our future through science

Bioceramics at the CSIR: Past, Present and Future

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OVERVIEW

Bioceramics are ceramic materials used to replace, repair or augment damaged or missing parts of the body [**1**]. For example, hydroxyapatite (HA = $Ca_{10}(PO_4)_6(OH)_2$) and tricalcium phosphate (TCP = $Ca_3(PO_4)_2$) are bioceramics commonly used in dental implant and synthetic bone graft applications. Together with the Bone Research Laboratory of the University of the Witwatersrand, the CSIR Bioceramics group's initial research into synthetic porous HA revealed geometrically induced osteoinduction in primates [**2**], i.e. the spontaneous formation of bone *in vivo* at implant sites where bone formation is not expected without exogenously supplied growth factors (e.g. the bone morphogenetic proteins).

Further materials research [**3,4**] led into the development of the now well known Eyeborn® orbital implant (synthetic eye) between 2000 and 2003. Successful clinical trials of the product (PCT/IB02/04481) - carried out by ophthalmologists at the Pretoria Eye Institute – were followed by its official launch into the market in March 2004. Since then some 240 implants have been sold, and transfer of the manufacturing technology to a local ceramics firm is currently in progress [**5**].

Harnessing this research momentum (see also, e.g., [**6,7**]), we plan to extend our bioceramics research into the field of synthetic bone substitute materials. Almost a billion dollar industry worldwide, bone substitutes are required for the grafting of synthetic bone into defects arising from (for example) trauma, tumour resection and congenital conditions [**8**]. There is great local demand for bone substitutes due to the nation's unacceptably high rates of trauma, but as most graft material is imported, the costs remain beyond most South Africans. We hope to address this clear national need in our research by developing cost effective hydroxyapatite and tricalcium phosphate bone substitutes materials.

THE EYEBORN ORBITAL IMPLANT

- A biocompatible and bioactive orbit volume filler required in cases of enucleation / evisceration of damaged or diseased eyeball
- Manufactured as a macroporous, sintered HA sphere with smooth, non-porous cap to reduce conjunctival erosion
- Brittle nature of sintered HA not a problem in low load-bearing application

