Soft wool for strong bones

Researchers at the Swiss Federal Institute of Technology (ETH) in Zurich, Switzerland have developed a synthetic material made from a polymer and calcium phosphate, which is both flexible and osteoconductive. This unique 'bone wool' could potentially replace blocks and granules in bone substitution during orthopedic surgery.

What looks like regular cotton wool, is as soft as cotton wool, but is not cotton wool? While a simple appearance may be deceptive this cutting-edge biomaterial for guided bone regeneration has been designed to combine maximum flexibility, ease of use and osteoconductivity.

"Bone wool", as it is commonly referred to, is made from ultra-thin fibers which consist of 60% of polylactide-co-glycolide (PLGA), a polymer with a long track record of success in surgery, particularly orthopedics. Because of its biodegradability and biocompatibility, PLGA is commonly used for plates, screws and sutures.

Up to 40% of bone wool fibers consist of calcium phosphate, a mineral similar to natural bone with good osteoconductive properties. Calcium phosphate ceramics are currently used in various types of orthopedic and maxillofacial applications, mainly in the form of granules, block or cement.

New nano-techniques

Flame synthesis has recently made it possible to integrate calcium phosphate into a polymer in large quantities. It allows preparation of the mineral composition of bone in the form of nanoparticles.

Bone wool fibers are only 5 to 20 micrometers in diameter and contain 20 to 50 nanometer-sized calcium phosphate molecules. They are produced by electrospinning, which uses high voltages to draw very fine, typically micron-sized fibers from a liquid solution.

Its flexible texture makes bone wool easy to insert, extract, and to fit to any defect. It does not require special tools. It stays in place, absorbing blood and tissue liquid. Depending on the size and location of the defect, bone wool is absorbed by the body within three to six months.

Bones will benefit

The new biomaterial is suited for defects in all bones that are non-load bearing, notably in oral and maxillofacial surgery. Further it could be applied as bone filler, using additional internal fixations such as screws in critical size defects. It's equally suited for padding the space between an implant and the bone, thus preventing the formation of scar tissue in

