

Our Founders' Story

Ninth Grade Science Leads to Life-long Friendship

Sam Mazin, Ph.D. and Akshay Nanduri, the two co-founders of RefleXion Medical, first met in 1992. It was ninth grade Advanced Science at Thornlea Secondary School in Thornhill, Ontario, Canada, where the two became best friends. They worked together on multiple science projects, one where they measured gravity and were loyal members of their school's chess and bridge clubs. Mazin and Nanduri will tell you they were extremely competitive academically with one another, but this only strengthened their closeness. After high school, both men attended the University of Waterloo, each receiving a Bachelor of Applied Science in Computer Engineering.

Nanduri went on to receive his Master of Applied Science in Electrical Engineering at the University of Waterloo, where he was advised by Dr. En-hui Yang, one of the world's leading researchers in information theory and co-founder of SlipStream Data, Inc. Upon completion of his master's in 2003, Nanduri joined SlipStream as its first employee and later became director of software development, where he led a team of 10 engineers. In 2006, SlipStream was acquired by Research in Motion (BlackBerry), and in 2007, Nanduri left the company to pursue graduate work at MIT, where he received his MBA at the Sloan School of Management.

Mazin meanwhile, started his graduate work at Stanford University, where he too received a Master of Science in Electrical Engineering. In 2004, he decided to pursue a Ph.D. in Electrical Engineering at Stanford and his research was focused on the design of a novel X-ray computed tomography (CT) system, resulting in several journal papers and a patent, as well as the Joel Drillings Award from the American Heart Association (AHA). His work on a PET-based algorithm received the prestigious Cum Laude Award from the SPIE international medical imaging society.

The "Aha!" Moment to Turn Cancer on Itself

After earning his Ph.D. in 2007, Mazin started a postdoctoral position focused on medical imaging in the Radiological Sciences Lab at Stanford. Mazin's Ph.D. advisor, Norbert Pelc, Sc.D., who at the time was associate chair of the Department of Radiology, continued to advise Mazin during his postdoc research. The idea that would later become RefleXion, came to Mazin in 2007 when he attended a talk on campus by Radiation Physics Professor, Lei Xing. As Professor Xing was explaining how difficult it is to see tumors during cancer treatment, an idea formed for Mazin that he would pursue after leaving Stanford. Could cancer signal its location back to the therapy machine? Could positron emission tomography (PET) be used in a different way to enable the X-ray beam to be locked onto the tumor?

"An idea began to slowly take shape – to use the signals coming from the tumors themselves to guide radiation during treatment," says Mazin. "In essence, turning cancer on itself to destroy it."

The entrepreneurial spirit runs in the Mazin family. His father, Jack Mazin, developed fruit flavored raisins and founded the company, Amazin' Raisins in Ontario. Even though young Sam

Mazin never thought he would start a company, he found himself in 2007 thinking that he had to. So he called his best friend.

The Whiteboard with Wild Scribbling

Nanduri, who was completing his first year at MIT Sloan, remembers receiving the first of several phone calls from Mazin in late 2007 regarding his new idea in radiation oncology. Nanduri also remembers feeling skeptical about it. The MBA program at Sloan had a track focused on Entrepreneurship which culminated in a visit to Silicon Valley in Northern California. It was in January of 2008 when Nanduri went on one of these trips and was able to spend time with Mazin at Stanford to more fully discuss his idea. He remembers seeing a whiteboard in Mazin's dorm room with "wild scribbling" all over it and he said to his friend, "Maybe we should go get a beer."

Back at MIT after his Silicon Valley excursion, Nanduri continued to take courses focused on new ventures and Mazin did so as well through the Stanford Ignite program during the summer of 2008. At the same time, Mazin continuously worked on computer coding to simulate the machine he had already built in his mind. After almost a year of phone calls with Mazin, Nanduri reluctantly agreed to help him out and suggested they enter MIT's storied "100K" business plan competition – an institution-wide competition that helps turn breakthrough technology ideas into thriving companies. During this process, Nanduri and Mazin interviewed dozens of clinicians and something clicked for Nanduri. He realized his friend was onto something that could be extremely disruptive.

The team didn't win the competition. Instead they were one of five semi-finalists, but creating the plan helped the two understand the implications of the idea and it gave them exposure to business and medical thought leaders.

Nanduri Joins Mazin

The positive feedback they received from radiation oncologists during their research clearly validated that there is a need for seeing and treating cancer at the same time. This was the validation Nanduri needed to join Mazin.

"I started thinking about what I was going to do post-business school," says Nanduri. "I had this opportunity in front of me to change the world, work with my best friend, and all we needed was money. No problem – let's go do it!"

Nanduri moved from Boston in 2009 to the San Francisco Bay Area to join Mazin and the two worked out of Mazin's apartment in Menlo Park, California. RefleXion Medical was incorporated on March 17, 2009.