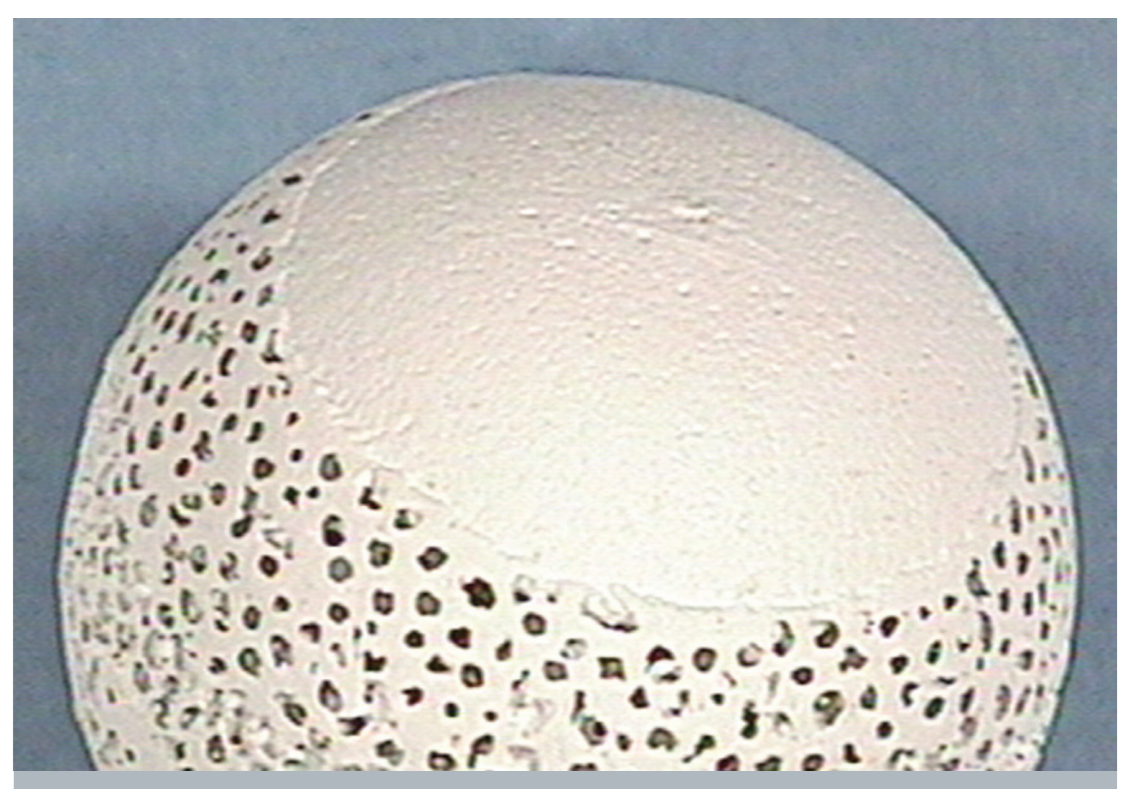

Figure 1: The Eyeborn® orbital implant

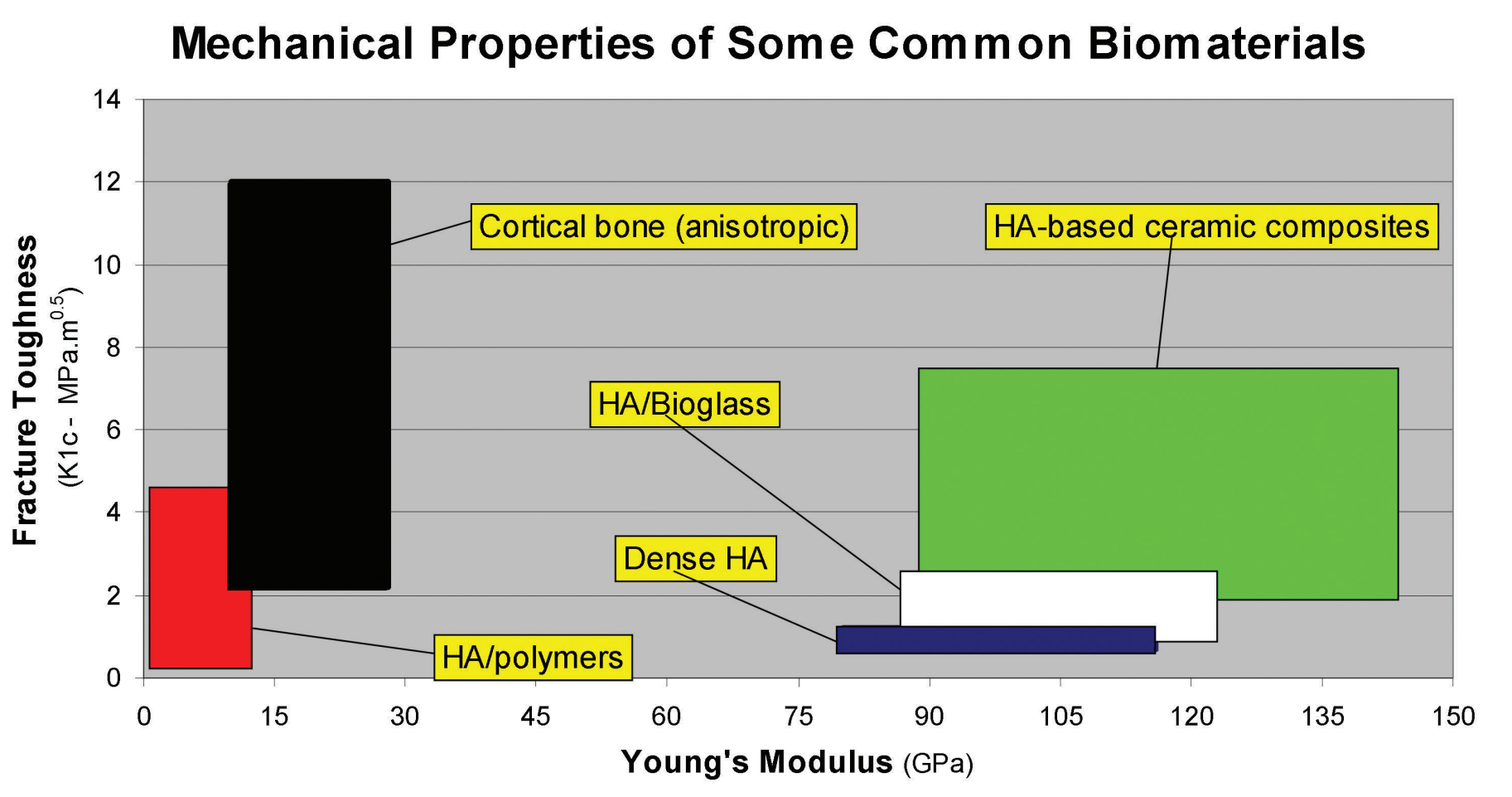

Figure 2: Mechanical properties of important biomaterials

- Macropores (0.7 -1mm diameter) allow tissue ingrowth
- Micropores (<5μm diameter) encourage protein and cellular attachment
  - improved eye muscle attachment
  - improved implant motility (psychological benefit)

