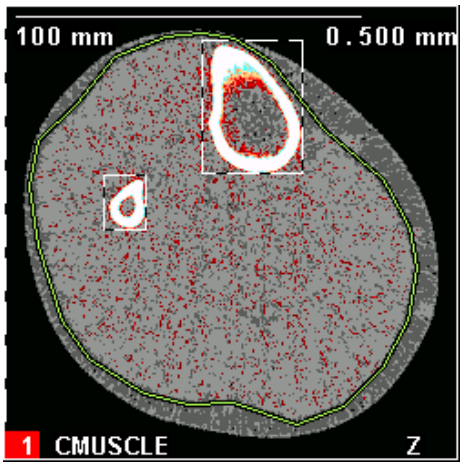
The High Bone Mass Study
Academic Rheumatology
Musculoskeletal Research Unit
Avon Orthopaedic Centre
Southmead Hospital
Bristol BS10 5NB
Tel 44 (0)117 323 2071
Fax 44 (0)117 323 2340

1st December 2012

The High Bone Mass Study Newsletter

Hello, and welcome to the 3rd edition of the annual High Bone Mass study update letter. As always it has been a busy year for the study; the main focus this year has been on continuing to analyse the huge amounts of data that have been collected so far from participants and their families. Recent data analysis has focussed on 3 main areas; bone structure, body composition (the proportions of fat, muscle and bone in High Bone Mass), and osteoarthritis.

The second full scientific paper from the study has recently been published in the journal "Bone" and assesses bone size and structure as measured by pQCT (the polo-shaped scanner that was used to measure the lower leg and forearm in those participants seen in Hull and Birmingham). This scanner enabled us to look in detail at bone structure (see picture), which we compared between HBM individuals and unaffected family members as well as with scans from the Hertfordshire cohort study (http://www.mrc.soton.ac.uk/herts), a large study of people from the general UK population with average bone density. Our results show that individuals with HBM have thicker bones, with a stronger bone shell (cortical bone) and a stronger internal bone structure (trabecular bone). Bones in HBM are also larger, particularly towards the ends of the bone. Our findings suggest that HBM may result from a combination of (1) more bone being formed in early life (when the bones are developing *e.g.* during puberty), and (2) less of a tendency to lose bone density in later adult life, which might otherwise be expected. The full scientific paper is available to read at the following link



(http://www.sciencedirect.com/science/article/pii/S8756328212013294), alternatively please contact us if you would like to request a copy.

Another scientific paper written this year, which will be published shortly in the Journal of Clinical Endocrinology and Metabolism (JCEM), has analysed proportions of fat and muscle mass in HBM, collectively termed "body composition", using the DXA scan information collected from participants seen in Birmingham, Cambridge, Hull and Sheffield. We have found an increase in the amount of body fat in women with HBM compared with unaffected relatives, but in men with HBM no increase in body fat was seen. The mechanism which explains these observations is still the focus of ongoing research work assessing metabolic/energy changes in HBM.

Lastly, we have completed a further scientific paper analysing the presence of osteoarthritis in HBM, particularly joint replacements. This has just been accepted for publication in the journal "Rheumatology". Our results have shown that joint replacements occur more frequently in HBM, even after taking into account differences in age, gender and bodyweight (this is important as increased bodyweight is known to increase osteoarthritis risk). We also compared the number of joint replacements seen in our HBM study participants over the age of 65 with data from a survey of the UK population in 2005 (the "Health Survey for England"), and again we saw an increase in joint replacements in HBM. On the other hand, joint pain was no more commonly reported in HBM. Dr Sarah Hardcastle (formerly Baker) presented these new findings at a national meeting in Manchester in July. Dr Hardcastle is currently working to assess signs of osteoarthritis on the X-rays performed across all our HBM study centres and we hope to report further findings from this work early next year.

All of these research publications are helping to raise awareness among both doctors and scientists about HBM. We are frequently asked questions by other doctors at conferences about HBM cases, and in response to this Dr Celia Gregson has recently written a review article, soon to be published in the journal "Rheumatology", which summarises what is currently known about HBM and provides a guide to doctors. If you would like to request a copy of this article, again please contact us.

Plenty of work is planned for the coming year. Excitingly, Arthritis Research UK (who already fund Dr Hardcastle) have awarded a prestigious Clinician Scientist Fellowship to Dr Celia Gregson, to enable her to further develop the ongoing work searching for genes related to HBM over the next 5 years (www.**arthritisresearchuk**.org/).

We are also pleased to report that early in the New Year we are planning a new phase of the study, inviting selected participants, who live close enough, to attend a clinic in Oxford for a detailed set of tests looking at changes to the way the body uses energy (metabolism). This will build upon the

body composition work described above. If you are eligible to receive an invitation, you will hear from us soon. Therefore, please do remember to keep us informed about any change in your contact details, providing you are happy to continue to hear news of the study. Of course if at any time you would prefer not to hear from us, please do let us know.

Once again, we would like to thank you for your time and continued interest; we are constantly encouraged and delighted by the enthusiasm of our study participants. Of course, we would again like to acknowledge our financial support from The Wellcome Trust, the National Institute for Health Research and Arthritis Research UK who have and are making it possible for this exciting work to continue.

From all of the team, Season's Greetings and all the best for the New Year.

With thanks and best wishes

Yours sincerely

Dr Celia Gregson

On behalf of:

Chief investigator: Prof Jon H Tobias, email: jon.tobias@bristol.ac.uk
Study co-ordinator: Dr Celia L Gregson, email: celia.gregson@bristol.ac.uk
Clinical research fellow: Dr Sarah A Hardcastle, email: sarah.hardcastle@bristol.ac.uk
Study administrator: Caroline Holder, email: caroline.holder@bristol.ac.uk
University of Bristol, website: http://www.bristol.ac.uk/clinicalsciencenorth/musculo/