The Transformers

Engineering meets medicine at NC State where a high-tech team is replacing missing bones, limbs and joints in dogs and cats.

By David Hunt

On the inside, the gleaming, expansive and antiseptically clean Terry Center on the campus of North Carolina State University looks much like any other world-class teaching hospital. The $72 million facility, which opened last year, has some of the most advanced medical equipment available, including a linear accelerator for cancer treatment, a 64-slice CT scanner for high-resolution diagnostic imaging and a biplane fluoroscopy unit for better visualization of congenital heart defects.

The enormous stone sculpture of a golden retriever out front is the first clue that the 110,000-square-foot medical center treats a different mix of clients than the Mayo Clinic. The facility's full name gives it away. This is the Randall B. Terry, Jr. Companion Animal Veterinary Medical Center, home to the high-tech future of veterinary medicine. In fact, if you still think of veterinary care along the lines of the 1980s TV show, "All Creatures Great and Small," think again. At NC State, veterinary medicine meets engineering, and the results are nothing short of groundbreaking.

Denis Marcellin-Little is a professor of orthopedic surgery and an expert in osteogenesis, the formation of bone tissue. His understanding of the field goes far beyond the theoretical. Under his leadership, the university has achieved remarkable success developing implants that fuse with an animal’s existing bone to replace damaged or missing limbs and joints.

He thinks his work at the medical center more closely resembles a big-budget adventure film than a BBC series about country doctors.

“It’s kind of dorky to say this,” he jokes, “but creating a treatment plan for a new patient is like the first 20 minutes of an action movie where they have to pull together a team of mercenaries. We need a specialist for this and a specialist for that.”

GLOBAL COLLABORATION

In fact, Marcellin-Little’s undoubted skill as a surgeon is surpassed only by his ability to wrangle large, multidisciplinary teams to create custom implants for his small patients. A recent project, the world’s first fully functioning feline knee replacement, developed for a 10-year-old tabby named Cyrano, involved more than a dozen collaborators in both medicine and manufacturing on two continents.

His main collaborator, and the one indispensable member of the team, works out of an office across campus in Daniels Hall, an older and imposing brick structure built in 1926. Like their work environments, the men are a study in contrasts. Swedish-born Ola Harrysson, associate professor of industrial and systems engineering, works with electron beams, 3-D models and an array of alloys. He led the effort to design, fabricate and finish Cyrano’s sophisticated knee replacement.

French-born Marcellin-Little is more at home working with tendons than titanium. But the professors have learned from each other. “The language of medicine and engineering are different,” Marcellin-Little says.

“When we began working together 10 years ago, we only understood each other’s disciplines a little bit,” adds Harrysson. “Today, he knows a lot more about engineering and I know a lot more about medicine.”

Their ability to bridge the divide has paid dividends in the operating room. It was especially important when they began working on the knee replacement for Cyrano.
“It was a state-of-the-art engineering project and a state-of-the-art surgical project,” Marcellin-Little says. “It’s easy to be very good in one area, but it’s hard to overachieve in multiple categories.”

In the end, after a six-month design and development phase and a six-hour surgery, Cyrano returned home to his Virginia farm with a new knee fashioned out of cobalt chromium. His prognosis is excellent, says Marcellin-Little, although the farm’s mouse population may not fare as well.

MANUFACTURING MIRACLE

If Marcellin-Little and his team make it look easy, that’s because they have a lot of practice. Cyrano was the seventh animal they’ve fitted with a custom prosthesis since 2005.

The hallmark of their work is the use of an innovative process called rapid prototyping to create custom bones and joints. The process, commonly called 3-D printing, uses an electron beam to melt layer after layer of a powdered resin or metal alloy to create a product — anything from a hammer to a toy soldier — from the ground up.

To an observer, it looks like magic.

“The finished metal part isn’t solid, but honeycombed with a porous latticework that allows the animal’s bone to grow into it. As a result of this free-form fabrication, it behaves more like a natural limb.”

In the beginning of the rapid prototyping industry, in the early 2000s, the focus was on creating tools, like wrenches and screwdrivers, out of steel. Harrysson was one of the first to see the potential for medical applications.

“In 2002 I attended a big rapid prototyping conference in Austin and I heard a couple of guys speaking Swedish, so I went over and introduced myself,” he says.

It was a lucky coincidence. Harrysson told the men, continued
executives with a company called Arcam AB, that they could make more money if their machines used titanium alloy.

“Who wants a hammer made out of titanium,” one asked. Harrysson smiled and quickly sketched out the dimensions of the market for prosthetic implants.

Three months later, the company’s CEO and sales manager dropped by Harrysson’s office in Daniels Hall and showed him titanium products created by Arcam’s new rapid prototyping machine. At Harrysson’s urging, NC State bought the first one.

Today, Arcam has 80 installations worldwide and is a leading manufacturer of rapid prototyping technology for the medical and aerospace industries. And they’re not alone. Total annual revenue for the industry now exceeds $1 billion and is expected to nearly quadruple by 2019.

SHARING SKILLS

With the growth of the industry, new educational opportunities have opened up for students in both engineering and medicine.

“I just redesigned one of my manufacturing courses,” Harrysson says. “We used to spend two weeks on rapid prototyping. Now the entire course is about product development and prototyping.”

The collaboration between the two professors has led to cross-disciplinary partnerships between their students, as well.