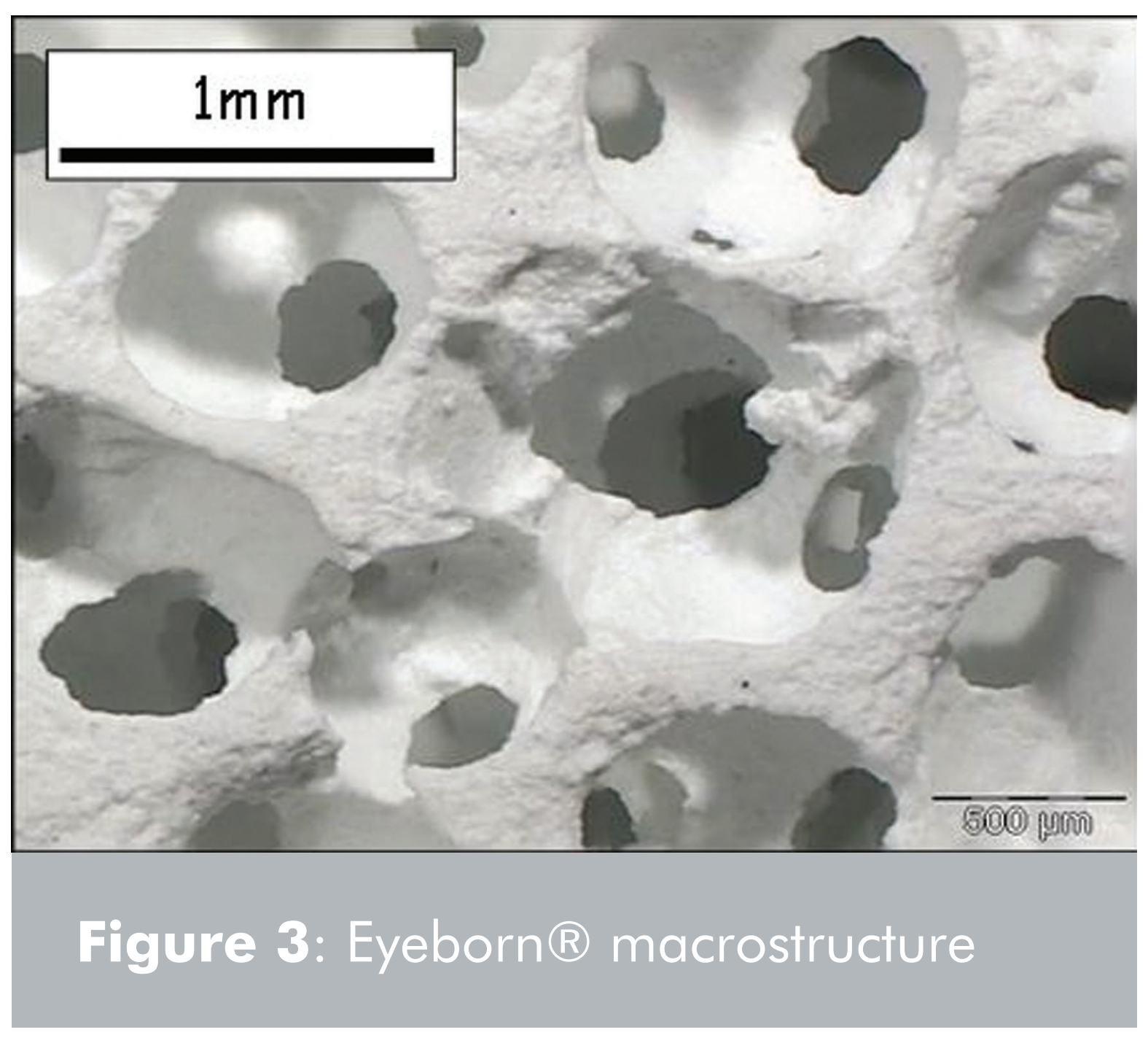

Figure 3: Eyeborn® macrostructure

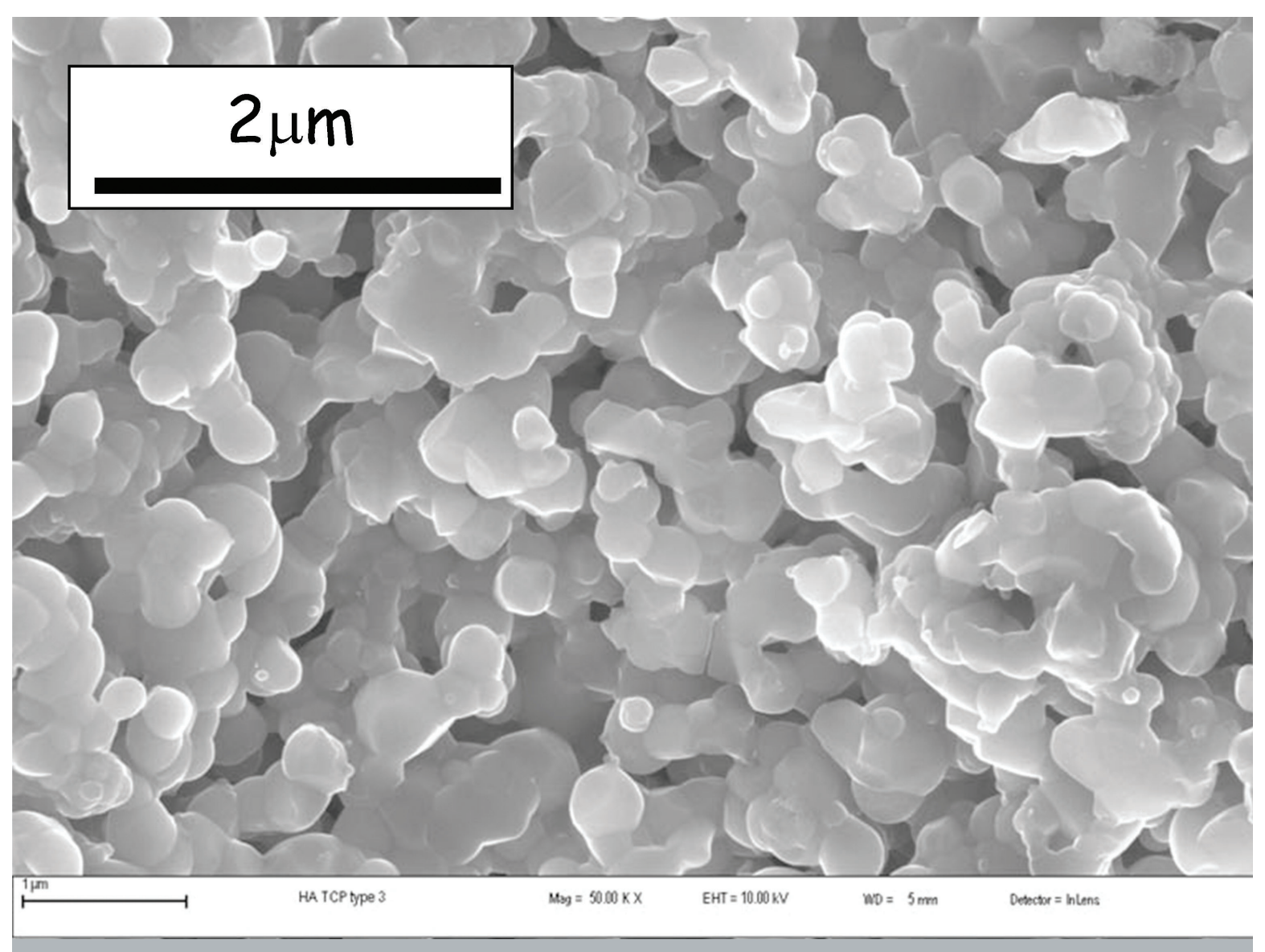

Figure 4: Eyeborn® microstructure

- More affordable than competitor imports
- Big impact on quality of life for the nation's patients
- Technology currently in transfer to local ceramics manufacturer

