Ottawa researchers enter home stretch in race to produce artificial heart

Charlotte Gray

Charlotte Gray, an Ottawa freelance writer, is a *CMAJ* contributing editor.

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In Brief

AN OTTAWA TEAM IS IN A FIERCE RACE TO PRODUCE an artificial heart. If it wins, the prize will be huge: a worldwide market worth billions of dollars. The team, led by Dr. Tofy Mussivand, brings together scientists and entrepreneurs. The goal is to produce a heart that improves patients' quality of life and doesn't leave them tethered to a machine in hospital. Current plans are to complete clinical tests by 2000 and to have a commercial product ready for market in 2001–2. Several other groups are also racing the clock.

En bref

UNE ÉQUIPE D'OTTAWA PARTICIPE À UNE COURSE ACHARNÉE pour produire un cœur artificiel. Si elle gagne, le prix sera énorme : un marché mondial de plusieurs milliards de dollars. Dirigée par le Dr Tofy Mussivand, l'équipe réunit des scientifiques et des entrepreneurs. Elle vise à produire un cœur qui améliorera la qualité de vie du patient et ne le laissera pas enchaîné à une machine à l'hôpital. Les plans actuels prévoient la fin des essais cliniques d'ici à l'an 2000 et la production d'un cœur prêt à commercialiser en 2001–2002. Plusieurs autres groupes participent aussi à cette course contre la montre.

As a Kurdish teenager, Tofy Mussivand was responsible for a herd of sheep on Turkey's Mount Ararat. "At night," he says, "I used to look up at the stars and wonder, 'What are they? How can I learn about them?' "

Decades later, Mussivand is still grappling with existential challenges. His primary preoccupation is whether he and his Ottawa-based team can develop an artificial heart that will allow people to live an ordinary life. But in the background of his ground-breaking work at the University of Ottawa Heart Institute is an equally important question. Can a single academic health care centre operating in a small country with limited research funding compete with the big boys — the American and Japanese biomedical corporations — to develop a product that has the potential to provide a massive return? The answer: quite possibly.

Dr. Tofy Mussivand discusses his project in terms that are disarmingly simple. Whether he is talking to an audience of peers, a group of mutual-fund managers or a reporter with no background in the sciences, he avoids jargon. "I love to teach," he explains.

He wants listeners to understand the significance of his work just as he yearned to understand the stars and, later in life, medical texts. Mussivand, who came to Canada in 1967 to study engineering, eventually settled in Alberta, where he worked for the provincial government. When he married a physician, he looked at her textbooks and was frustrated to discover that he couldn't understand them. "I then switched my attention from the stars to the human body," he explains.

When he was 37 he decided to return to school, and persuaded the University of Akron in Ohio to accept him as a doctoral student in a combined program in biomedical engineering and medical sciences. One of his professors there was al-

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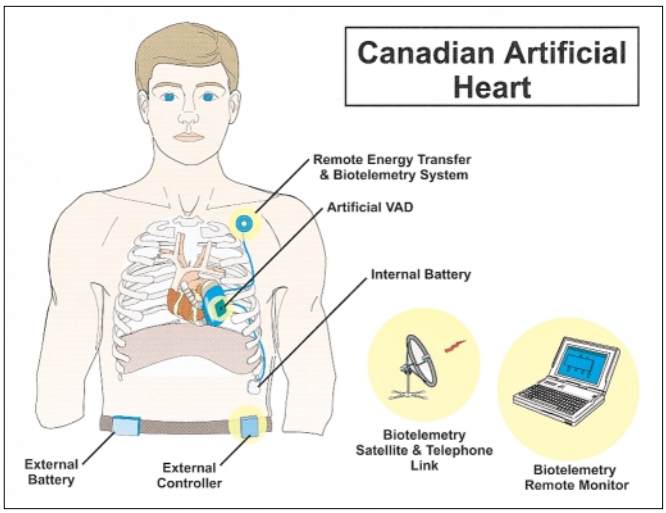
ready working on an artificial-heart project at the Cleveland Clinic, and when Mussivand graduated the professor asked whether he would like to join the project. "Can I start tomorrow?" he asked. Today, his enthusiasm remains undimmed.

