

PU TISSUE SCAFFOLDS ALLOW REGENERATION OF HUMAN ORGANS

By Louise McHenry, UTI reporter

Polyurethane is used for a wide variety of medical purposes. This versatile, biocompatible polymer is suitable for uses from wound dressings to catheters, but PU is also at the forefront of medical science, finding its place in unique, vital devices, which tackle advanced diseases and make huge differences to people's quality of life.

In London, Prof Alex Seifalian and his team of postdoctoral students from University College London (UCL) have developed a nanocomposite called POSS-PCU (polyhedral oligomeric silsesquioxane-poly (carbonate-urea) urethane) which can be used for bypasses, stents and as tissue scaffolds for building new tracheas and even noses.

Work on the material began around 2001/2002, when Seifalian and his team started research into nanocomposite polymers, using



Prof Seifalian shows a synthetic trachea

nanoparticles to enhance the mechanical behaviour of the polymer and its biocompatibility. The base of the nanocomposite is PCU, which is synthesised with POSS, a nanoparticle of 1.5 nanometres. Bayer MaterialScience supplies the raw

materials used.

Seifalian and his team tested a number of polymers and nanoparticles before settling on POSS-PCU, he told UTI in a 22 Aug telephone interview. The material itself is not expensive to make, Seifalian said, and if required, a body part such as a trachea can be made in one week in the lab.

In the lab, the team can make up to one litre of POSS-PCU. On a commercial scale, Hybrid Plastics in the US and Rosehill Polymers in the UK have been approved to make the material.

Initially, the team worked on cardiovascular devices such as stents and blood vessels. Seifalian then expanded to other organs. To make a replacement organ such as a trachea, Seifalian receives a CT scan from the patient's hospital from which he makes a glass mould of "exactly the same shape and size" as the organ to be replaced. "Then we grow the polymer around that glass; we take away the glass and we're left with the scaffold," he explained.

While the polymer is 'growing' around the glass, doctors take stem cells (cells from the body which can divide and differentiate into specialised cell types) from the patient. Seifalian then introduces these to the scaffold along with a 'growth factor' to help convert the cell into the right cell type for the specific organ.

The scaffold is then implanted into the patient where it should last "for as long as a person lives," as it is non-biodegradable, Seifalian said. And because it includes the patient's stem cells, it's biocompatible and

HEART-ASSIST DEVICES

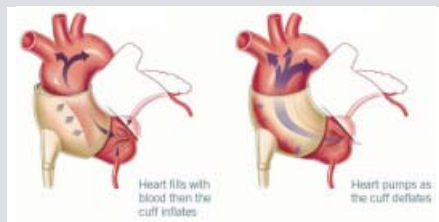
Sufferers of heart disease in Europe may soon have another option to help reduce the symptoms of this chronic illness, which causes shortness of breath and angina. Sunshine Heart Inc. of Minneapolis, Minnesota, hopes to receive the CE Mark for its C-Pulse heart-assist device by the first quarter of 2012, which will allow the company to market its device aimed at treating the clinical symptoms associated with Class 3 and ambulatory Class 4 heart failure.

The device consists of a cuff, made using segmented polyurethane (SPU) and thermoplastic polycarbonate urethane, and a motor, which drives the device. The cuff fits around the ascending aorta, providing a secondary pulse, which eases the workload on the left ventricle and helps increase blood flow to the coronary arteries.

Kevin Bassatt, vice president, R&D & quality at Sunshine Heart, told UTI in an 11 Oct telephone interview that the company has recently completed a feasibility trial in the US. The successful completion of this study allows the company to apply for the CE mark in Europe, a mandatory declaration that a product meets European requirements on health,



Kevin Bassatt, VP R&D



C-Pulse's 'balloon' inflates & deflates to help pump blood around the body safely and environmental protection.

In the US, the C-Pulse device needs to undergo a further pivotal study, "in the 270-patient range," Bassatt said, which the company hopes to carry out in the next two-and-a half to three years, subject to FDA (US Food and Drug Administration) approval.

