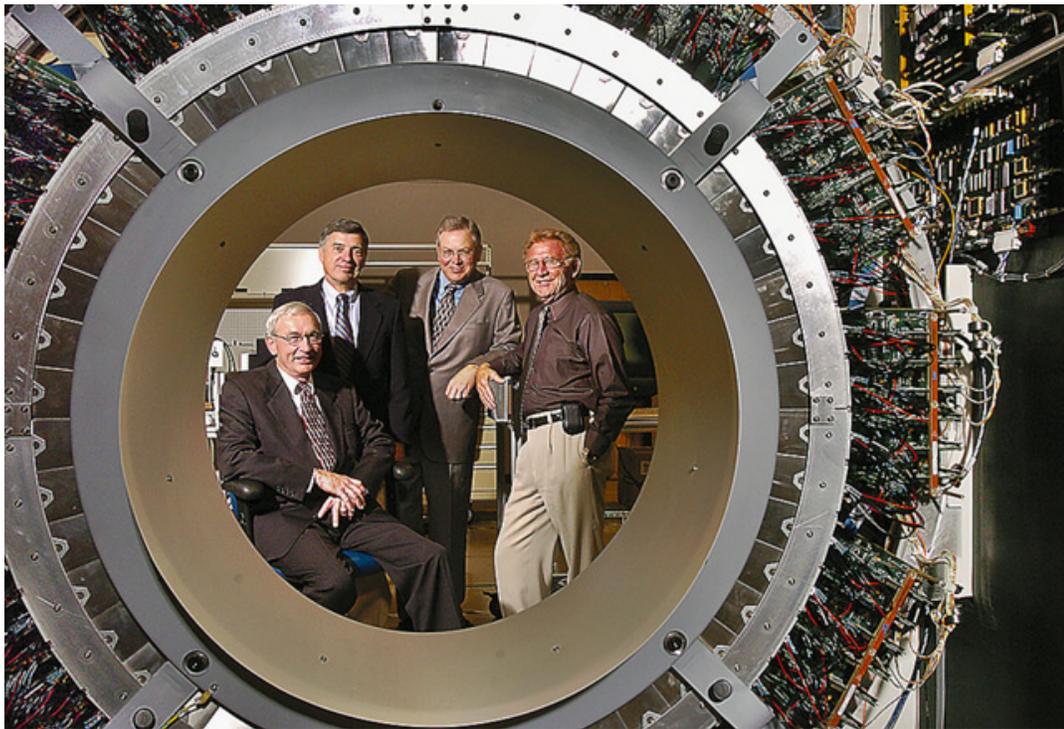


Local engineers made lasting impact on detection, treatment of diseases



The founders of CTI, from left, Kelly Milam, Terry Douglass, Mike Crabtree, and Ronald Nutt were photographed through the opening of a PET tomograph on the West Knoxville production line shortly after the company's sale to Siemens was announced.

By Kay Brookshire

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Diagrams sketched 36 years ago by three university researchers and several engineers in an Oak Ridge office evolved into technology that today is used to detect cancer, heart disease, Alzheimer's and other diseases as well as aid in their treatment.

"For us as oncologists, it has helped make tumor staging much

more accurate. It allows us to better predict how a patient responds to treatment. It avoids unnecessary surgery and makes treatment recommendations more accurate," says Dr. Richard Grapski, an oncologist at Thompson Cancer Survival Center in Knoxville. "It is going to revolutionize how we treat people with cancer."

The technology is medical imaging scanners using positron emission tomography, commonly known as PET scanners. Four electrical engineers who sat at that conference table founded CTI Molecular Imaging to produce and market the PET scanners in 1983 and continued to improve the technology for broader applications.

Siemens acquired CTI for nearly \$1 billion in 2005, and the company continues to employ about 500 people at its Knoxville operation.

Its founders, however, measure the company's success by the estimated 3.5 million people worldwide who have undergone PET scans in the past year and the impact of the technology on detection, management and treatment of disease.