"At Cleveland, I discovered that millions of people around the world were dying of heart disease," he says. "And guess what — there was no solution."

The best available treatment for end-stage disease is a heart transplant, but the problems are legion because demand far outstrips supply, the cost is huge and post-transplant patients face a lifetime of medication and medical surveillance. The more Mussivand studied existing options, the more committed he became to the concept of an implantable artificial heart. He saw the project foremost as an engineering challenge. "The human body is a masterpiece of God and fluid dynamics," he argues. "Can we reproduce it?"

University of Ottawa Heart Institute



Schematic drawing shows how EVAD would operate. The system can be monitored via biotelemetry.

The Cleveland team was not the only group taking on the challenge, because several other US centres were already at work. In Canada, Dr. Wilbert Keon had established a heart-transplant program at the Heart Institute in 1984, when it was only 8 years old. When he decided that his team should build a prototype implantable electrohydraulic ventricular assist device (EVAD), he began searching for a project manager. Keon kept hearing Mussivand's name, and invited him to come to Ottawa.

Mussivand's first reaction was that Canada was too cold. Besides, he loved the work he was doing in Cleveland. However, his wife and children, all Canadians, wanted to come home, and so Mussivand moved to Ottawa in 1989. Today, besides being a professor in the University of Ottawa's Faculty of Medicine, he heads the Heart Institute's Cardiovascular Devices Division and leads the Canadian Artificial Heart Program.

"I'm a simple-minded person myself," says Mussivand, "so I like things to be simple." Soon after arriving in Canada, he sat down with his colleagues to list the key attributes of an artificial heart. They decided that it should fit in the chest like a human heart. It should allow for remote power transfer so that no hoses or tubes had to protrude through the skin. There should also be wireless monitoring and control, and it needed to be compatible with blood and tissue to eliminate the risk of clotting.

The key point was that the patient's quality of life would have to be improved by the device: patients could not be left tethered by tubes to huge machines, or left unable to care for themselves. Finally, the device should be affordable. "It should cost less than a heart transplant," Mussivand explains. "Ideally, much less."

To a layperson each of the attributes sounds eminently reasonable, yet none is simple and each involves a major biomedical-engineering or medical challenge. To achieve remote power transfer, for instance, the Ottawa team had to develop a component that transferred a strong electrical current through the skin without requiring perforation. To achieve wireless monitoring and control, which would allow the heart's operation to be altered noninvasively, the team had to develop new telemedicine technology.

In 1993, Mussivand and his team unveiled a prototype of their EVAD that weighed only 500 g. It is a sign of the Ottawa team's creativity that none of the competitors, such as Thermo Cardiosystems Inc. of Woburn, Mass., or the Novacor Division of Baxter Healthcare Corporation, has produced an artificial heart that meets Mussivand's criteria. Most are considerably heavier than the Ottawa model, fit in the abdomen and not the chest, require permanent openings in the skin and impair a user's quality of life. Four of the Ottawa team's innovations are patentable, and other research centres are now buying EVAD components.

Given the technical complexity and cost of developing an artificial heart, why are there so many competitors? It is a simple matter of demand and potential profits. Cardiovascular disease is the number-one cause of death in the West, and about half of the deaths are directly attributable to heart failure; about 500 000 Americans and 44 000 Canadians die of heart failure each year, and 40% of those who die are younger than 65. Unfortunately, demand far outstrips the supply of donor hearts.

This means the potential market for artificial hearts is

so huge that American analysts say the worldwide market could be worth $3 billion annually by early in the next century. Little wonder that many American companies have tried to persuade Mussivand to move south again. "I'm monogamous," he says to the Americans who come courting.

