

## Targeted chemotherapy shows early signs of slowing tumor growth with less toxicity

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Surviving neuroblastoma as a child can come with just as many challenges as the cancer itself, mainly because of the toxic effects of chemotherapy. But a team of surgeons is in the nascent stages of developing a more targeted method of treating neuroblastoma patients with chemotherapy and lower toxicity. Their research results were presented at the 2015 Clinical Congress of the American College of Surgeons.

Neuroblastoma is a rare childhood cancer, with only about 700 new cases each year, mostly affecting children who are one to two years old, reports the American Cancer Society. The cancer normally presents as a <u>tumor</u> in the adrenal glands.

Normally, treatment of high risk patients involves a surgical procedure to biopsy the tumor, followed by several rounds of chemotherapy to shrink the tumor, then another operation to resect the rest of the tumor, explains Bill Chiu, MD, FACS, assistant professor of surgery at the University of Illinois in Chicago. The more cancerous tissue the surgeon can resect, the higher that patient's chance of survival and the lower the patient's chance of recurrence.

The good news is that current treatment protocol has achieved high five-year survival rates. More than 90 percent of those young children with neuroblastoma in the lower risk or intermediate risk groups get to celebrate their 6th or 7th birthday, reports American Cancer Society.<sup>2</sup>



The bad news is the adverse effect of the chemotherapy. "Chemotherapy is usually given intravenously through a central line. It goes through the body and every cell in the body will experience the chemo," explains Dr. Chiu. "Chemotherapy is basically poison. You're hoping that the poison will kill the tumor before it kills the host."

Some of the more serious late effects of chemotherapy for children include cardiomyopathy, neuropathy, infertility, growth problems, learning difficulties, or even secondary cancers, according to the American Society for Clinical Oncology.<sup>3</sup>

Dr. Chiu and his team have begun developing a more targeted method to deliver the chemotherapy: "The ultimate goal is to create an alternative way to deliver chemotherapy to people with neuroblastoma so we can increase the dosage of chemotherapy but, at the same time, decrease the systemic toxicity," he says.

The targeted method involves implanting a device directly into the center of the tumor. The device contains a chemotherapy-loaded silk sponge. The silk fabric binds to the chemo-therapy agent, allowing Chiu and his team to tune the agent's release. The amount of silk used determines how much of the drug is released.

"Silk has been used in humans for a long time. Certain sutures are made from silk," Dr. Chiu says. "There's very little inflammatory reaction with silk."

In a mouse model, Dr. Chiu and his team simulated neuroblastoma tumor growth in the mice's <u>adrenal glands</u>. They then looked at how the tumors responded to two chemotherapy agents, vincristine and doxorubicin.

They compared delivery methods for the same dosages of each agent.



One set of mice received vincristine delivered intravenously, while another set received it through the <u>sustained release</u> of the silk sponge implanted into the center of the tumor. With the sustained release, half of the <u>chemotherapy agents</u> were released immediately, while the remainder was released over the following 20 days.

Then, they measured tumor growth using ultrasound.

Though the targeted delivery of doxorubicin was not more effective than intravenous delivery, results showed that sustained release of vincristine on the silk sponge device slowed the rate of the tumor's growth more effectively than delivering it intravenously. Tumors usually reach 1000mm<sup>3</sup> in about 10 days. With the sustained release of vincristine it took 30 days for the tumor to reach the same size.

"This approach can complement the traditional systemic chemotherapy," Dr. Chiu explained. "I don't see this protocol replacing systemic chemotherapy altogether, but this method could be a helpful adjunct to the overall treatment plan."

The next steps include more preclinical research to refine the delivery method, dosage, and chemotherapy drug combinations. Ultimately, Dr. Chiu's team seeks to add another effective option to help patients beat neuroblastoma.

"The way we deliver <u>chemotherapy</u> hasn't changed much in the last 50 years. The cycles may change. The dose may vary, but we're always giving it intravenously," Dr. Chiu explains. "But a complementary way to give it in a targeted way—such as going directly to the tumor and giving a lot of it—can decrease the systemic toxicity and hopefully prevent secondary malignancies."

**More information:** 1. American Cancer Society. What are the key



statistics about neuroblastoma? Available at: <a href="https://www.cancer.org/cancer/neurobla.co.stoma-key-statistics">www.cancer.org/cancer/neurobla.co.stoma-key-statistics</a>. Accessed September 16, 2015.

- 2. American Cancer Society. Survival rates for neuroblastoma based on risk groups. Available at: <a href="https://www.cancer.org/cancer/neurobla.com/stoma-survival-rates">www.cancer.org/cancer/neurobla.com/stoma-survival-rates</a>. Accessed September 16, 2015.
- 3. American Society of Clinical Oncology. Cancer.net. Late Effects of Childhood Cancer. Available at: <a href="www.cancer.net/navigating-canc">www.cancer.net/navigating-canc</a> ... cts-childhood-cancer. Accessed September 16, 2015.

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