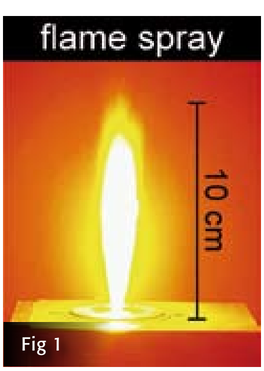


Fig 1

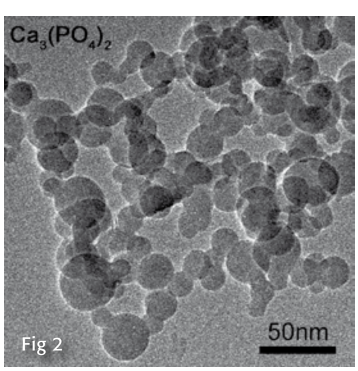


Fig 2

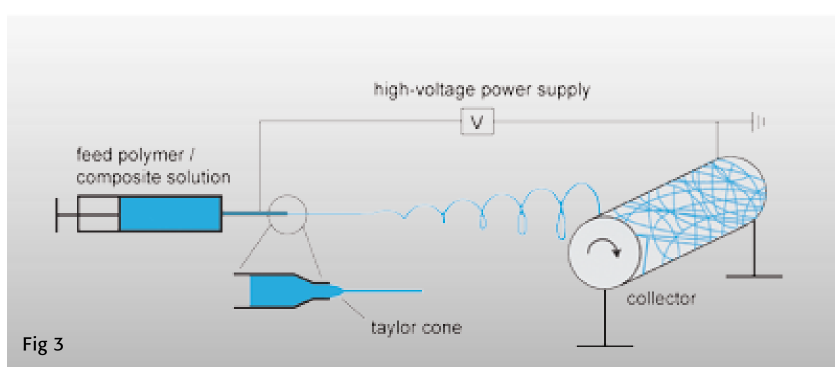


Fig 3

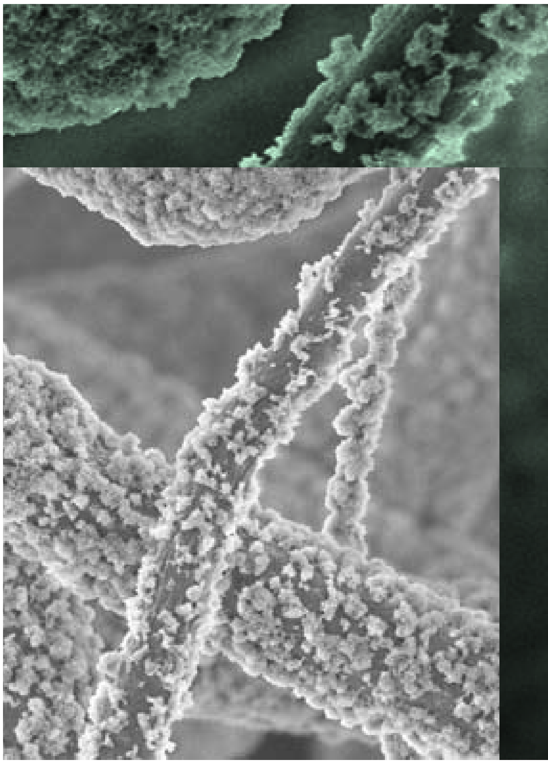


Fig 5

spaces, reducing pain and generally facilitating the integration of an implant by the body`s own bone material. Bone wool is also expected to be used for bone augmentation.

Study results hopeful

The pre-clinical data are promising. An in vivo study with rabbits has proved the formation of new bone tissue in calvarial defects after only four weeks. By adding silver to the calcium phosphate nanoparticles the material was rendered antibacterial without losing its bioactivity.

In a second in vivo study with Swiss alpine sheep, bone formation and biocompatibility of the material was investigated by introducing PLGA /calcium phosphate scaffolds with and without silver nanoparticles in drill hole defects in femur and humerus bones. The next step being considered is indication studies for methods like sinus lift or socket preservation. If everything goes to plan, bone wool will enter clinical phase I trials in 2011.

FDA clearance for bone wool is expected to go smoothly, as both PLGA and calcium phosphate are already approved substances. The researchers of ETH Zurich expect bone wool to be on the market in three to five years.

Fig1 The burning spray of a flame synthesis, which produces nanon calcium phosphate. The particles leave the flame at the top where they are collected on a filter.

Fig 2 Nano calcium phosphate.

Fig 3 Electrospinning: PLGA/nano calcium phosphate solutions are feed with a syringe. High voltages are applied on the tip of a metallic needle which results, due to electrostatic repulsion, in the formation of a taylor cone and a charged liquid jet. The micron-sized fibers are collected on a rotating drum.

Fig 4 Bone wool consists of a PLGA/nano calcium phosphate matrix which allows rapid mineralization. Already after tow days immersion in a body-fluid like solution, calcium deficient hydroxyapatite is formed on the fibers.

Fig 5 Bone wool can easily be plugged into bone defects.

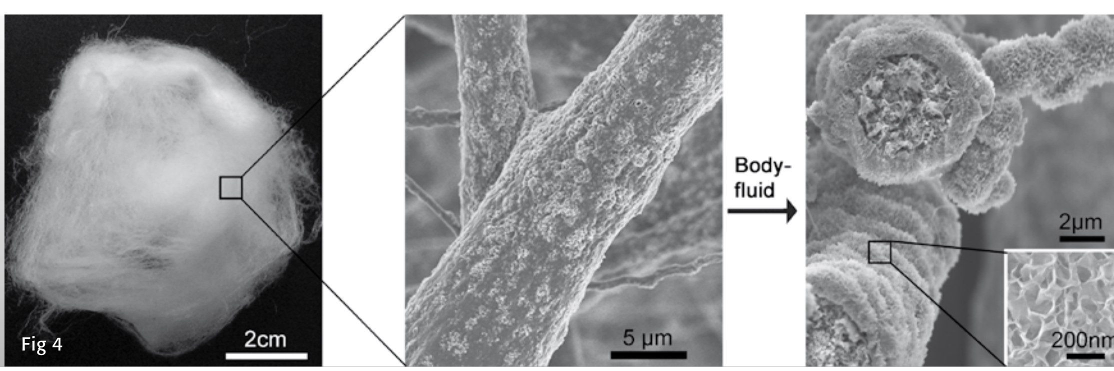
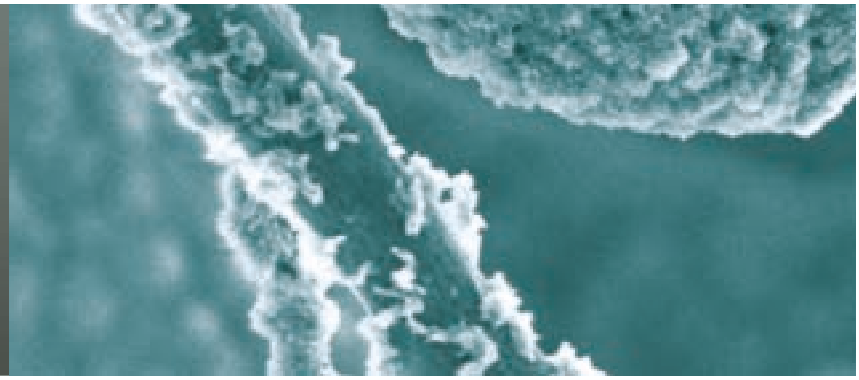