“In our research, we try to pair up engineering students with veterinary students,” Harrysson says. “The vet students teach the engineering students to do dissection. Some vet students spend their whole summer in the engineering lab working with materials.”

For his part, Marcellin-Little sees the collaboration as making a difference where it counts the most. “At the end of the day, my entire job is about helping patients,” he says.

He doesn’t mean just cats and dogs. The work he’s done with Harrysson over the past decade has made them both pioneers in the field of transdermal osseointegration, the direct skeletal connection between living bone and a load-bearing implant. The implications for human orthopedic treatment are exciting.

“All the progress we make in free-form fabrication very quickly gets translated to human prosthetic research,” he says. “Free-form transdermal osseointegration will cross over at some point to human patients.”

Still, there’s work to do perfecting the process, especially to reduce the rehabilitation time and guard against infection. Marcellin-Little is proud of the progress that’s been made at NC State, but he’ll wait to take a bow.

“I’m a long-distance runner,” he says. “I’m not interested in getting a medal two days after surgery.”
GLOBAL TEAMWORK DRIVES INNOVATION

Meet the team assembled by NC State experts Denis Marcellin-Little and Ola Harrysson to develop the world’s first fully functioning feline knee replacement. More details are online at research.ncsu.edu. Follow the Results link.

- **Anke Langenbach**, Diplomate of the American College of Veterinary Surgeons
  The Hope Center, Vienna, Va.

- **Steve Withrow**, Diplomate of the American College of Veterinary Surgeons
  Director of the Animal Cancer Center, Colorado State University

- **Tim Horn**
  Ph.D. candidate at NC State

- **Christopher Sidebotham**, President
  **Greg Van Der Meulen**, Director of research and development
  BioMedtrix LLC, Boonton, N.J.

- **Bill Liska**, Diplomate of the American College of Veterinary Surgeons
  Gulf Coast Veterinary Specialists, Houston, Texas

- **Caroline Webster**
  Undergraduate in biomedical engineering at NC State

- **EOS (EOS GmbH - Electro Optical Systems)**
  Krailling, Germany

- **Duncan Lascelles**, Diplomate of the American College of Veterinary Surgeons
  Orthopedic surgeon and professor of surgery and pain management at NC State

- **Simon Roe**, Diplomate of the American College of Veterinary Surgeons
  Orthopedic surgeon and professor of orthopedic surgery at NC State

- **Nancy Doyle**, MPT
  Gulf Coast Veterinary Specialists, Houston, Texas

- **Toni Kwan**
  Senior resident, Small Animal Surgery at NC State

- **Joanne Tuohy**
  Resident, Small Animal Surgery at NC State

- **Jonathan Hash**
  Technician, NC State Orthopedic Research Laboratory

- **Dawn Kaplan**
  Clinical technician at NC State

- **Anke Langenbach**, Diplomate of the American College of Veterinary Surgeons
  The Hope Center, Vienna, Va.

- **Steve Withrow**, Diplomate of the American College of Veterinary Surgeons
  Director of the Animal Cancer Center, Colorado State University

- **Tim Horn**
  Ph.D. candidate at NC State

- **Christopher Sidebotham**, President
  **Greg Van Der Meulen**, Director of research and development
  BioMedtrix LLC, Boonton, N.J.

- **Bill Liska**, Diplomate of the American College of Veterinary Surgeons
  Gulf Coast Veterinary Specialists, Houston, Texas

- **Caroline Webster**
  Undergraduate in biomedical engineering at NC State

- **EOS (EOS GmbH - Electro Optical Systems)**
  Krailling, Germany

- **Duncan Lascelles**, Diplomate of the American College of Veterinary Surgeons
  Orthopedic surgeon and professor of surgery and pain management at NC State

- **Simon Roe**, Diplomate of the American College of Veterinary Surgeons
  Orthopedic surgeon and professor of orthopedic surgery at NC State

- **Nancy Doyle**, MPT
  Gulf Coast Veterinary Specialists, Houston, Texas

- **Toni Kwan**
  Senior resident, Small Animal Surgery at NC State

- **Joanne Tuohy**
  Resident, Small Animal Surgery at NC State

- **Jonathan Hash**
  Technician, NC State Orthopedic Research Laboratory

- **Dawn Kaplan**
  Clinical technician at NC State

PIONEERS IN OSSEointegration

NC State leads the world in the development of transdermal osseointegration, the direct skeletal connection between living bone and a load-bearing implant. These pioneering patients have been treated in recent years:

- **2005 — George Bailey**, a cat born without the lower half of his hind legs, is fitted with a titanium post connected to an artificial limb.

- **2007 — Pez**, a dog with a large hole in the roof of his mouth, is fitted with a custom implant.

- **2008 — Mr. Franz**, a cat, is fitted with a custom foot implant.

- **2008 — Cassidy**, a three-legged German shepherd mix, receives a new limb.

- **2009 — A dog**, whose owner does not want publicity, receives a custom implant.

- **2011 — Zeus**, a Siberian husky with a missing foot, is fitted with an artificial foot. He is the first patient to receive an implant for a front limb.

- **2012 — Cyrano**, a cat, receives the world’s first fully functioning feline total knee replacement.

- **2012 — Jack**, an American Staffordshire terrier mix, is fitted with bilateral implants for his missing hind legs.