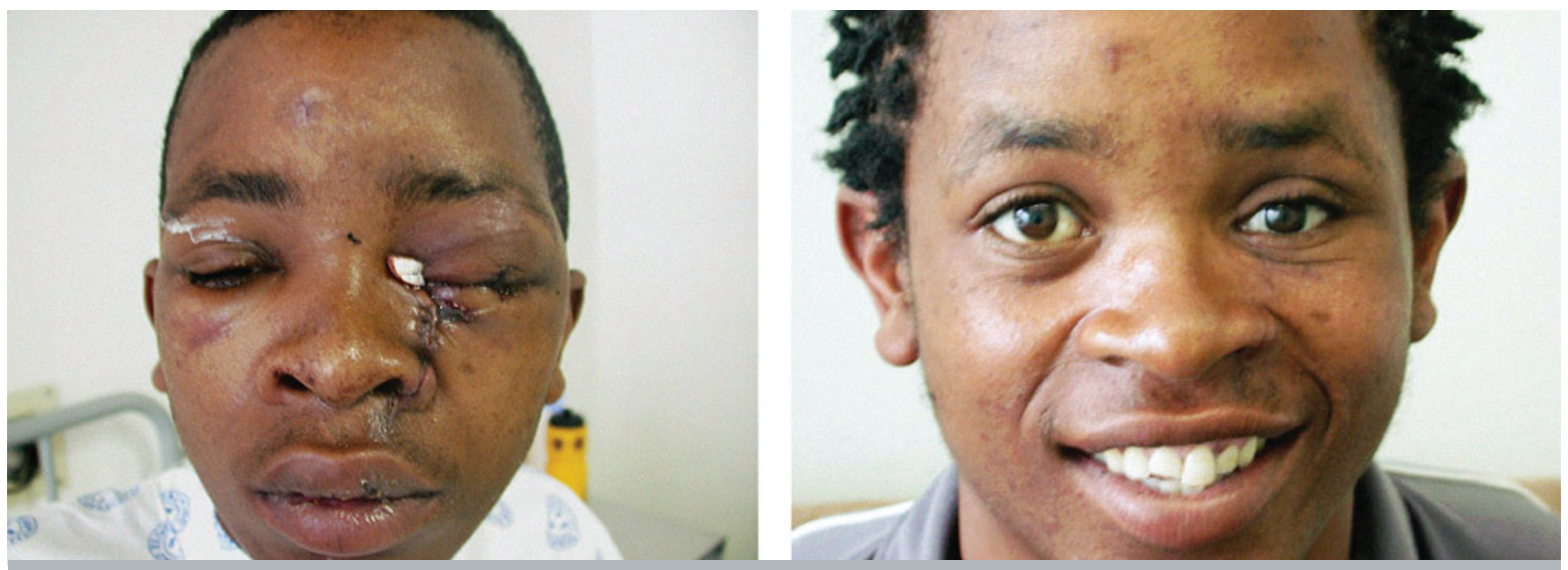

Figure 5: Patient before (left) and after (right) Eyeborn® procedure

INITIAL BONE SUBSTITUTE INVESTIGATIONS

- Bone is a nanocomposite of HA and collagen, so (porous) HA is an important material for synthetic bone substitutes, especially in nanoparticle form
- Collaboration with Bone Research Laboratory at University of Witwatersrand
- Early *in vivo* trials with porous HA revealed geometrically induced osteoinduction
  - Spontaneous formation of new bone tissue in concavities at extra-skeletal sites without exogenously supplied bone growth factors

