

# A battle over the rights to tumor tissue

By Stacey Burling  
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All Niki Perry wanted was pieces of her own brain, and she got angrier by the day as she tried to get them.

She needed samples of her brain tumor this spring to enter clinical trials she hoped might save her life.

What she got, she said, was delay and disappointment. Plus insight into what she sees as a new battleground: who controls what happens to tiny bits of tumor tissue saved after surgery. This tissue is growing more precious as scientists unlock its potential to target treatments to a specific person's cancer.

When Perry had surgery in September, she knew better than most patients how valuable the deadly cells in her tumor might be someday.

A frequent participant in brain-cancer

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message boards and an aficionado of new research, Perry knew she might want to enter a European cancer vaccine clinical trial or seek genetic testing that would require frozen pieces of her tumor. She said she asked her surgeon at Thomas Jefferson University Hospital to freeze some just in case.

Freezing tumor cells in a form that can be used for vaccines or advanced genetic testing is unusual. Doctors always put some of the tumor, preserved in formalin and embedded in wax, in slides and small blocks for diagnosis and later testing. Perry knew she would want that, too.

When in March she requested the frozen tissue and her slides, Perry said she ran into

weeks of red tape and a Catch-22. She says Jefferson balked at sending slides to another hospital until she was officially in a trial there. But she needed the tissue to enter the trial. Jefferson finally mailed the slides at the end of May and she picked up the tissue blocks herself at the hospital. To her dismay, she learned there was no frozen tissue.

The 37-year-old South Philadelphia woman, who has had speech problems since the surgery and now communicates more easily by e-mail, wrote that she felt "helpless" and "enraged" as she fought for the tissue. She felt the hospital, which has said it will not comment on her individual case, got "in the way of my trying to save my own life."

Cancer surgeons at Jefferson usually do not freeze tumor tissue, and Peter McCue, who runs Jefferson's anatomic pathology laboratory, said he did not receive instructions to save frozen cells. He said Perry should not have had trouble getting slides.

Perry's experience is unusual, but she says she's seeing more complaints on message boards from patients having trouble getting tissue sent from one hospital to another.

Some doctors agree with her. They say problems with tissue-sharing likely will worsen as the era of "personalized" cancer treatment unfolds. Individualized care is spurring higher demand for tissue, creating nascent tensions between research and treatment. That's making tumor cells a hot commodity, one that patients — bewildered and terrified by a life-threatening diagnosis — often give little thought.

Cancer treatment protocols already contain acronyms for biomarkers — HER2, EGFR, KRAS — that determine which drugs will be used. Memorial Sloan-Kettering Cancer Center does genetic profil-

ing of most of its lung-cancer cases. Swedish Medical Center in Seattle routinely profiles brain tumors.

This is where cancer treatment is heading. The trend has huge fiscal, medical, and social implications. Instead of everyone getting the same chemo cocktail, patients will get treatments aimed at specific mutations in their cancer. They can avoid side effects from drugs that won't help them and can avoid paying for expensive treatments that won't work.

Gregory Foltz, a neurosurgeon who directs brain-tumor treatment at Swedish, says genetic profiling done with frozen brain-tumor tissue may identify the most aggressive forms of a disease that can kill in months. That will help patients make key decisions, like whether to quit a job or enroll in a riskier trial. Companies can justify drugs with smaller target markets. One lung-cancer treatment in development, for example, seems to work well, but only for 3 percent of patients.

Tumor tissue is the keystone of the new science, and its use is fraught with complex, unanswered questions. When cancer patients have surgery, they usually sign consent forms allowing their tumor to be used for research, although hospitals say patient needs should trump science. Tumor tissue might not only save a patient's life — or the lives of other patients years later — but reveal scary genetic truths about him, his family, or his ethnic group. You can't legally sell tissue itself, but its secrets might help a drug company make millions.

So who really owns this stuff and has the right to make decisions about it?

You might think the obvious answer is the patient. But that's actually not clear. C. Mitchell Goldman, a health-care lawyer at Duane Morris L.L.P., expects more lawsuits as more uses for

**At issue is its potential in developing treatments.**



tissue emerge.

"There's not a body of settled law around this issue," he said. It's "fertile for litigation once it becomes clear that having control of this tissue for future use will become important."

