Bone in contention

Bone has been used by mankind since prehistoric times, when human and animal bones were used in tools and weapons. The recreation of its structure is now stimulating new approaches in the field of tissue engineering, and is also providing the inspiration for biomimetic materials and structures, writes Ian Salusbury.

Bone has a highly complex, hierarchical make-up, with different structures at different length scales. There are two levels of composite structure present – at the microstructural scale there are bundles of hollow fibres (osteons), which consist of lamella and pores, while at the nanoscale the lamella are made up of fibres consisting of collagen, a protein, within a matrix of calcium phosphate mineral (hydroxyapatite). The combination and configuration of these components makes for strong and lightweight structures.

In the human body there are two types of bone. Cortical (or compact) bone forms the outer load-bearing shell of the key support bones in the skeleton, and within this there is trabecular (or cancellous) bone, which is also present at the ends of long bones. Trabecular bone has a honeycomb-like texture, with pores that range in size.

The exact structure within the bone depends on the loads that are repeatedly placed upon it, which explains how archaeologists can deduce whether the skeletal remains they find were of right or left-handed people. It also explains the bone loss that astronauts experience when on missions in space – they can lose 1-2% of bone mass per month.

This same condition, osteoporosis, is of course a major medical problem on Earth. As the human body ages, there is a loss of bone mass. This particularly affects post-menopausal women, but as life expectancy increases it is becoming more widespread. This has led to the use of artificial implants for hip replacements. However, patients often live for more than 30 years after they have an implant and the implants often fail, resulting in further operations.

In addition to reducing the suffering of patients and conserving National Heath Service resources, this is a key industrial area for the UK. A recent Foresight report on smart materials stated that the UK currently holds 'world-class status in biomaterials, implants, external prostheses and tissue engineering areas' and that further development was reliant on 'the development of biocompatible components and devices'.

Efforts have been made to improve the biocompatibility of implants by coating them with a synthetic hydroxyapatite layer, for example, but it seems that such implants are still prone to failure. Therefore, new approaches are being sought which will enable the body to regenerate itself, and key to this is understanding and recreating the structure of bone.

Professor Brian Derby from Manchester University displays scaffolds that could be used to generate new bone

Building on success

The idea behind regenerative medicine is that a scaffold is seeded with tissue cells taken from the patient. Once the scaffold has been implanted in the body, the natural processes of laying down bone take place, blood vessels infiltrate the structure and when the scaffold eventually degrades, it would be as though it was never there. In the words of Dr Julian Jones of Imperial College, UK, 'the scaffold guides and stimulates *in situ* regeneration'.

It is vital for the scaffold to mimic the structure of trabecular bone. Not only does the structure have the required mechanical properties such as a high strength to weight ratio, but also the interconnected pore network allows for blood vessels to infiltrate the structure and so ensure its successful absorption into the body.

Scaffolds can be made in various ways. Dr Aldo Boccaccini and his group, also working at Imperial College, are using a biodegradable polymer composite scaffold. As Boccaccini explains 'composites with tailored physical, biological and mechanical properties, as well as predictable degradation behaviour, can be produced combining bioresorbable polymers and bioactive inorganic phases.'

Jones is pursuing a different approach, and generates bioactive glass scaffolds through the sol-gel process. The silicon and calcium ions that are released as the scaffold degrades mean that human growth factors do not need to be incorporated within the scaffold before implantation – the polymer composites incorporate bioactive glass partly for this purpose.

In order to characterise the materials they have synthesised, the researchers are using a recently purchased X-ray computed tomography system. Structures can be imaged in three dimensions and so the pore network of the implant can be inspected from all angles, at resolutions near the micron level. The technique is non-destructive, which would allow implants to be analysed for quality control before implantation.

A number of other techniques are being pursued for the creation of the scaffolds. Inkjet printing is the subject of preliminary studies by a number of groups, including those of Professor Brian Derby at the University of Manchester, in collaboration with the Tissue Engineering International Research Consortium. Derby notes that one of the main advantages of this technique is in being able to lay down cell material and scaffold at the same time, and thus avoiding problems with poor cell infiltration into the centre of the scaffold that other techniques encounter (see *Materials World*, February 2005, p6).