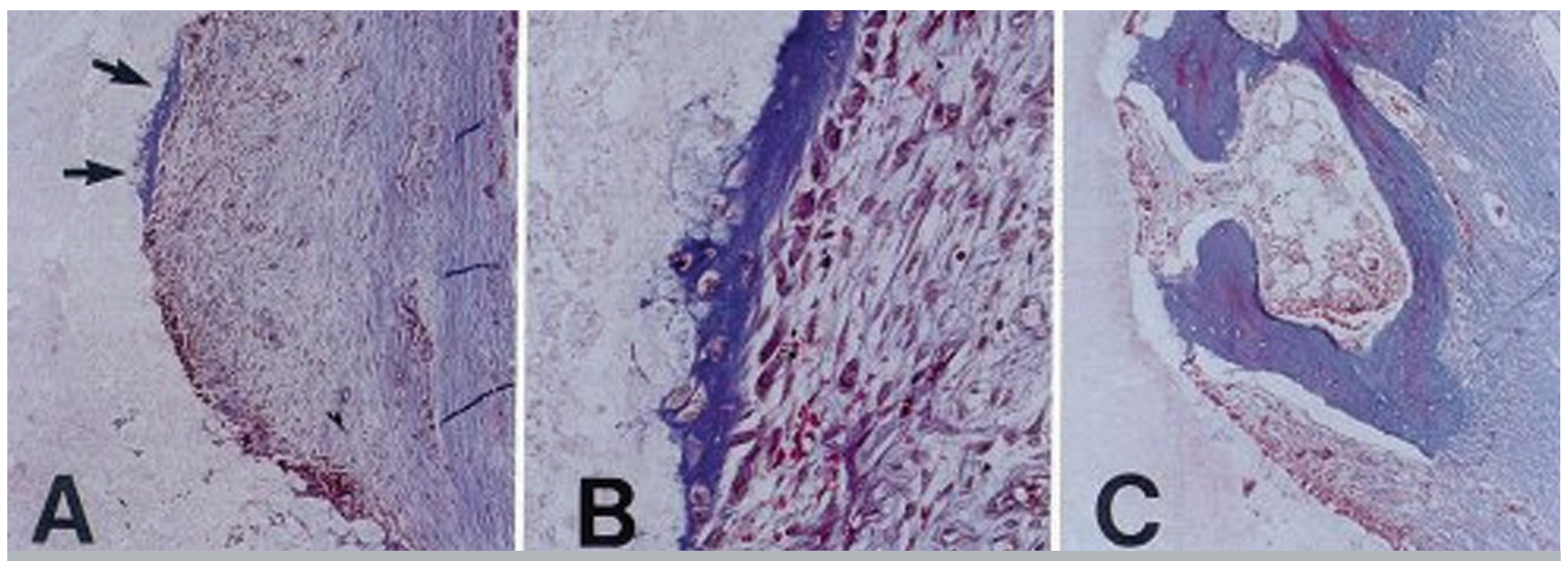

Figure 6: Osteoinduction in geometric concavities of HA

FUTURE RESEARCH: LOAD BEARING BONE SUBSTITUTES

- Sintered HA is brittle, low strength - only suitable for low load-bearing applications (e.g orbital implants)
- HA-polymer composites currently best candidates for load-bearing applications
- Sintering temp^{0}C strongly affects mechanical properties & bioactivity

