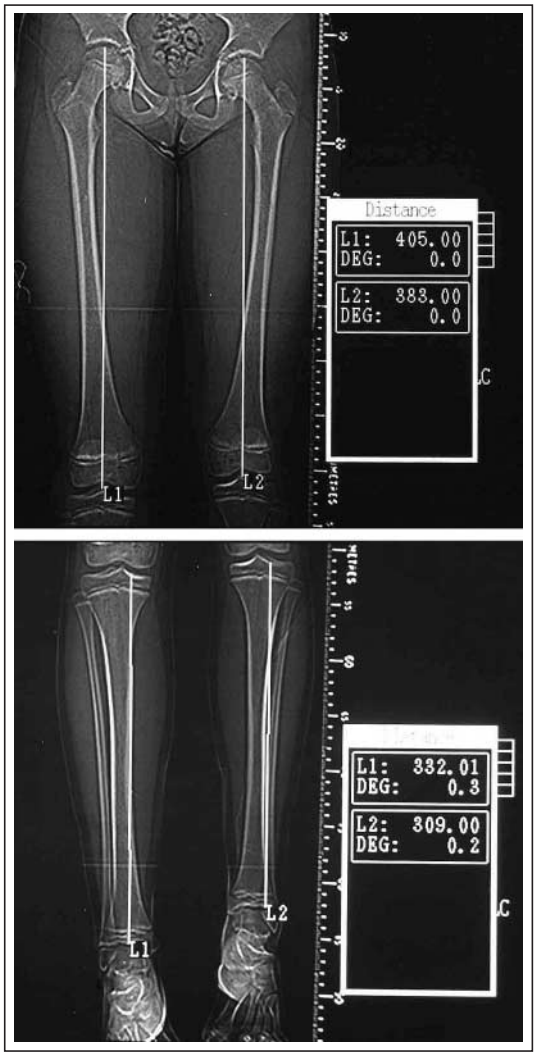
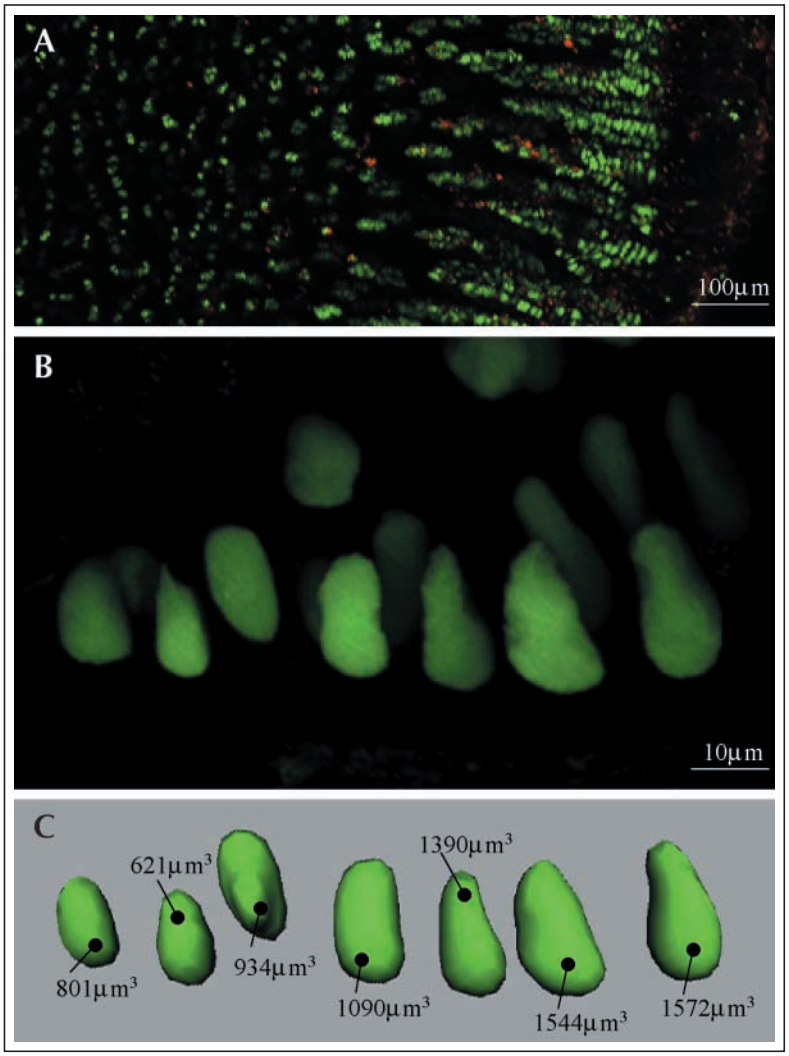
Looking at the living human growth plate