Fig 4

Nano bone mineral

The mineral composition of bone can now be synthesized in the form of 20 to 50 nanometer particles (0.02–0.05 micrometers). This allows easy application in flexible polymers where the nano bone mineral induces bioactivity and enables osteoconductivity.



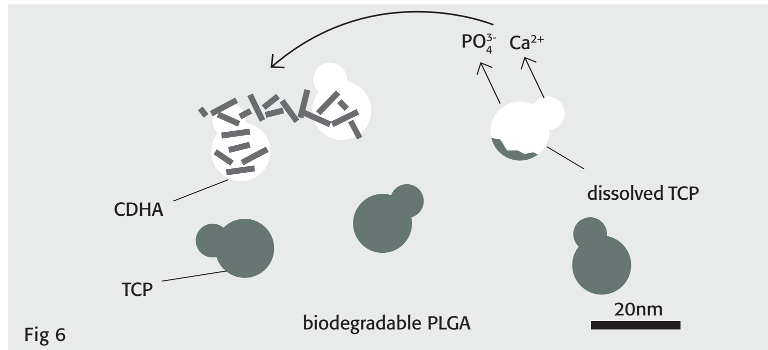


Fig 6

Interview with Wendelin Stark, chemist at ETH Zurich, Switzerland

No bone substitute material to date is woolly in texture. How did you come upon the idea of bone wool?

We asked orthopaedic and oral surgeons about their experiences with the currently available reconstructive bone materials and found that they are not very convenient to work with. Granules cannot be homogenously distributed in the defects and are easily washed out during the rinse. Blocks in their turn use up a lot of time during surgery because they are difficult to shape, and cement may leak into blood vessels. So we knew we had to develop a material that would not present these problems. At the same time, it struck us in our discussions with oral surgeons that they simply love cotton wool. They use it for almost everything, from routine preoperative mouth swabs to placing it under temporary fillings as space holders. So one of my PhD students, Oliver Schneider, came up to me one day and said we must produce cotton bone wool. And that's what we did.

What were the main challenges?

Finding out what a really "good" product for the working doctors is in the first place! Also, we had to work with FDA approved materials, which limited our options. Another challenge was homogenously distributing the nano particles in the polymer solution, which is a prerequisite for cotton wool like texture.

There has been an effort in recent years to develop new synthetic bone substitute materials but none has made it in the operating theatre. Why should bone wool succeed?

Many new materials for guided bone regeneration are technically excellent, but at the end of the day a surgeon must be able to handle it easily. If new material is complicated in use, for example if a special tool or application aid is needed, or if it requires the mixing of two components, application is much fussier, more instruments need to be laid out, sterilized and so on. The principle for bone substitute materials is: Less is better, safer, easier to plan and easier to check. Bone wool fulfills these requirements. Also, bone wool easily fits into any kind of cavity, which is useful for complex shape bone defects. There have been bone substitute materials on the market made from the same components as our bone wool, that is PLGA and calcium phosphate, but they have the form of plates, screws and the like, and are thus very close to conventional steel-osteosynthesis. The novelty of bone wool is its texture of cotton-wool-like, open, voluminous fibres and the integration of calcium phosphate in the form of highly reactive, that is osteoconductive nanoparticles.

Which advantages may bone wool offer to the patient?

