

Department of Medicine
Bone Histomorphometry Service

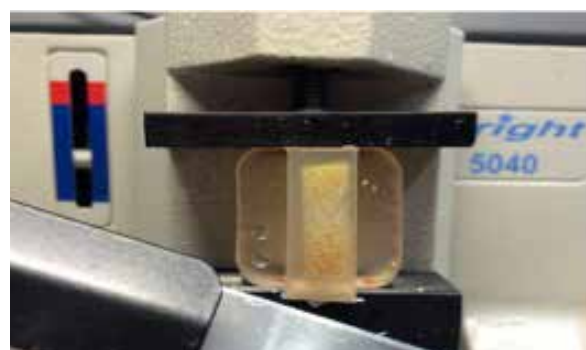
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Bone histomorphometry service

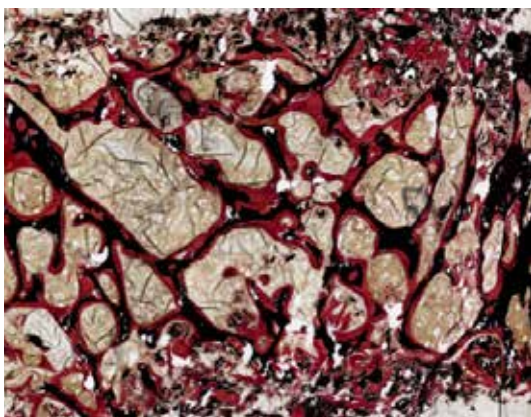
There are various imaging and biochemical tests which examine the structure and activity of bone. However, for many bone diseases, a bone biopsy is the 'gold standard' diagnostic technique. For example, the technique is useful for determining whether osteoporosis is high or low turnover in origin which will then inform treatment choices. Likewise, in patients with renal disease who may have osteomalacia, secondary hyperparathyroidism or adynamic bone disease; treatment can be tailored to the specific pathology once the diagnosis is made. Taking the antibiotic tetracycline (or demeclocycline) at certain intervals before the biopsy, creates fluorescence in the patient's bone which enables the measurement of bone formation rate

Bone biopsies are ideally taken from the iliac crest with a 6 – 8mm trephine. This transiliac core gives the best chance of obtaining a good biopsy with two cortices and intervening trabecular bone. The procedure can be carried out on a day case basis (except for patients with complex medical needs) and complications are minimal. The biopsy is placed in 70% ethanol at room temperature for fixation and transfer to the lab – this particular fixative is best for preserving the tetracycline labels. Bone samples without antibiotic labelling, or from other surgical sites can be analysed but may provide less information.

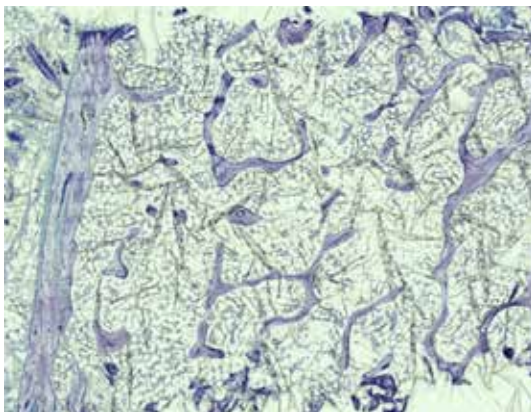
In order to assess the metabolic status of the bone it should be examined in its natural mineralised state (unlike bone sent to routine pathology labs which is decalcified so that it can be processed and embedded in paraffin wax). Hence, for bone histomorphometry, samples are processed in their undecalcified state which necessitates embedding in a resin of comparable hardness to bone – we use LR White, a methacrylate resin. Once embedded the resin blocks are sectioned on a heavy duty microtome with a tungsten carbide knife.



Sections are then stained with either von Kossa or toluidine blue stains: von Kossa staining shows mineralized bone in black and unmineralised osteoid in red; toluidine blue stains cells as well as bone and under polarized light displays bone lamellae well. Alcian blue staining after von Kossa staining allows visualisation of cellular detail in the bone marrow.