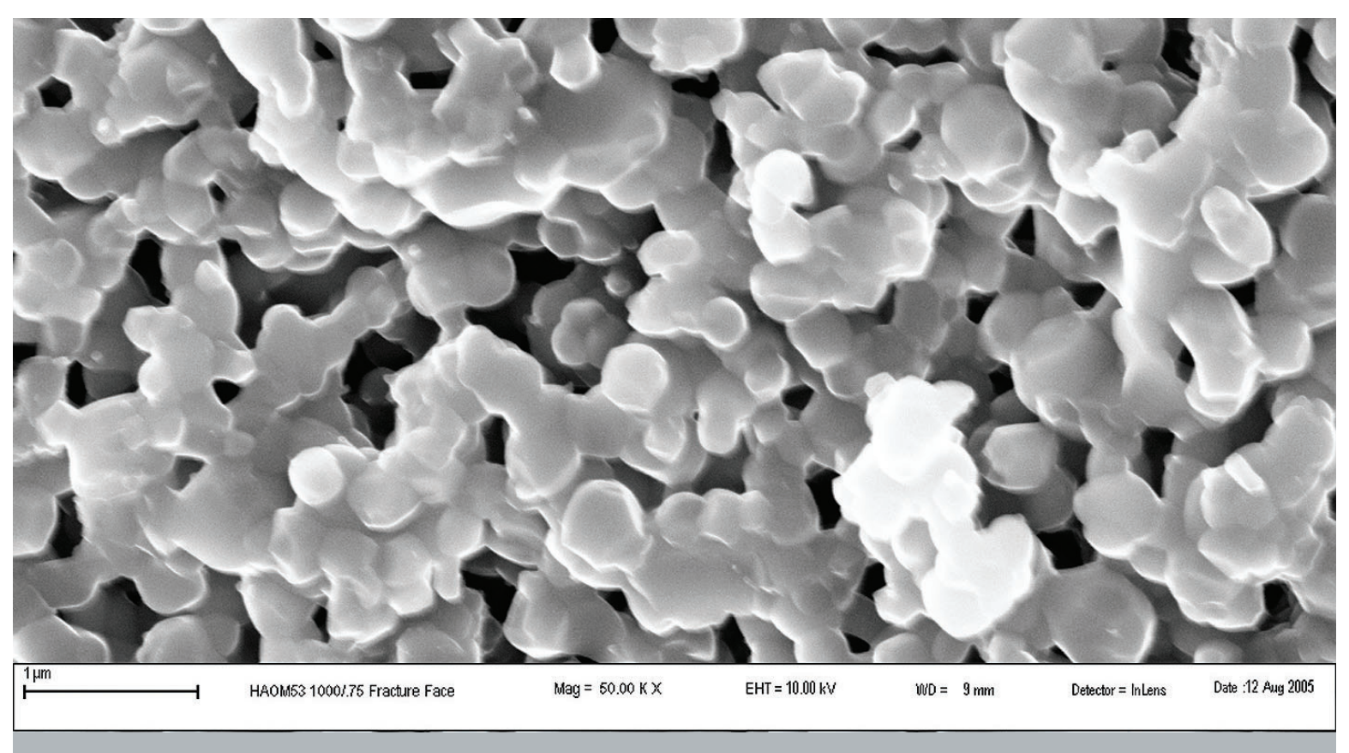

Figure 7: HA sintered at 1000°C

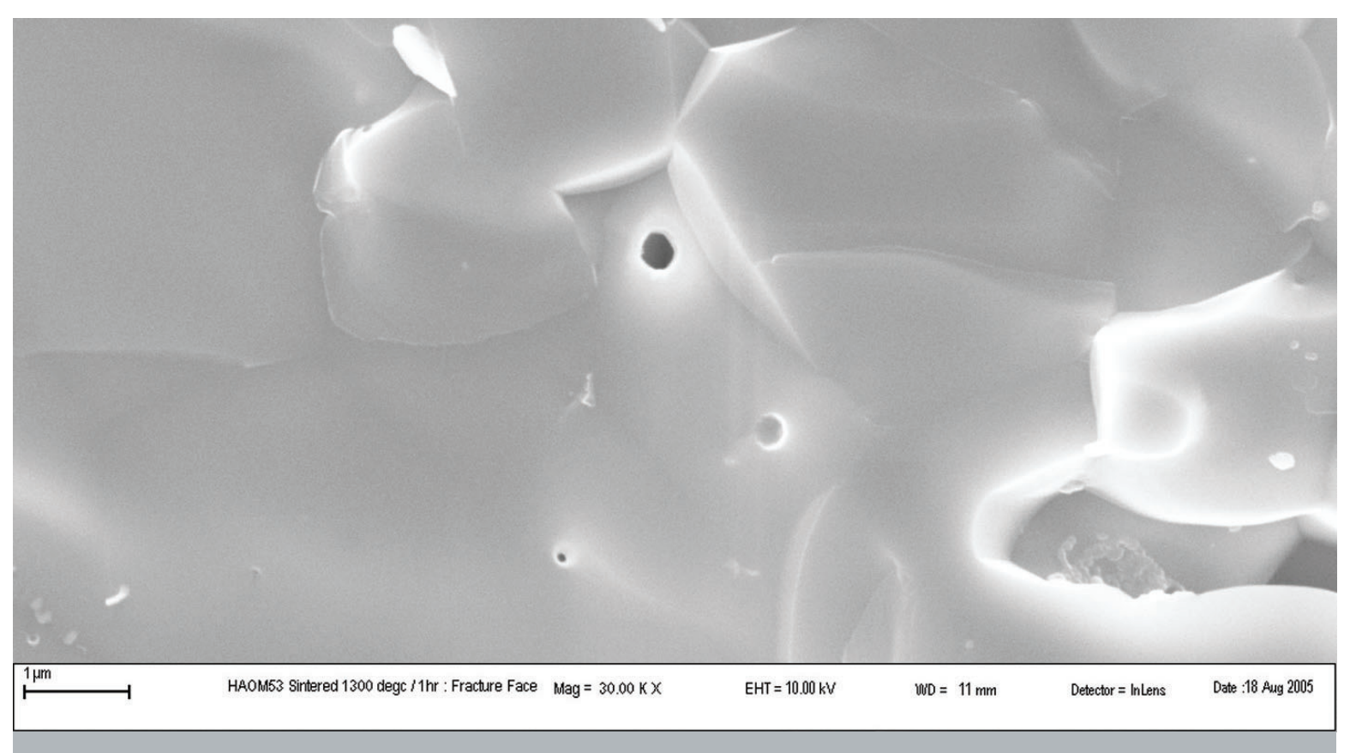

Figure 8: HA sintered at 1300°C

- Implant resorption (in situ biodegradation) and replacement with natural host tissue provides the ultimate healing
- HA is non-resorbable, but TCP is resorbable (rate ~months to years)
  - varying phase content of biphasic HA/TCP material allows control of resorption rate, thus can tailor for specific application