"We know in about a third of the cases that treatment has changed as a result of doing a PET scan. You can see the number of lives that are impacted because treatment was changed, hopefully to be more effective," says Terry Douglass, a founder and the first president/CEO of CTI. "That is the biggest reward out of the whole effort that we put out for this."

Douglass and the other founders, Mike Crabtree, Kelly Milam and Ronald Nutt, put up their houses as collateral and borrowed \$2 million to finance the startup business when the market for PET scanners was limited mostly to universities.

"We pledged our houses and some automobiles," Nutt recalls. "It was scary. It was all we had. We bet all the material things we had, and started it up."

Michael Phelps, then an assistant professor at Washington University in St. Louis, planted the seed for the business when he called EG&G ORTEC in Oak Ridge, where the men who would become CTI's founders all worked, to ask about components researchers might use to build a new type of medical imaging scanner.

"He was a very insightful and entrepreneurial-type person," Milam says of Phelps, now a professor and department chair at the University of California-Los Angeles.

EG&G ORTEC makes nuclear and electronic instruments, primarily used by nuclear physicists in laboratories, which Phelps thought could be applied to measurements of the human body.

Douglass, then chief life sciences engineer for ORTEC, invited Phelps to East Tennessee to talk more. Phelps later bought some components and the company gave him others to try to create a prototype. Soon, ORTEC was building the scanning devices.

By 1983, Douglass was ORTEC's president and charged with selling parts of the business that weren't consistent with the company's new mission, including the PET scanner work.

He and Crabtree left the company and with Nutt and Milam, who had departed earlier and were working elsewhere, to launch CTI.

"It really seemed to us that this was something that we needed

in health care, and we could do the things to make it a reality, make clinical PET a reality. That was our mission statement," Douglass says.

The partners brought different and complimentary skills to the business, Douglass says.

"As president of ORTEC, strategy was kind of my expertise. Then Ron Nutt was in research and development - that was his focus. Kelly was in manufacturing and operations, and Mike was systems and software and marketing. We had complimentary interests and skills."

The new company set up shop in a small office in West Knoxville, gutted space for manufacturing and started producing PET scanners to meet the first half-dozen orders, Nutt said.

With its own research and development program and 22 employees, CTI soon replaced the technology it had acquired from ORTEC with a new scanner, beginning the innovation that kept CTI ahead of its later competitors.

The scanners were pricey - from \$500,000 to \$2 million.

"Only a handful of institutions worldwide could afford this technology," Nutt says.

That helped keep the young company focused, Crabtree says. "If you miss your forecast by one or two a year, it has a dramatic effect."

Positron emission tomography makes computerized pictures of the body after a patient has been injected with a radiopharmaceutical, a radioactive drug with a very short half-life. Sugar, or glucose, is an energy source for most areas of the

body, and a radioactive tag is placed on sugar molecules, with the scanner showing those areas using more energy. Cancer cells use more energy than normal cells, so PET detects that abnormal activity. While CT (computed tomography) scans, developed before PET scanners, give an anatomical view of the body, PET scans give a metabolic view.

As the patient lies on a table that moves through the PET scanner, the scanner's cameras detect gamma rays emitted from the patient. They are converted into electrical signals, processed by a computer to generate images.

One problem CTI solved was how to provide radiopharmaceuticals to PET scanner clients. CTI purchased a business that made cyclotrons, the particle accelerators that produce the short-lived isotopes needed in PET scans.

In 1989, CTI established radiopharmaceutical distribution centers, which later became CTI PETNet.

CTI's partnership with Siemens began in 1985 when Siemens invested \$2.5 million in CTI. Two years later, the firms created a joint venture.

"They didn't just grab our technology and leave us high and dry," Milam says. "They bought 49.9 percent of the company, which gave us controlling interest."

The partners recall 1994 as the year the company didn't make money.

U.S. hospitals feared ordering expensive machinery until they knew the results of then-First Lady Hillary Clinton's health-care reform effort.

