Glass bones

Developments in bioactive glass are set to change the way broken bones are treated. Neutron Scientist Dr Martyn Bull from the ISIS neutron research centre, Didcot, UK, discusses

Scientists are developing a new type of glass that releases calcium into the body as it dissolves. This could enable patients to regrow bones and may signal an alternative to bone transplants.

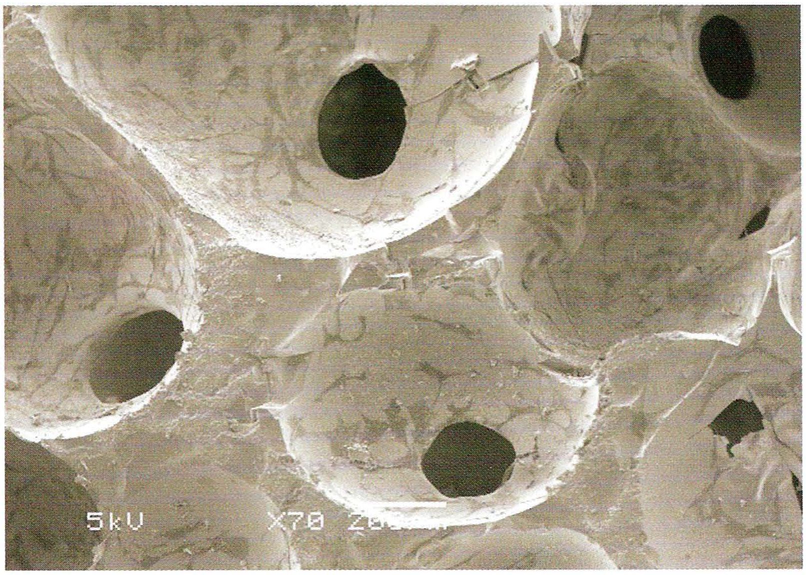
The porous glass acts as an active template for bone growth, without leaving behind traces of itself or toxic chemicals. As it dissolves it releases calcium and other elements such as silicon into the adjacent body fluids, stimulating bone growth.

This technology could be helpful for elderly patients whose bones are slow to heal, as the number of so-called 'active' cells – those that allow healing – reduces with age. Every year thousands of elderly patients suffer broken hips and have to undergo hip replacements. The bioactive glass might prevent the need for this surgery by encouraging healthy bone to grow in weakened areas.

The first bioactive glass was invented by Larry Hench in 1969 and is now a commercial product (from Novabone Products, Jacksonville, USA) in particle form. Recently, Dr Julian Jones of Imperial College, London, UK, has led research into a different direction (see *Materials World*, October 2006, pp21-23).

The particles fill bone defects well, but a porous material that can degrade as the bone regenerates would be better. In 2001, Drs Sepulveda and Jones produced the first porous bioactive glass scaffold with an interconnected pore structure similar to porous bone. This was achieved by foaming sol-gel-derived bioactive glasses.

Below: Bioactive glass forms a bone matrix. Picture reproduced with permission from Julian Jones et al. *Biomaterials*, 2007



Jones developed the material to have mechanical properties similar to bone, and in doing so, discovered that human bone cells growing on the material could produce new bone without the addition of growth factors or hormones – demonstrating that the glass has potential for regenerating bone defects.

The glass activates genes present in human bone cells, which encode the proteins controlling the cell cycle. This forms a bone matrix and rapid mineralisation of the bone nodules. The release of soluble silica and calcium ions from the glass in specific concentrations activates genes, but this only occurs when the timing sequence of the cell cycle is matched by that of the glass surface reactions and a controlled release of the ions.

