

Photodynamic Therapy: A Light At The End Of The Tunnel For Cancer Patients

Roswell Park Cancer Institute



Almost a decade ago, a woman in her 60s was in extreme pain from a tongue tumor that was spreading along the floor of her mouth. The cancer surgeon whom she consulted removed the lining of her mouth with a laser incision and cut out the tumor. Two months later, the woman's pain level was the same as before surgery and the tumor returned. The surgeon repeated the procedure, yet three months later there was no progress.

"This was a case of the cure being worse than the disease," says Nestor R. Rigual, M.D., a head and neck surgeon at Roswell Park Cancer Institute in Buffalo, N.Y., who struggled with this woman's case.

Recognizing that what he was doing wasn't working, Rigual consulted Thomas J. Dougherty, Ph.D., at Roswell Park who had invented a light-targeted cancer therapy called photodynamic therapy or PDT. Dougherty was then head of the PDT Center. Rigual's patient was a good candidate because her lesion was accessible. With the woman's approval, Rigual treated her with PDT.

“The initial result was quite dramatic,” Rigual says. “The disease went away for more than a year.”

Shining a Light on the Matter

“PDT is an entirely unique concept in cancer treatment,” says Richard R. Matner, Ph.D., director of technology transfer and commercial development at Roswell Park Cancer Institute. “It’s possible that one application may be able to control a cancer, but multiple applications are possible since the treatment is nontoxic.”

Where the light strikes the tumor cell, Matner explains, it releases oxygen and, simply put, “It’s killed.” Matner experienced the treatment himself when a basal cell carcinoma on his shoulder “disappeared” with a single treatment of PDT.

As an alternative cancer therapy, PDT dramatically reduces many of the side effects of standard treatments that include surgery, radiation and chemo or hormone therapies. Unlike radiation or surgery, there are no permanent or deleterious effects like scarring with PDT.

If PDT doesn’t work, says Rigual, “you haven’t burned any bridges” to try other treatments, which is an important concept in medicine.

“*Rather than using toxic radiation to kill cells, a surgeon shines a light at the tumor. This powerful beam of light, directed by a tiny diode laser or endoscope via a particular wavelength that fits in a briefcase-size pack, creates energy that destroys vessels by stopping blood supply. The tumors then starve to death.*

“PDT’s impact is akin to a combination of chemotherapy and radiation,” says Matner. “It takes the best of each and eliminates the worst of each.”

Bringing PDT Into the Light

The first indication that light could damage living organisms was discovered by a German scientist in 1900. He found that a single-cell paramecium was killed when a fluorescein-type dye was added and then exposed to light. Years later, others recognized the role that the oxygen played — and this ultimately became known as the photodynamic effect.

“My first exposure to this phenomenon was accidental,” says Dougherty. “I was testing a potential radiation sensitizer that I had made for its cellular toxicity using a fluorescein derivative that produces fluorescence to remain in live cells but not in dead ones. I was told to do this testing in subdued light since light would kill all the cells in the presence of this stain.”

Like a curious scientist, Dougherty found this intriguing, and so he tried it. “Sure enough,” he says, “all of the cells died.”

And an area of cancer research was born.

His first experiments using fluorescein as the PDT photosensitizer on mice “sort of” worked, says Dougherty. “It slowed the growth but didn’t kill the tumor.

“I soon realized two problems with using fluorescein,” he continues. “First, it produces very little singlet oxygen when activated by light, and, second, the light needed to activate it does not penetrate very far into the tissue. I needed a drug — a photosensitizer — that could be activated by red light (which penetrated tissue the deepest) and produced

large amount of the oxygen needed to kill the cells. I chose a class of compounds called porphyrins since they possess both of these properties. When porphyrins were used, the tumors on the mice completely disappeared.”

The results stunned the researcher. “I couldn’t believe it,” says Dougherty, “I repeated the experiment at least a dozen times!”

Many more experiments took place on numerous mice. Then, with permission from the U.S. Food and Drug Administration (FDA) to start clinical trials on a few brave people with advanced cancers (some who suffered a great deal of pain from overtreatment until the researchers got the dosages right), Dougherty, with the help of many others including various pharmaceutical companies, achieved the one-chance-in-a-thousand odds for FDA approval in 1995.

Not everyone saw the light of PDT at first. Some of the researchers from Roswell, including Dougherty, created a company to commercialize the original compound that Dougherty had identified and patented, called Photofrin. Funding was first provided by the National Cancer Institute in 1974 as a grant and renewed many times over the course of their research. Financial support also came from The Oncologic Foundation of Buffalo. These funders, along with money from Johnson & Johnson for the Photofrin rights, officially launched and carried the program.

When the Photofrin was licensed to the company, it, in conjunction with Lederle Laboratories, obtained approvals for obstructive esophageal cancer in 1995 and for lung cancer in 1998. When Axcan Pharma of Quebec obtained the license from the company, the group earned approval for high-grade dysplasia in Barrett’s esophagus in 2003.

At that time, Barbara Henderson, Ph.D., and current head of the PDT Center at Roswell Park, discovered that destruction of the tumor blood vessels, in addition to the tumor cells, was key to the complete destruction of the tumor. Henderson helped change medical minds with this finding. “She translated the PDT technology into patients,” says Matner.

But there was still a concern with one of the side effects of the drug, says Dougherty. “There was skin phototoxicity, which meant that patients had to stay out of the sun for six to eight weeks after the procedure.”

Ultimately this problem was solved by Ravindra Pandey, Ph.D., a chemist at Roswell. He worked on a series of compounds that would be as effective as Photofrin, but without the skin toxicity. The breakthrough came when Pandey synthesized compounds that reduced skin phototoxicity from several weeks to three or four days. This dramatically impacted quality of life for patients following the PDT cancer treatment.

How Brightly the Light Can Shine

PDT has been used for essentially every conceivable cancer as well as many noncancer indications. Some of the most promising are cancers of the head, neck and bile duct. The only approved noncancer uses are for vision loss and skin lesions. It is approved in the United States, Canada, Europe and Japan for palliative use and cure for certain cancers of the esophagus, lung, skin, cervix and bladder (bladder cancer is not yet approved in the United States).

Pandey’s new photosensitizer has been licensed in China and in India where it will be used for treatment of head and neck cancers that are prevalent in these countries. This will greatly expand the number of patients who can benefit from PDT.

As for the woman whose tongue cancer was treated with PDT by Rigual over a decade ago — she is in her 70s now and cancer free. At the rate it is being studied and applied, PDT is not only likely to extend the lives of many more people with cancer, but will allow clinicians to make earlier and more precise diagnoses that will

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