ONCOLOGY DEVICES

HIL Applied Medical Ltd.

Ultra-compact proton accelerator for treating cancer

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Business: Ultra-compact, high-performance particle accelerator
Founded: November 2010
Founders: Shmuel Eisenmann, PhD, CEO; Arie Zigler, PhD, Chief Scientist (Hebrew University of Jerusalem)
Employees: 5
Financing To Date: $1.7 million
Investors: Israel's Office of the Chief Scientist; Hebrew University of Jerusalem; Undisclosed venture capital firms; Angel investors
Board Of Directors: Oded Tamir (InSightec Ltd.); Arie Zigler; Guy Shinar, PhD (formerly, X Technologies Inc.); Judith Zilberstein (Maayan Ventures); David Akunis (Medvest LLC)
Scientific Advisory Board: Yves Jongen (Ion Beam Applications SA [IBA]); Alfred Smith, PhD (formerly, The University of Texas MD Anderson Cancer Center, Houston); Zelig Tochner, MD (Roberts Proton Therapy Center, University of Pennsylvania)

HIL Applied Medical Ltd. is developing a smaller, lighter, and more compact particle accelerator for proton therapy that has the potential to dramatically change the way cancer patients are currently being treated with radiation, and at much lower infrastructure, operating, and maintenance costs. "Most of radiation therapy today relies on very high energy X-ray," says founder and CEO Shmuel Eisenmann. "Although these X-rays are very effective at destroying tumors, they cause a lot of damage to healthy tissue around the tumor." On the other hand, proton-beam therapy is a form of highly focused radiation that uses charged particles and "can reduce collateral damage to the tumor by up to sixfold," Eisenmann says. "However, a particle accelerator is needed to bring the protons to about two-thirds the speed of light; then the protons are focused and directed toward the tumor inside the patient."

Today's proton accelerators – based on advances made in the 1930s and 1940s – are huge, complex machines, weighing more than a fully loaded 747 jumbo jet; it costs between $150 million and $250 million to build a stand-alone center, with typically four or five treatment rooms (75,000 to 110,000 square feet total). Because of such prohibitive costs, there are only 11 operating proton therapy facilities in the US. But there are between 250,000 and 300,000 eligible cancer patients a year for proton therapy, so these 11 centers can only meet 2% to 5% of the clinical demand, even by operating 24/7.

HIL's technology significantly reduces the cost of building and equipping a proton therapy center "to the level where practically any community hospital can afford one," says Sagi Brink-Danan, VP of business development. "It also becomes a profit center within about three years," he adds. For a single-room facility, which is what most hospitals desire, the cost is on the order of $12 million to $14 million. "There are a few other companies that offer single-room facilities, but they cost around $40 million each," Brink-Danan says. The key to such drastic cost savings is HIL's high-power laser-based proton accelerator, as opposed to the massive magnets and radiofrequency (RF) electric fields currently used for acceleration. "We shoot the laser beam on a physical target that has nano-engineered features," Eisenmann says.

The interaction between the laser and the physical target produces and accelerates the protons within the span of a fraction of a millimeter. This results in a beam of fast protons that can be shaped and directed precisely toward a tumor using magnetic elements (particle-focusing optics). Inside the tumor, the protons collide with DNA, causing sufficient damage to destroy the cancerous cells. "The Bragg peak is the mechanism by which protons deposit most of their energy in the tumor while sparing the surrounding tissue," Eisenmann explains.

Another advantage of HIL's laser-based technology is that it requires substantially less radiation shielding, compared with conventional accelerators that generate excessive unwanted radiation and are, therefore, housed in concrete vaults up to 18-feet thick. "As much as 25% of the facility cost for these traditional proton therapy centers is for concrete reinforcement," Brink-Danan says.

Proton therapy is used to treat solid tumors, usually before they metastasize, representing about 300,000 new patients yearly in the US alone, and roughly one million patients worldwide, for an aggregate potential market of $30 billion to $40 billion annually.

Eisenmann and company chief scientist Arie Zigler founded HIL in November 2010, following lengthy research at the **Hebrew University of Jerusalem** headed by Zigler, who is a full professor in the department of physics. HIL has one issued and six pending patents, one of which is owned by Hebrew University and licensed to the company. "In those early days, we successfully demonstrated proton acceleration by laser, but it was nowhere near the two-thirds speed of light needed to treat patients," says Eisenmann, who earned both a masters and a PhD in physics under Zigler and specializes in high-powered lasers, electro-optics, nonlinear optics, plasma physics, and laser accelerators. A titanium sapphire laser of 800 nm was chosen as the platform because of its ability to produce a temporally "clean" laser pulse without sacrificing too much energy.