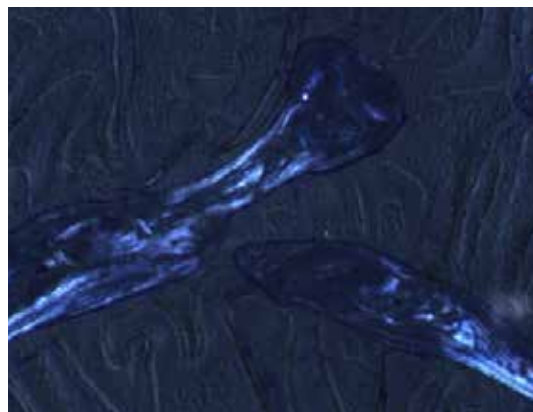


Undecalcified bone, von Kossa staining, mag x40: Osteomalacia, thickened osteoid seams on almost every mineralised bone surface.

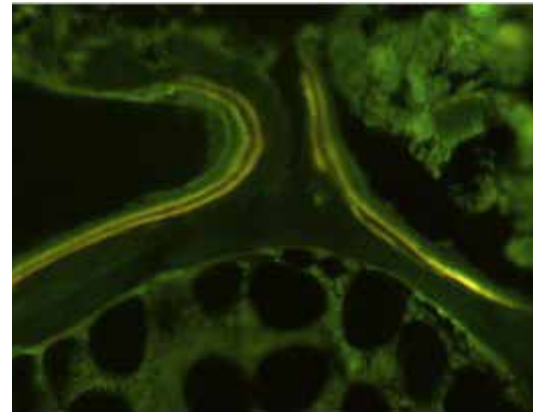


Undecalcified bone, toluidine blue staining, mag x100: osteoporosis, thin trabeculae and cortices.

In order to assess the presence and rate of mineralisation, patients can be given two short courses of tetracycline antibiotics prior to biopsy: the antibiotic is taken up by the mineralising bone and fluoresces under UV light, best seen on an unstained section.



Undecalcified bone, toluidine blue stain, mag x100 viewed under polarized light: lamellae within trabecular bone.



Undecalcified bone, unstained, mag x100 viewed under UV light: two mineralisation fronts highlighted by double tetracycline labels.

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Biopsy logistics

A typical antibiotic fluorochrome labelling regime:

**Tetracycline 250 mg x 8 tablets:
one tablet twice a day**

OR

**Demeclocycline 150mg x 16
tablets: two tablets twice a day**

in the following pattern:

Day 1

Day 2

Then leave a ten-day gap

Day 3

Day 4

Biopsy taken 3 – 5 days later.

Biopsy logistics

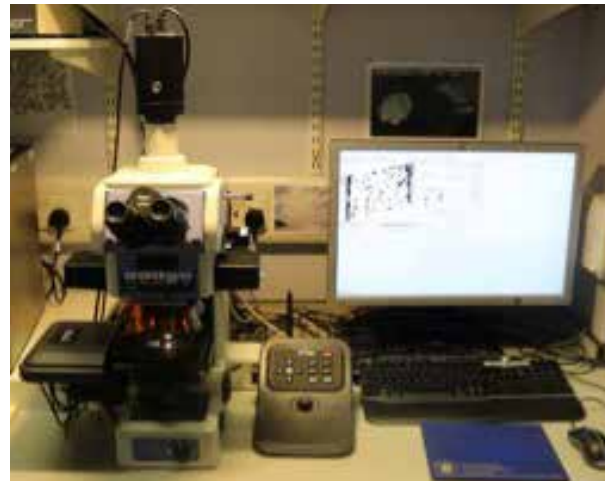
Iliac crest biopsies are traditionally taken from an area 2cm below and 2cm anteriorly of the anterior superior iliac spine while the patient is under general anaesthetic or sedation. They should be taken with a 'crown drill' corer of diameter >6mm. We prefer two samples per patient: one >6mm core for undecalcified metabolic assessment in our lab and one Jamshidi needle core for routine decalcified examination in the pathology lab to exclude malignancy. Biopsies can be sent to us in a universal tube containing 70% ethanol, along with a copy of the consent form (preferably also with research consent) and as much clinical detail as possible in order to aid interpretation. Please contact us for packaging and transportation details.

About bone histomorphometry in Cambridge

The Bone Research Laboratory was set up within the Department of Medicine in the University of Cambridge by Prof Juliet Compston in the 1990s. Part of the remit of the lab was bone histomorphometry which was carried out by Dr Shobna Vedi and reported by Prof Compston. Since Dr Vedi's and Prof Compston's retirement Dr Ken Poole has continued to provide the reporting service with Dr Linda Skingle who was trained by Dr Vedi and Prof Compston.

Digital images of whole mounted sections are made with a QImaging camera attached to the computer using Surveyor software from Objective Imaging.