Penn bioethicist Arthur Caplan thinks hospitals will have to reserve more tissue for patient use. "The notion of 'I-might-want-it-myself' has just emerged in the last few years," he said. "There's no point in having personalized medicine and mapping the genome if you can't get your tissues shipped."

The evolving problem is that doctors and researchers need more tissue now, and in new forms, while there may be less of it. Early detection and needle biopsies have shrunk the size of tumor samples in some diseases, notably breast cancer. Even though brain tumors like Perry's may be large, surgical techniques often yield little usable tissue.

Doctors are doing more tests on tumors, both before and after treatment. In some trials, they're using live tumor cells to make medicines or profile genes. Academic centers such as Hospital of the University of Pennsylvania are augmenting their diagnostic tissue banks with new frozen repositories earmarked for research. Penn's costs \$250,000 to \$300,000 a year to maintain, said Michael Feldman, a pathologist who runs the new program.

Carolyn Compton, director of the National Cancer Institute's office of biorepository and biospecimen research, said sharing is suffering. Trouble acquiring tissue, she said, is one of "the most common and pervasive issues" in NCI-sponsored clinical trials. The

percentage of tissue that researchers can get from other hospitals has gone from 90 to 75 or 80 and it's still falling.

"There's been a growing difficulty," Compton said, "in getting those tumor samples out of the institution where the patient had their surgery."

Frozen tissue used for immune therapies like the one Perry wanted is especially challenging. It must be sterile and stored in a way that preserves cell viability. This is very expensive. Even research powerhouses like Penn usually don't freeze tissue that way.

Plus, sharing is impractical because different trials use different freezing methods, said David Berd, who is testing an ovarian cancer vaccine at Cancer Treatment Centers of America.

The bottom line, researchers said, is that patients who want vaccines that use frozen tissue either have to have surgery in a hospital that's doing the clinical trial or they have to ask for special treatment before the operation.

That's asking a lot of patients. "They're in a state of shock and they get rushed into surgery right away before they hardly know what hit them," said Linda Powers, an owner of Northwest Biotherapeutics, a Bethesda, Md., company that's testing a brain-cancer vaccine.

George Coukos, ovarian cancer research director at Hospital of the University of Pennsylvania, wants to create a regional bank to store specially treated fresh cancer tissue. He needs it for two new immune-therapy trials.

After the need for tissue slowed recruitment to Northwest's trials, Powers set up HealthBank, a private frozen-tissue bank where patients pay to store their own tissue — if they can persuade their surgeon to help.

Since tissue

banking began a few months ago, two hospitals have refused to participate.

"Their policy was that it was their material to use," Powers

said. "Once it comes out of the patient in their institution, it belongs to them, not to the patient."

While some cancer experts think private banks might help, others were critical.

"These things are not regulated. There are no standards. It's the Wild West," Compton said. "Until this is all standardized and regulated, I'd say you're just throwing your money away."

There's another Catch-22. Pathologists, who are required to keep tumor samples for several years, are increasingly worried about releasing tissue that might be needed later for new treatments, Compton said. Meanwhile, development of those treatments hinges on tissue.

Jefferson's McCue thinks researchers hungry for tissue increasingly are asking for samples as the "ticket" into clinical trials, even though they're not really essential.

Patients don't realize how small the samples are. Years from now, when a more promising trial starts, McCue doesn't want to have to say there's nothing left. Then "we've blown our stake at the poker table," he said.

Should cancer patients consider all this when they have surgery? Most doctors think that's unrealistic.

"Hopefully, as we move more toward personalized medicine, the medical community will think about it so patients don't have to," said Linda Liau, a neurosurgeon who directs UCLA's brain-tumor program.

Perry is still steaming over avenues now blocked because there is no frozen tissue.

"I am utterly crushed by not having access to what I truly believe is the best, most amazing trial ever," she said, referring to a vaccine trial in Belgium. The trial that needed her slides rejected her because her cancer had spread.

She's weighing less-appealing alternatives now.

"I'm totally freaking out day after day," she said, "desperately digging for something that holds promise."

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**Some doctors agree problems over the rights may worsen as "personalized" treatment grows.**



ED HILLE / Staff Photographer

**Niki Perry of South Philadelphia** battled Thomas Jefferson University Hospital to win possession of her tumor tissue.



DAVID M WARREN / Staff Photographer

**Federico Valdivieso** checks on frozen tissue samples at the Hospital of the University of Pennsylvania.