"We got no orders in the United States that year. We survived

that year on orders from Europe," Nutt says.

As medical uses of PET scanning became more significant in the 1990s, CTI dealt with regulatory and reimbursement barriers.

Company officials enlisted the aid of U.S. senators, including Bill Frist of Tennessee and Ted Stevens of Alaska, to receive Food and Drug Administration approval for use of radiopharmaceuticals with PET scanners, a goal achieved in 1997. They also sought approval for Medicare reimbursement of the procedure, which opened the market for the imaging scanner in 1998.

"Once reimbursement was approved, then that opened the flood gates. It allowed economic models to flourish, so that clinicians and physicians could order PET scans and know that they were going to be reimbursed for it, or the patient would be reimbursed for it," Crabtree explains.

Nutt adds, "We were the only people doing it for years. When it became clinically viable, General Electric entered the market, and later Philips (Electronics)."

CTI's continued research and development efforts, however, allowed it to retain about 60 to 70 percent of the market, according to Milam.

"We kept changing and improving the product faster than our competitors did," Milam says. "We were the ones that led in the market all along with innovative solutions."

Used initially in brain research at universities, PET scanning was put to use clinically at first to explore cardiac problems. By the mid-1990s, researchers demonstrated that PET scans could identify tumors much earlier than existing CT scans and

determine whether they were cancerous. Today, about 95 percent of the use of PET scanning is directed toward cancer detection and treatment planning.

Nutt says the impact of PET scans is difficult to measure, but he points to the recent finding that the cancer death rate has dropped and notes smoking cessation, early detection of cancer and proper cancer treatment are cited as reasons by the National Institutes of Health.

"PET has impacted two out of the three," he says. "We can detect cancer earlier than any other technology."

In 1995, Nutt and physicist David Townsend built the first medical imaging device that combined PET and CT technology, detecting both anatomical details and metabolic processes at the same time. Approved for use by the FDA in 1999, the PET/CT scanner was named Time magazine's medical invention of the year in 2000. The scanner allows physicians to determine not only size of a tumor, but also success of treatment within a short time.

In 2002, CTI conducted an initial public offering selling stock on the Nasdaq market. In 2003, Douglass stepped down as president and CEO, remaining as chairman, and was succeeded by co-founder Nutt. Milam and Crabtree had already left - Milam to retire and Crabtree to continue as an entrepreneur.

In 2005, the German electronics and electronic engineering giant Siemens bought CTI, making it part of its Siemens Molecular Imaging Group.

About 3,000 PET scanners are operating around the world, including a half-dozen in Knoxville.

"We were a young company that grew steadily. We worked very hard, and we were thankful for a lot of things that happened. Some we controlled and some we didn't," Crabtree says.

"Anybody who thinks they are smart enough that they can do all those things without a little luck, they are not being totally honest with themselves."

1972: Early PET experiments at Washington University

1973: Washington University post-graduate Michael Phelps approaches ORTEC about developing the first PET scanner

1974: First human PET scan

1981: Science magazine publishes PET scans of the human brain

1983: Terry Douglass, Ron Nutt, Michael Phelps, Mike Crabtree and Kelly Milam launch CTI Molecular Imaging

1987: CTI PET Systems formed as a joint venture with Siemens to bring together CTI's PET experience with Siemens' global distribution network. Division later becomes CPS Innovations. Siemens pays \$30 million to own 49.9 percent of CTI's manufacturing operation.

1992: Develops the first whole body imaging capability.

1998: Invents the combined PET/CT scanner and demonstrates the first clinical image using this scan.

2000: PET/CT scanner receives Time magazine's Medical Invention of the Year.

2002: An initial public offering of CTI stock made on the Nasdaq Stock Market

2003: Founding president and CEO Terry Douglass steps down

and is succeeded by co-founder Ron Nutt. Douglass remains chairman.

2005: CTI announces and completes sale to Siemens.