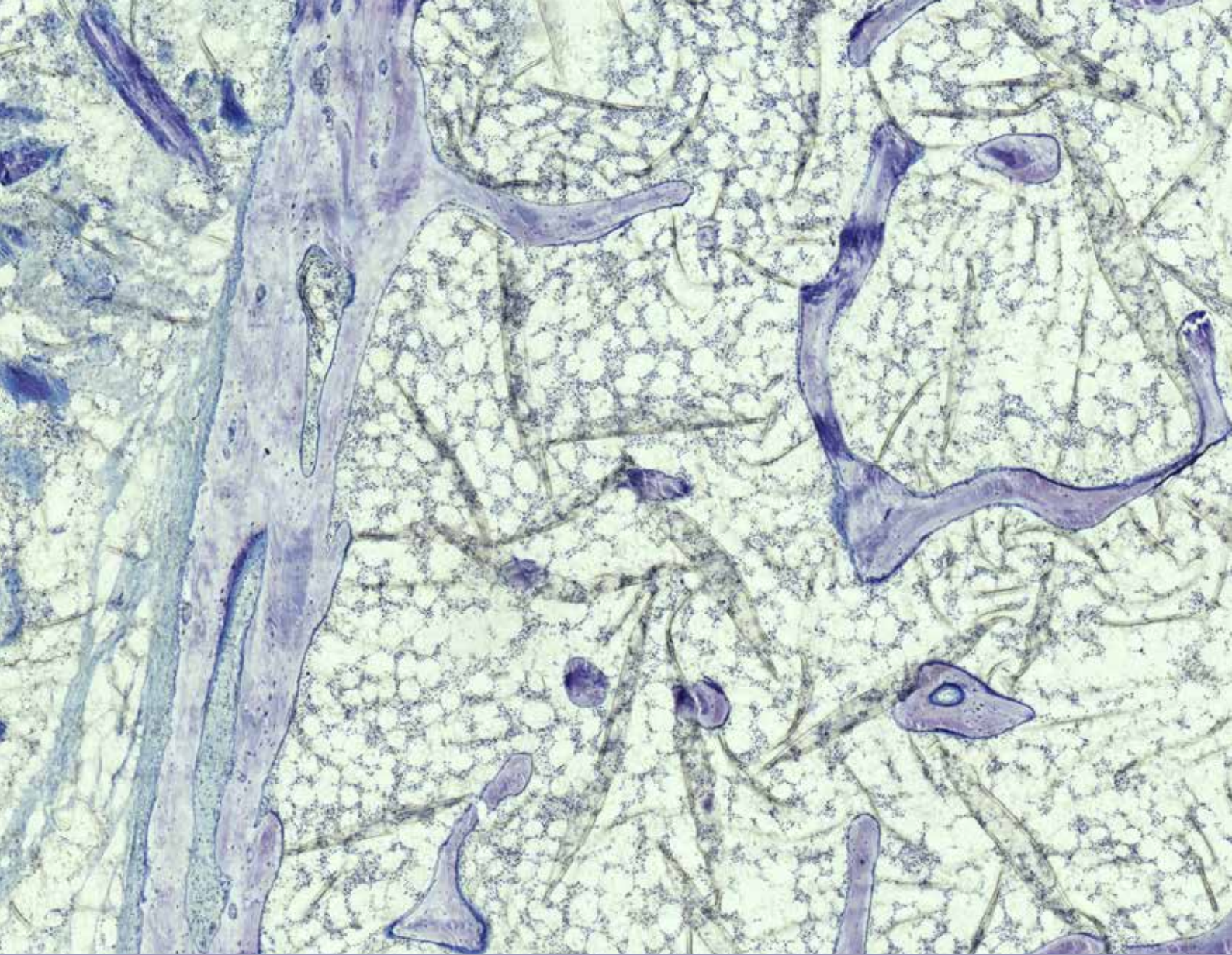
Diagnostic biopsies are reported qualitatively; the report being paired with a report on a second decalcified trephine core analysed by the NHS pathology lab to exclude malignancy. Occasionally a quantitation (of bone volume and/or osteoid volume/thickness) in accordance with standard nomenclature (ASBMR committee) is provided and compared with published normal ranges. Research samples are analysed quantitatively using Bioquant Osteo II software providing a range of static and dynamic measurements.



Microscope, camera and computer set up for analysis

Time from receipt of a diagnostic biopsy to a report being published is usually about 4 weeks.

The diagnostic bone biopsy service is provided at a cost which covers our time, equipment maintenance and consumables and is currently **£368.55 +VAT/biopsy.**



Contact information:

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