Images courtesy of Dr. James S. Huntley



Images courtesy of Dr. Peter G. Bush

A baby girl was noted soon after birth to have a form of hemihypertrophy affecting her limbs (right longer than left), but not her trunk or face. She was followed by the regional orthopedic team for several years with respect to her leg length discrepancy. At 10 years of age the discrepancy in length was 4 cm, as assessed by "block testing" (the patient stands with feet flat on the ground, and the shorter leg is raised by a series of graduated blocks until the examiner judges the pelvis to be level by palpating both iliac crests). A CT scanogram confirmed the 4-cm discrepancy (Fig. 1) and showed that the difference was equally attributable to tibia and femur. The patient underwent surgical ablation of the growth plate (epiphysiodesis) of her right distal femur and proximal tibia 2 months after the assessment. The timing of the procedure was chosen to allow equalization of the limb lengths at maturity.[1–4] The postoperative course was uncomplicated, and the patient was discharged the next day. Two years later, she remains under follow-up with respect to equalization.

With parental consent and permission from the Lothian Research Ethics Committee (Edinburgh), tissue from the original osteotome cut was retained and maintained in aseptic culture. Confocal laser scanning microscopy and fluorescent dyes (calcein-AM and propidium iodide) were used to image human chondrocytes living in situ in the growth plate (Fig. 2). Living chondrocytes are seen as green, and dead chondrocytes and bone material are seen as red (Fig. 2A). Under low power (Fig. 2A [magnification ×10]), from left to right, the cartilaginous region, proliferating cell zone, hypertrophic cell zone and osteogenic zone are seen. At higher power (Fig. 2B [magnification ×63]) a small group of cells within the central region of a column of cells in the hypertrophic zone is identified. These cells were selected for computerized estimation of cell volume[5] and were surface-rendered in Fig. 2C to illustrate morphology.

Discrepancies in leg length can arise from many congenital and acquired conditions (including physeal injury, osteomyelitis, hemiatrophy, hemihypertrophy, partial gigantism, arteriovenous fistulas, poliomyelitis, cerebral palsy, neurofibromatosis and Perthes' disease).[1,2] The cause is more often growth inhibition than growth promotion (as occurs in hemihypertrophy). Significant discrepancies have several sequelae, including a pelvic tilt (with compensatory scoliosis), gait problems and back pain. Discrepancies of less than 2 cm are unlikely to be significant. For those of 2–5 cm, epiphysiodesis of the longer limb is the preferred treatment.[1,2] Discrepancies of more than 5 cm are usually treated with a limb-lengthening procedure, which can be combined with contralateral epiphysiodesis.

The physis, or growth plate, is a disc of tissue situated between the metaphysis and epiphysis of long bones and is responsible for growth in bone length.[4] At the epiphyseal side, mitotic activity (in the proliferative zone) is followed by chondrocyte volume expansion (in the hypertrophic zone) and finally cell death in the juxta-metaphyseal region. The products of cellular degradation are then incorporated into the metaphyseal bone front. Some have described this process as apoptosis,[4,6] although the morphological correlates are atypical.[7] Little is known about the processes underlying the cellular changes in the physis except that the rate and extent of chondrocyte swelling correlate with the degree of bone elongation.[8–10] Most studies have used traditional techniques (e.g., chemical fixation for histological analysis and tissue sectioning, or enzymatic isolation of chondrocytes) or animal models to examine the physis.[6–10] With confocal laser scanning microscopy, problems associated with these techniques are avoided and the cells are closer to the in vivo state. Novel views of the human growth plate, such as those seen in Fig. 2, not only are visually appealing but also provide a bridge between the clinical and basic sciences and permit a better understanding of bone elongation.

James S. Huntley
Lecturer in orthopedics and trauma
Department of Orthopaedics
New Royal Infirmary of Edinburgh
Peter G. Bush
Postdoctoral fellow
School of Biomedical and Clinical Laboratory Sciences
University Medical School, Edinburgh
Andrew C. Hall
Senior lecturer in physiology
School of Biomedical and Clinical Laboratory Sciences
University Medical School, Edinburgh
Malcolm F. Macnicol
Consultant orthopedic surgeon
Royal Hospital for Sick Children
Edinburgh, Scotland

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