Fisher, an associate professor of neurology and pediatrics at the Lucile Packard Children's Hospital at Stanford University, which is offering lower doses of radiation for medulloblastoma. "What will these children be like when they grow up?"

Treatments for other childhood cancers such as leukemia and Hodgkin's disease also involve neurological side effects because they can require whole-body radiation that affects the brain. These diseases are more common than medulloblastoma, which affects about 500 children a year, nationally. By contrast, 3,250 children a year are diagnosed with leukemia, and 1,700 with lymphomas such as Hodgkins.

The effects are especially devastating with medulloblastoma, where patients must undergo not just whole-brain radiation, but also an extra, higher dose directed at the site of the tumor. The new therapy lowers the dose for the whole-brain radiation in hopes of minimizing damage to healthy tissue, though the dose to the tumor site is the same.

The new therapy is being offered in two clinical trials at more than 120 major **cancer** centers in the U.S., Canada, and Australia, including the Lucile Packard Children's Hospital, Children's Hospital of Philadelphia, Massachusetts General Hospital in Boston, and Children's Hospital of Pittsburgh.

In the trials, **cancer** researchers are lowering the radiation dose from the current standard of 2340 centigray, or cGy, to 1800 cGy (cGy is a measure of radiation absorbed by the body). Stanford's Dr. Fisher says a 2340 cGy radiation dose is the equivalent of having 2,340 CT scans or more than 100,000 X-rays. Doctors say that if survival rates drop by more than 10%, the trials will be stopped early. So far, doctors haven't seen "an undue proportion of recurrence," Dr. Fisher says.

The benefits of the lower dose still are far from certain. A small pilot study published in October 2004 involving seven children treated with the lower radiation showed negative results. One child relapsed two months after completing radiation and died. Two others relapsed and required further radiation and chemotherapy but survived. In the paper, the researchers concluded that the 1800 cGy dose "may not be adequate" to prevent recurrence.

Regina Jakacki, the principal investigator on the study, says another disturbing finding was that despite the lower radiation dose, most of the children still had significant learning disabilities, and every one of them experienced difficulties in school. "We may be kidding ourselves that reducing the dose will make a difference in their long-term outcome, and it could decrease their chances of survival," says Dr. Jakacki, director of the pediatric neuro-oncology program at Children's Hospital of Pittsburgh, which is participating in one of the current lower-dose trials.

At least one prominent **cancer** center, St. Jude Children's Research Hospital in Memphis, Tenn., decided not to participate in the current trials. Concern over the results of the Pittsburgh trial was a major factor, says Larry E. Kun, the head of the department of radiological sciences at St. Jude.

For parents, the decision is intensely painful. Max Letizi, now 17 years old, was diagnosed at age 13 with medulloblastoma after he began experiencing double vision and headaches. Five days later, he had surgery. When doctors at the Lucile Packard Children's Hospital offered the possibility of a lower radiation dose, Max's mother, Terry Letizi, says she and her husband agonized about what to do.

In choosing the lower radiation dose, Mrs. Letizi says they knew it could potentially reduce Max's chance of survival, but they felt the chance of preserving a normal life for their son was worth the risk. "It would have been cataclysmic, the juxtaposition of who he was before and who he was after," she says.

Today, four years after his treatment, Max is a junior in high school in Penngrove, Calif. He hasn't had a recurrence of his **cancer** in four years. But even with the lower radiation dose, he has experienced side effects. He gets straight A's in school, but his mother says it takes him longer to process information. He finishes tests in the allotted time, she says, but is usually among the last to do so. His balance is off, so he can't do certain things like skateboard. "Making this choice was the most traumatic thing I ever did," Mrs. Letizi says.

Meryl Shader and her husband, Paul Seave, made a different choice. Their son, Sawyer Shader-Seave, was diagnosed with medulloblastoma at the age of 4. Three days later, he had surgery. The couple wrestled about whether to choose the lower, 1800 cGy radiation dose or the standard one. When they asked Stanford's Dr. Fisher if Sawyer would still be able to go to college some day, Dr. Fisher said he didn't know. In a child so young, the doctor explained, the risk of long-term cognitive damage was very high. "I was shocked to hear the doctors say that there were things that Sawyer might not be able to do," says Ms. Shader, a published author and creative-writing teacher.

Ms. Shader says her husband said, "If Sawyer doesn't make it, we'll want to kill ourselves." They told Dr. Fisher they wanted Sawyer to receive the standard, higher radiation dose.

Today, Sawyer is eight and in the third grade in Sacramento, Calif. He is doing well in school, but has needed certain accommodations: It takes him a long time to write, so in spelling tests he writes only the word while the other children write a full sentence that uses the spelling word. When he does school projects, he dictates his answers to his mother, who types his reports for him. Still, his mother says he is a creative child, inventing a board game that his teacher liked so much that she now uses it in class during free time.

Dr. Fisher has told the couple that the effects of radiation can continue for years, so Sawyer is likely to experience further cognitive deterioration. When asked if she regrets their decision, Ms. Shader says she didn't and that above all, she is grateful her son is alive: "It was an impossible decision. I try not to think about what might have been."

Weighing the Trade-Offs

For more information on efforts to minimize the side effects from **cancer** treatments, the following sites can help.

-- www.survivorshipguidelines.org

The Children's Oncology Group developed a set of guidelines on the latest ways to monitor and treat effects of **cancer** treatment in children.

-- http://braintumor.org/patient_info/connecting_and_coping/nbtf_conferences/listen.html

A teleconference sponsored by the Children's Brain Tumor Foundation and the National Brain Tumor Foundation on long-term effects on pediatric brain-tumor survivors.

-- www.braintumor.org

The National Brain Tumor Foundation's site has information on treatments and their effects, including radiation options.

-- www.cbtf.org

The Children's Brain Tumor Foundation site is geared to the problems of pediatric brain-tumor survivors.

-- <http://cancer.gov/clinicaltrials/COG-ACNS0331>

Information on the national Children's Oncology Group study of lower radiation doses in children with medulloblastoma.

-- <http://researchportfolio.cancer.gov>

A database of National **Cancer** Institutesupported research and trials on brain tumors.

-- www.massgeneral.org/cancer/cancer_pediheonc_clinicalresearch.htm#brain

Information on a proton-beam-therapy trial for medulloblastoma at Massachusetts General Hospital

-- www.nci.nih.gov/search/viewclinicaltrials.aspx?cdrid=69075&version=patient&protocolsearchid=1466379

Information about a low-dose radiation trial open to children with medulloblastoma ages 3 to 18.

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