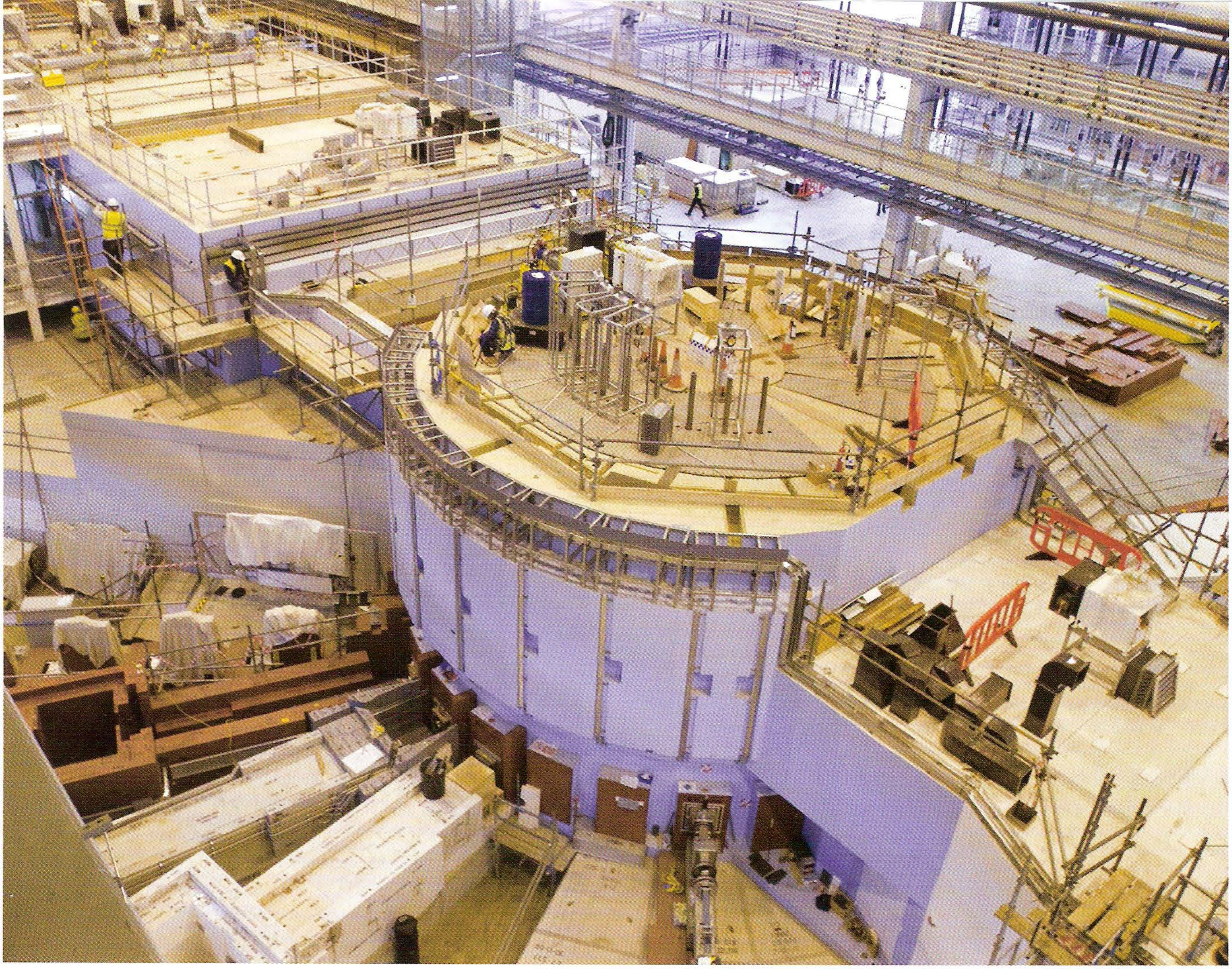
The presence of calcium in the glass is critical in terms of stability and bioactivity. To understand the interactions better, Jones collaborated with Professors Bob Newport at the University of Kent and Mark Smith at the University of Warwick, both UK, who investigated, at an atomic level, how the nanostructure of the glass affected its properties.

Calcium concentration

Newport's experiments were conducted at the Science and Technology Facilities Council's ISIS neutron source, a world-leading centre for research in physical and life sciences, in Didcot, UK. The ISIS source uses neutron scattering to penetrate materials and reveal their molecular structure through beams of neutrons and sensitive detectors. Research showed exactly how the calcium is held in the glass and how, and at what speed, it is released into the body.

By comparing samples made with natural calcium and with a calcium isotope, it was possible to isolate the complex and subtle contribution of calcium from that of all other atoms present.

Calcium ions are bound within the silicate glass



network in a sophisticated fashion, with each ion bound to six neighbouring oxygen atoms – only some of those atoms are bound to the silicon atoms of the host glass. This ensures that the calcium can leave the glass and enter the surrounding body fluid relatively easily. The resulting surface charge on the glass, and changes to the pH of the body fluid, drive redeposition of calcium, but now in the form of hydroxycarbonate apatite, which is similar to bone mineral. Crucially, the increased calcium concentration in the surrounding body fluid also serves as a signal to the appropriate cells to stimulate new bone growth.

Strong stuff

Further research is planned at the ISIS Second Target Station, which will open on the same site later this year. This will investigate glass/polymer hybrids and could assist the development of mechanically stronger versions that would be available for medical use in joint replacement.

According to Newport, the new Nimrod instrument, which is a near- and intermediate-range order diffractometer, will offer greater insight into the subtle balance between short-, medium- and long-range interactions found in many materials. It being built at ISIS and will be crucial in understanding more about the process and relationships between the atomic and mesoscopic structure of sol-gel materials. This will be important for the study of phase separation in metal-silica sol-gel glasses, and the growth of bone minerals in bioactive glasses.

Andrew Taylor, Director of the ISIS neutron source, believes the new facility will make a big impact, 'with the coming of the Second Target Station we will have even more capacity to contribute to improving every-day life in areas as diverse as healthcare, engineering and information technology. This includes experiments with bioactive glass. To allow people to remain active and contribute to society for longer, the need for new materials to replace and repair worn out and damaged tissues becomes ever more important'.

Jones believes that with continued funding, especially for pre-clinical trials, and favourable research results, clinical trials on this form of bioactive glass could take place within five years. Commercial partners NovaThera, Cambridge, and Bioceramic Therapeutics, London, will have a key role to play in this.

'With continued support from the EPSRC we believe that this research will have a significant impact on the lives of not just the elderly, but people who may have been injured in road traffic accidents, had tumours removed, or those who suffer from diseases such as osteoporosis,' adds Jones.

Further information

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Main image: Construction of the ISIS Second Target Station in Didcot, UK. Above: The new bioactive glass could enable knee joints to regrow