Professor William Wagner of Pittsburgh University is the Editor of a new journal in this field, *Acta Biomaterialia*. He confirms that papers are being submitted from all over the world on this topic, and believes that those researchers working on ceramics are becoming more sophisticated in their application of cell biology, and are catching up on their colleagues in the polymer area in this respect.

Boning up

The pace of development seems likely to accelerate in this interdisciplinary research area, but it is not just with respect to use in the body that the study of bone is of research interest. Bone has also inspired developments in other fields of materials engineering.

Gustav Eiffel was inspired to design his tower based on studies of the structure of the thighbone. The bone curves as it enters the hip joint, and the trabeculae inside strengthen the bone in exactly the directions and to the degree required. The structure of the tower, the tallest man-made structure in the world when it was constructed in 1889, is an intricate network of metal studs and braces, mimicking the effect of the trabeculae.

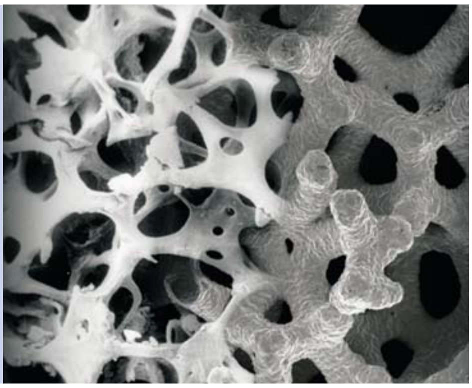
Researchers in the Department of Architecture and Civil Engineering at the University of Bath have completed modelling that suggests that the structures of bones could go on to inspire more radical structures of buildings and bridges. Dr Chris Williams