Surgery will be shorter, which reduces the risk for complications or failures, and bone may grow faster. Also, implant life spans may be longer because implants can be anchored better with bone wool, which reduces osteoporosis on the weight-bearing part of the bone. Better anchoring can also reduce pain because pressure is better distributed, for example of the head of the femur on the acetabular surface.

Bone wool has been designed for application in non-load bearing bones. Can it also be used for spine and hip surgery?

It could be used to pad spinal cages, which would not only anchor the cages better but also protect the soft structures like cartilage and neurons from being damaged by the hardness of the spinal

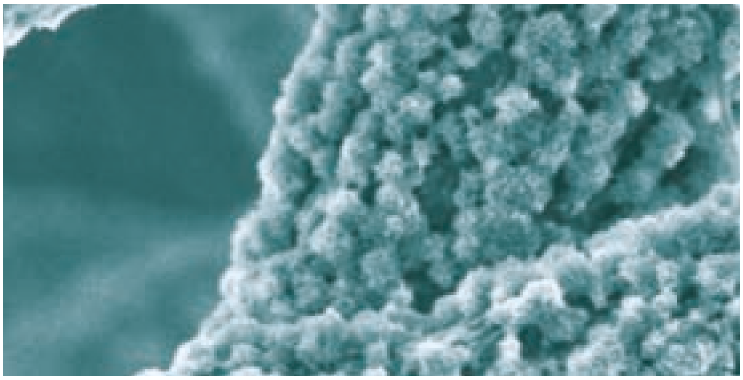


Fig 6 Highly reactive calcium phosphate nano particles are integrated into biodegradable PLGA by electrospinning. The formed fibers allow fast mineralization due to the reactive nano particles.

cages. Certainly, bone wool is also better than cement in the case of collapsed disc space because it maintains the spine segment's mobility. And, as mentioned before, bone wool may be of generally good use for padding of implants, also of hip implants.

What are your visions for the future?

I would like to develop multifunctional material, for example bone wool that contains regulatory proteins which will further stimulate bone growth, to be applied, for example, in osteoporotic areas. I would also like to develop three-dimensional, membrane-type structures with anisotropic properties, that is, which induce on one side, for example, bone growth and on the other side cartilage growth. They could be used, for example, for comminuted fractures in the foot. Functional physics would then have to stimulate the tissue.

What is your personal motivation for your work on bone wool?

I have always believed that the natural sciences have a performance mandate within society, and I've felt that with bones our research group is able to fulfil that. I have always been fascinated by bones because they are stable and yet constantly rebuilt. They are mainly inorganic but nature still finds a way to work with them. Generally speaking, I feel that natural scientists can bring a lot to medicine if they listen to the doctors first.

Prof Dr Wendelin J Stark
Wendelin Stark has been Assistant Professor of Catalysis at the Institute for Chemical and Bioengineering of the Federal Institute of Technology, Zürich since 2004. His research focuses on functional materials and their interface to chemistry (catalysis) and biology.

New products

Further protection for healing hands

In May of this year, Ansell launched a product that aims to provide a new layer of protection for surgeons against exposure to viruses and bacteria. GAMMEX® powder-free gloves incorporate an inner coating of skin-friendly antimicrobial agent that protects surgeons from blood-borne pathogens in the event of a breach. Ansell's lab test results report that their antimicrobial technology (AMT) consistently kills over 99 % of Hepatitis C1 and 99 percent of HIV-1 within 60 seconds of exposure. The result of intensive and collaborative research at Ansell, the GAMMEX® powder-free gloves are now being rolled out for use by doctors in Australia. Ansell plans to make the gloves progressively available within the Americas, Europe, and Asia Pacific.
www.ansell.com

New RPI instrument offers better indication of fracture risk

Rather than using the traditional DEXA scan to measure bone mineral density (BMD), Active Life Technologies' new BioDent instrument instead measures bone mechanical properties in vivo in patients. A reference point indentation (RPI) tool, the BioDent 1000 uses a needle within a hypodermic needle to apply steady pressure to create small holes–microindentations– in the bones of the tibia. The further the needle is able to penetrate the bone, the weaker the bone's mechanical properties. New clinical tests have validated the performance of BioDent in more accurately assessing fracture risk in osteoporotic patients. Intentionally designed for practical use in clinics in the future, BioDent has the potential to improve clinicians' prognostications.
www.activelifetech.com