"Let me show you what we're up to," says Mussivand, leading me along a fifth-floor corridor at the Heart Institute. Each door bears a different plaque to mark donors such as Northern Telecom and the Ottawa Jewish community. In one room, he showed me a laptop computer linked to a video screen, which allowed me to see the artificial heart in operation. A graphic and numeric display revealed what was happening within the EVAD. With a few keystrokes, Mussivand altered its beat rate.

We then entered the laboratory where the device was located, in a plaster cast of a male torso. I watched the EVAD, connected to an internal battery implanted below it and without any protruding wires, beat on. The internal battery can hold a 45-minute charge, enough to allow a person to go swimming. An external battery, usually slotted into a belt, can last 6–8 hours. An external controller lodged on the same belt can accept power from a wall socket.

"What do you call the prototype?" I ask.

"The technicians call him DAVE — EVAD backwards," Mussivand chortles. "I like to call him Tofy's smarter twin."

The Cardiovascular Devices Division has 64 paid employees. In addition, Mussivand relies on an extensive network of volunteer scientists, entrepreneurs and electronics experts. "We have persuaded some of the best academics and clinicians available to help us, because they are interested," Mussivand observes. "They can see that their work with us will make a major contribution to alleviating pain. We have tried to capitalize on their excitement at being at the front end of science."

But they must also rely on government to contribute to the division's annual budget of $4 million to $10 million. This contribution is continually under threat as federal and provincial research funding, and provincial health budgets, are slashed. "We have almost lost the project several times," he comments. "I have become a professional beggar."

That's where DAVE comes in. DAVE, who has chestnut hair and a swimmer's pectoral muscles, is not just a pretty face with a beating heart: he is an extremely effective salesperson. He demonstrates to people who can't spell systolic exactly how the EVAD functions. Potential donors and investors are introduced to him on walk-through tours of the facility. There have been many of these since a pair of Ottawa's most savvy entrepreneurs, Ottawa Senators' owner Rod Bryden and Corel Corporation chair Michael Cowpland, began backing the Heart Institute's project.

In April 1996 WorldHeart Corporation was incorporated by its owners — Bryden, Cowpland, the Heart Institute and Mussivand. It was a neat marriage of entrepreneurial chutzpa and scientific expertise. Mussivand is president, with Keon serving as vice-president. Bryden is the chair and chief executive officer, while Cowpland is a director. The announcement had barely been made when Bryden began giving the EVAD (or HeartSaver, as it was quickly renamed), the right spin. The device, he said, "has the prospect of being, if not the only alternative, the preferred alternative for thousands and thousands of people whose other option is dying."

By mid-December, WorldHeart had completed an $18.7 million initial public share offering that will fuel its development efforts for the next 18 months. But that is only the beginning. The company will need a further $50 million to keep to its schedule of completed clinical trials by the year 2000 and initial commercial production by 2001–2. It warns potential investors that the stock "should not be purchased by people who cannot afford the loss of their entire investment."

Mussivand acknowledges that many hurdles lie ahead. "The most difficult problem now is to find the problems," he says. The artificial heart has kept a calf alive for 4 days; the next stage is a 3-month trial. Mussivand is determined to keep to schedule.

Within Ottawa there is a lot of excitement about WorldHeart, which builds on the high-tech knowledge that is already driving the local economy. Eventually, it could bring a lot of jobs to the capital.

"We have to capture and hold the market to be successful," warns Keon. "One of our competitors might get there first." However, if the HeartSaver is indeed first off the mark, it has the "potential of a Corel or a Newbridge," two of the powerhouses currently driving the new Ottawa economy.

The curious aspect of the EVAD market is that the success of the HeartSaver will not depend on a choice made by consumers. Instead, a few thousand thoracic surgeons throughout the world will make the final decision about which of 2 or 3 competing products, which will probably reach the market about the same time, is most appropriate for their patients.

The Heart Institute has already established its credibility within the profession by the quality of its publications and research, but Mussivand still has to spend a great deal of his time flying around the world delivering his message to surgeons.

"I hate flying," he says ruefully. "I'm an engineer. I know how many things can go wrong." ?