C-Pulse is manufactured using two key urethane materials, supplied by DSM-PTG. Biospan SPU is used for the 'balloon' of the cuff which inflates and deflates to pump the blood. "It was chosen for its mechanical characteristics," Bassatt explained. He noted that the SPU is resistant to flex fatigue, has a long flex life, is biostable and very high-strength. "It's constantly inflating and deflating, millions and millions of cycles," he said. The 'gasline' connecting the cuff to the driver is made using DSM-PTG's proprietary Bionate, a medical grade thermoplastic PCU that is harder and less flexible.

C-Pulse is different to many other heart-assist devices used at the moment as it does not have contact with the bloodstream, reducing the likelihood



Jim Yearick

of clots, explained Jim Yearick of Sunshine Heart in an 11 Oct telephone interview. He claimed that devices currently used for Class 4 heart disease, known as LVADs (Left Ventricular Assist Devices), cost in the region of \$80 000 - \$120 000. "[C-Pulse] is about 60 percent of that cost,"

Yearick said. The two Sunshine Heart executives commented that it is difficult to judge the device's exact cost, as production has not been scaled up to commercial level.

Elsewhere, NeoCardial Technologies llc of Minnesota, is in the early stages of testing its heart assist device "off-site," according to managing partner, Allan Robinson. As with C-Pulse, NeoCardial's device, made using a urethane-silicone material, has no direct blood contact.

However, the device is designed to be placed around the ventricles of the heart to "gently compress the ventricles during the systolic [when the heart is contracting] phase," Robinson told UTI in an 8 Sept email.

Robinson said he was unable to discuss the various manufacturers of the urethane-silicone copolymers being tested but added, "More than one of their materials show promise as to ease of assembly and performance."

GenOsteo

For start-up company GenOsteo, polyurethane plays an essential part in the creation of its bone graft material, which can be used with adult stem cells to restore bone lost because of trauma or disease. GenOsteo's Prof Joo Ong, of the department of biomedical engineering at University of Texas, San Antonio, told UTI in a 6 Sept telephone interview that the bone graft can be used for large defects, such as gunshot or blast wounds.



Some of the shapes available of GenOsteo's bone scaffold

Polyurethane foam is used as the base material. The foam forms a template onto which a calcium phosphate 'slurry' is applied. The PU is then burnt out and what remains is the bone scaffold. "[PU] is a starting material," Ong said, "but without that material, we wouldn't be able to come out with the end product."

In March 2011, GenOsteo announced an agreement with Austin, Texas-based SpineSmith Partners to commercialise the scaffold once US FDA-approval is received. "GenOsteo's role is the development and refining the technology. SpineSmith's role is to market and sell it," Ong said.

The scaffold will be an 'off-the-shelf' product, meaning a surgeon can just select the size they need and put it in the patient. "If it's just a hole... in the arm, in the skull, that's easy," Ong commented. "There are fillers that you can put it and fill it easily. But if it's a custom-made product like a jaw, we would probably need, at the most, seven days to get it ready."

The scaffold, which is currently awaiting US and international patents, has not yet been used on humans but Ong noted that it is unlikely to be rejected by the body as calcium phosphate "is found naturally in the bone anyway."



A synthetic nose being formed in a reactor

should be accepted by the patient's body.

The material has already been used successfully in humans. The first synthetic organ transplant took place in Sweden in June, when a cancer patient from Eritrea received a trachea. Seifalian says he has made tracheas for patients in Austria and Italy, and has even been challenged to make one for a ten-month-old baby in New York. "[It's] a bit different. It has to grow with the child, it's not the same as an adult one," Seifalian commented.

Other "very successful" implants include a tear duct, which

includes silver nanoparticles for antibacterial properties, and a leg bypass. He expects to have the first human coronary artery bypass soon.

The professor of nanotechnology and regenerative medicine at UCL is also in the process of making his first POSS-PCU nose for a patient with cancer. This involves inserting the nose scaffold into the skin of the patient's arm where blood

vessels and skin will start to grow through and around it, before cutting the nose out of the arm and attaching it to the patient's face. "This is a compassionate case," Seifalian said. "There's a hole on his face and his children get scared." Seifalian's passion for his work is clear and he notes that his research would have no interest to him if it didn't have a direct relationship to patients.

"Internationally, I think we are a unique place," he commented, adding that currently each of his PhD team is developing one human part – larynx, skin, liver, parts of the lymphatic system. Seifalian laughed, "[People say] 'one day you'll make a plastic person'."