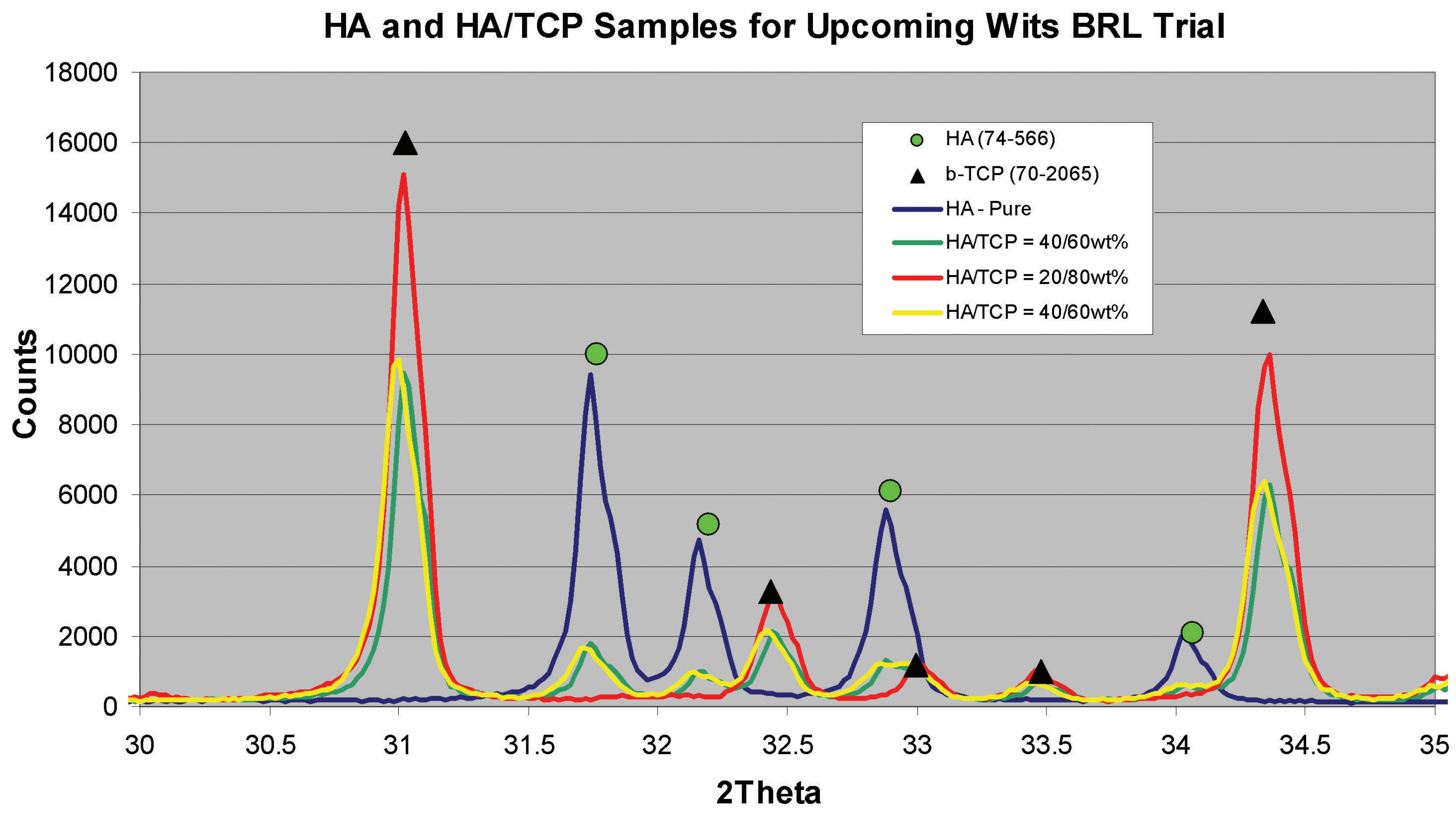

Figure 9: XRD traces of various biphasic HA/TCP mixes

Questions to Address

- What is optimum sintering temperature and cycle?
- What is optimum (starting) HA/TCP phase content ratio?
- Which polymers are best suited for load-bearing composites?

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