"High-power ultra-short-pulse laser systems do not produce just one pulse at a time," Eisenmann says. "Each 'main pulse' is preceded by one or more 'pre-pulses' that are typically several orders of magnitude less energetic than the main pulse. But in the case of high-power lasers, these pre-pulses are energetic enough to completely ionize our nano-structured target before the main pulse even arrives. Devising new ways to control the timing and limit the amplitude of these pre-pulses in order to optimize the laser-target interaction has been a major challenge."

Moreover, to generate proton beams that are suitable for treating cancer, "one needs to produce enough protons per second [flux] to treat an entire tumor within the desired time frame, typically one to three minutes, and also accelerate the protons to high enough energies [speeds] to reach the desired depth within the body, to cover the entire tumor," Eisenmann notes.

Besides his academic appointment, Zigler co-founded X Technologies Inc. (interventional cardiac devices) in 1999, which was acquired by Guidant Corp. in 2003 and is now part of Boston Scientific Corp. Brink-Danan was the founding CEO of Perfuzia Medical Inc. (treatment of chronic wounds) in 2009, and prior to that served as VP at SRS Medical Inc. (a female urinary device) and manager for US operations at Mazor Robotics Ltd. (orthopedic and neurosurgical robots).

HIL's technology consists of four primary components: the laser, an interaction chamber, a nano-structured target, and particle-focusing optics. The radiation oncologist first arranges for the patient to undergo a computed tomography (CT) scan. Results from the scan are used with advanced treatment planning software, resulting in a treatment plan for radiating the tumor while minimizing damage to surrounding tissue. The patient is then brought into a treatment room, where he or she lies on a robotic bed. A rotating gantry surrounds the patient and directs the proton beam, according to the treatment plan, directly to the tumor.

The laser, which is housed in an adjacent room, produces an ultra-short pulse that travels through a set of mirrors and vacuum tubes and into the interaction chamber, which is situated on the rotating gantry about 10 feet from the patient. "In the interaction chamber, the laser beam [pulse] interacts with the nano-engineered target, which is a very small piece of material that resembles a forest of ice crystals," Brink-Danan explains. Once the laser beam hits those crystals, the protons are accelerated very quickly. The beam is then directly and precisely shot at the tumor through a set of magnetic lenses [focusing optics].

A treatment session takes on average 20 minutes, of which proton beam exposure lasts from one to three minutes, but there is no patient discomfort. A course of treatment ranges from three to 40 sessions, scheduled daily. "Anyone trained and certified in proton beam therapy will be able to use a system based on our technology as easily as any other system," Brink-Danan says. "Our system will also require a lot less maintenance and tweaking." This is significant, since today's centers typically require 15 full-time vendor employees for ongoing maintenance, compared with an estimated one or two full-time employees for HIL technology.

Competitor next-generation proton therapy technologies from **Mevion Medical Systems Inc.** (*Mevion S250*) and **Compact Particle Acceleration Corp.** (CPAC) are trying to achieve similar goals, but employ very different technologies. The Mevion S250 uses a combination of an electric field and electromagnets for its super-conducting, gantry-mounted accelerator that weighs 10 times more than HIL technology and is larger. Conversely, the CPAC system under development will use primarily electric fields to accelerate the protons. "Although these two competing technologies likely provide the same efficacy for treating cancer patients, our technology may enable proton therapy systems that are considerably less expensive and do not take up nearly as much space," says Brink-Danan, who does not expect the need for new reimbursement codes.

The first beta installation of HIL's technology is not expected for another five to six years. "But at any time, a strategic partner (e.g., market-leader Belgium-based **Ion Beam Applications SA** [IBA] or CA-based **Varian Medical Systems Inc.**), either active in proton therapy or radiation therapy at large, could step into the picture and adopt our technology," says Brink-Danan.

HIL has raised two rounds of seed financing and a $500,000 round capitalized by an Israeli VC firm that closed in October. A Series A round of as much as $5 million should conclude sometime next year, targeting top-tier VCs in Israel, Europe, and the US, as well as a number of potential strategic investors.

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– Bob Kronemyer