Also, in 2009, while a postdoc in Radiology at Stanford, Mazin was accepted to the 2009 Ewing Marion Kauffman Foundation (USA) Postdoctoral Entrepreneurship program, designed to help scientists commercialize innovative technology. The timing of this program was very opportunistic – it gave him a year to do research, develop his technology and get paid for it. Mazin and Nanduri entered other contests as well, including Stanford BASES and the Santa

Clara Boomer competition. Again, the competitions gave them exposure, this time with potential investors and venture capital groups.

All-Nighters

The two co-founders began many weeks of all-night coding sessions in Mazin's apartment. Using a refurbished personal computer and open-source software packages, they created a complete physics software simulation framework that modeled key aspects of their proposed system.

This work was instrumental in obtaining a Small Business Innovation Research grant from the U.S. National Cancer Institute in 2011 to carry out the first PET imaging experiments in collaboration with the Stanford Cancer Institute.

Early Advisors, Investors and Key Partnerships

Mazin and Nanduri first met Jay Watkins, an industry veteran with years of experience guiding and investing in medical device startups, in 2009. The meeting originated through Mazin's support from the Kauffman Postdoc program, as Watkins was involved in the interviews and selection of the 13 scientists for the program.

Watkins joined the RefleXion Board of Directors as Chair the next year because he was inspired by Mazin's vision. According to Nanduri and Mazin, Watkins, who often referred to the two co-founders as "delusional optimists," was a significant advisory figure to them early on, and to this day, he remains Chairman of the Board and has been instrumental in introducing the company to many of its key institutional investors.

RefleXion's early investors included David Auerbach, co-founder of IMPAC Medical Systems. Through the relationship with Auerbach, Mazin and Nanduri also met one of IMPAC's first employees, Todd Powell, who went on to lead IMPAC through an acquisition by Elekta, a world-wide giant in the field of radiation oncology. After an 11-year executive tenure at Elekta, Powell joined RefleXion as president and CEO and a member of its Board of Directors in 2017, bringing 25-plus years of medical and radiation oncology expertise to the company.

Other early investors included Professor Jonathan J. Fleming, a life sciences venture capitalist and lecturer at MIT, as well as Stanford's Chair of Radiology and pioneer in Nuclear Medicine, Sam Gambhir, M.D., Ph.D., and his wife, Aruna Gambhir.

From the beginning, RefleXion has forged key partnerships with academic institutions, research entities, and companies that have been instrumental in solidifying the company's position in intellectual property and clinician acceptance. Their low-key approach, especially during the cash-constrained climate that existed when the company was founded, helped build credibility with the medical and radiation-oncology communities.

RefleXion's grassroots seed financing approach has been beneficial as well. Radiation oncologists and industry executives who saw the potential of the technology and ultimately

invested in RefleXion have become advisers who continue to contribute to the ongoing success of the company today.

A Decade Later

St. Patrick's Day 2019 marked RefleXion Medical's 10-year anniversary. This was celebrated with the grand opening of the company's 50,000-square-foot manufacturing facility, which includes six state-of-the-art testing vaults for the RefleXion® X1 systems—machines that combine PET detectors with traditional radiation therapy in an entirely new way to deliver treatment to cancer patients.

It's been a long but rewarding decade for the company they founded. Despite launching a company during one of medical technology's darkest times when conventional venture capitalists were eschewing capital equipment, total investment to date is \$450M in equity funding from a top-tier investment syndicate that includes pharmaceutical giants Pfizer and J&J. The interest in RefleXion by these investors is a testament to RefleXion's bold vision of changing the treatment of cancer from single tumor therapy to the ability to treat metastatic disease.

An impressive internal team and an advisory board made up of KOLs and renowned industry veterans underpin RefleXion's success to date. In addition to Todd Powell, who assumed the roles of president and CEO in 2017, Martyn Webster joined the team as CFO in 2018, bringing specific expertise in medical device startups and fundraising, and Thorsten Melcher, Ph.D., a top-tier oncology industry leader, with a background in both radiotherapy and pharmacology, joined the company as CBO in 2019. In 2020, Sean Shirvani, M.D., assumed the role of CMO, bringing over 15 years of clinical and industry experience, including as a faculty radiation oncologist and medical director at MD Anderson Cancer Center's Arizona affiliate. To date, the company employs 240 people and is growing rapidly.

The RefleXion X1 machine with SCINTIX® biology-guided radiotherapy (BgRT) was granted Breakthrough Device Designation for lung tumors and received marketing clearance under the De Novo pathway by the U.S. Food and Drug Administration (FDA) for primary and metastatic lung or bone tumors. The RefleXion X1 is also cleared for stereotactic body radiotherapy (SBRT), stereotactic radiosurgery (SRS), and intensity modulated radiotherapy (IMRT).

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Media Contact:

Amy Cook
acook@reflexion.com