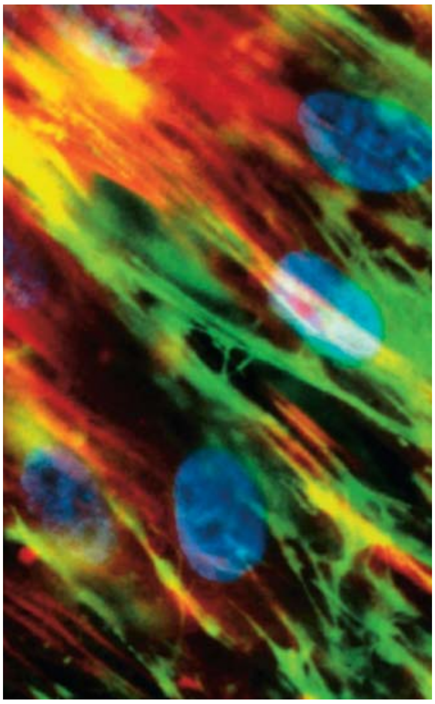
Inspired implants

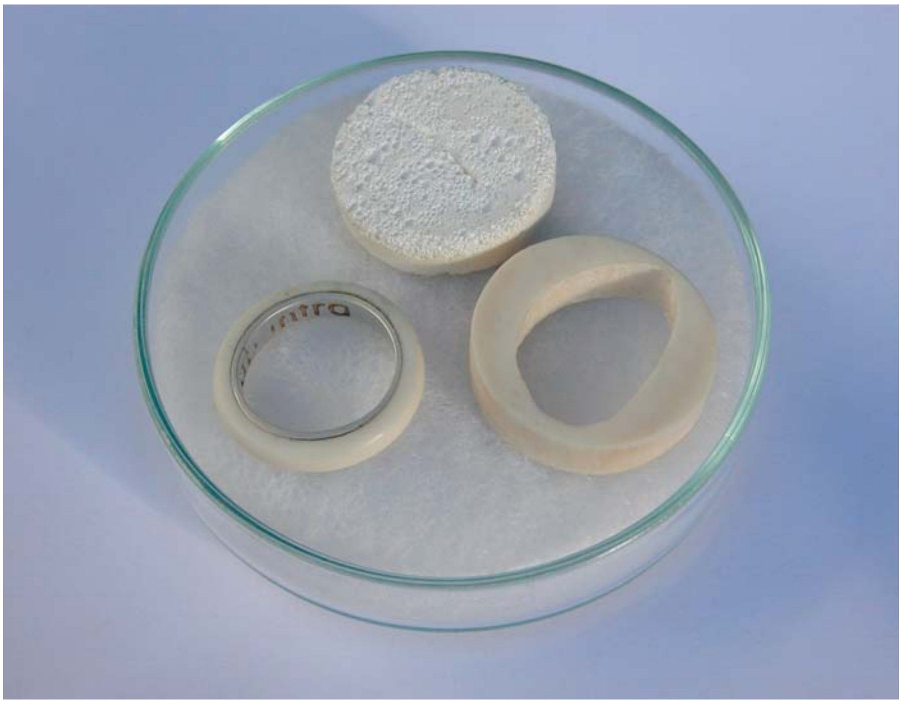
The structure of bone has also inspired the design of metals for use in the body. Zimmer produces a material called Trabecular Metal™, which is used in a range of implants including those for hips and knees. Trabecular Metal consists of tantalum, formed into a network that is 80% porous. This gives the material high strength to weight ratio, and the compressive strength and elastic modulus are said to be more similar to bone than other prosthetic load-bearing materials.

Implants can be made in a variety of complex shapes, using a vapour deposition process. New bone fills the majority of the porous structure within eight weeks of implantation, and within the same period soft tissue adheres to the surfaces and blood vessels also pervade the structure.

Tantalum is unaffected by body fluids and causes no adverse tissue reactions, so it is also widely used in surgical equipment.







A set of wedding rings made from bone is being used to raise awareness of issues surrounding tissue engineering in the UK. Samples will be harvested from a volunteer couple and grown to produce bone tissue which will then be carved to their design specifications (left). The concentric growth of circles of bone crystal are illustrated by fluorescent labels given at weekly intervals during bone growth. Clockwise from top on right – the porous, bioactive ceramic scaffold on which tissue growth takes place, a model of the ring using a combination of cow marrow-bone and etched silver, and a sample of cow marrow to illustrate the final bone sample (Images: Biojewellery.com)

explained that natural structures like bones 'tend to flow into each other', which makes for a better structure. 'They also have different hierarchies of scale and adapt themselves to stresses,' says Williams, 'whereas man-made structures tend to be made up of more simple shapes.' He is interested in both the structural and aesthetic possibilities this approach would offer. Such structures would also be more sustainable, as they would be made of the most efficient amount of material.

Hole new approach

Animal bone is also a source of biomimetic materials research. A feature of a horse bone has led one research team to consider how it might be applied in high-tech composite material – the leg bone has a hole in it, where blood vessels enter. This hole does not weaken the structure to the extent that a drilled hole in a man-made structure would do, which is usually compensated for by making the material around the hole thicker. Increasing the thickness means increasing the weight, a disadvantage in many applications (such as aerospace, where extra weight means higher fuel costs). When Andrew Rapoff and Raphael Haftka at the University of Florida modelled the effect, and then tested a hole reinforced with polyurethane foam, they found that the strength was greatly increased and are seeking to develop fibre reinforced composites on this basis. It seems unlikely that one particular form of bone engineering will catch on though. According to *New Scientist* magazine, one lucky engaged couple are being offered the chance of having wedding rings created out of their partner's bone. The couple would each have to supply bone cell samples (for example a sliver could be taken from the jaw bone during a wisdom tooth extraction), which would be grown on a ring-shaped scaffold. A designer would then consult the couple on how the rough bone circles should be customised. This is actually part of a recent Government-sponsored initiative in the UK to raise awareness of issues regarding tissue engineering, rather than a new fashion trend, and is certainly an eye-catching approach to illustrating the possibilities and ethical questions that this field may open up.

Engineer Gustav Eiffel copied the curved structure of the thighbone to give strength to his famous tower in Paris, France

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