REVIEW

Quantitative radiography of osteoarthritis

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Radiography is important in the diagnosis of osteoarthritis (OA) as the features described in the pathology of the disease can be visualised, with joint space narrowing generally thought to reflect cartilage loss.¹ Plain film radiography provides excellent detail of bony features but is generally poor at defining soft tissue structures, except with the help of an invasive procedure involving the introduction of a contrast medium. These characteristics together with the ready availability and ease of interpretation of radiographs has led to its use in confirming a clinically suspected diagnosis of OA, based on the appearance of characteristic radiographic features.² Different methods of scoring the extent of these features have been developed and have been used as criteria both for diagnosis and to classify the base line status and progression of the disease in clinical studies. In spite of recent attempts at improving methods of scoring joint damage,^{3–4} none of the different systems available^{3–8} have been widely adopted, largely due to the different emphasis that is placed on various radiographic features by different investigators, and the generally held notion that OA progresses slowly.⁹

Scoring systems, although an essential and widely used method for assessing disease progression, suffer from a number of limitations. They are based on two assumptions, first that the change in any one *x* ray feature is linear and constant during the course of disease, and second, that the relationship between the different *x* ray features is constant. Thus scoring radiographs does not take into account that different radiographic features may progress at different rates and at different times. To achieve an understanding of the relative significance of various radiographic features, a far better knowledge is required of the natural history and outcome of the disease, of which little or nothing is at present known.¹⁰ In this instance all radiographic features need to be studied with equal importance. This can best be done by taking direct measurements of the distribution and size of each feature accurately and reproducibly and determining the relative rates of change in their dimension with time.

Quantitative assessments of the structural changes in peripheral joints with OA are based on measurements of distance and area in the radiographic image. Such measurements are obtained either directly from the radiograph, or with the increased use of computer imaging, from digitised *x* ray films. Currently, direct measurement of *x* ray features are made from both standard and microfocal radiographs. The advantages and limitations of these two imaging modalities are described, and the

results of their application in quantifying disease progression are outlined. Where it has been possible to obtain precise measurements of changes in *x* ray features, this has provided new insight into the natural history of OA and a number of these findings are described. Increasingly the concept of quantitative radiography is being accepted by rheumatologists and radiologists as the means of obtaining information about joint structure. To this end the last section in this paper outlines a range of factors which need to be optimised and standardised to improve quantitative standard radiography.

Standard radiography

The radiographic image is a shadow of the differential absorption of *x* rays by the tissues of the joint, where radiographic appearance of bony structures appears white to light grey and the radio-transparent soft tissues dark grey to black (fig 1).

Advantages Standard radiography is simple, cheap, easily accessible and well understood. The radiographs provide a permanent record which can be assessed at any stage during the disease process permitting their use in both prospective and retrospective studies. This is important in the study of a disease such as OA which progresses slowly.⁹

Limitations The relatively large size of the *x* ray source of standard *x* ray tubes (usually 1 mm and at best 0.3 mm in diameter) demands that the object is placed close to the *x* ray plate resulting in little or no radiographic magnification. Bony margins are poorly defined due to the limited spatial resolution (the smallest object recorded in the film ranges from 0.1–0.2 mm) and to penumbral blurring. Secondary *x* ray scatter, even when largely removed with a Bucky grid, reduces the overall contrast of the shadow image recorded in the film.

Apart from those investigators who have developed special stereotaxic devices for examining leg alignment^{11–12} or knee joint motion,¹³ there is no accepted method for positioning a joint for radiography which ensures that it is in precisely the same position for each patient and on successive occasions. With the work of Ahlback⁷ and Leach *et al*¹⁴ radiographs of the knee are now taken weight bearing with the joint fully extended. Although this is the view described in recent studies,^{15–18} many studies do not define the radiographic position of the joint.^{9–19} Alternative views of the knee, in the semi-flexed²⁰ or tunnel²¹ position have been recommended as providing more

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Figure 1 Standard radiographic appearance of osteoarthritic knee joints showing different degrees of joint space narrowing, subchondral sclerosis and osteophytosis. The antero-posterior radiographs of the knee have been taken from different patients and all show the joint in a different radio-anatomical position. The variability in the tilt of the tibial plateau makes it difficult to obtain accurate and reproducible measurements of joint space.

reliable assessment of joint space loss. The absence of any standards in the radio-anatomical positioning of joints results in variable radiographic images of a joint both within and between patients (fig 1), compromising the reliability of measurements obtained from any of the radiographic features. As shown recently,¹⁶ increased flexion of the knee can result in apparent joint space loss of up to 25% in the medial compartment. Another important variation that can occur during the radiographic procedure is in the position of the central ray of the x ray beam relative to the centre of the joint, that is, the joint space in the knee. Here, changes in the beam angle lead to either the anterior or posterior edges of a joint margin partially overlapping and obscuring the joint space (fig 1). The lack of control over x ray beam alignment results in the articular surfaces not lying parallel to the x ray beam and perpendicular to the x ray film, thus preventing accurate and reproducible measurement of joint space width. Fife *et al*¹⁶ found that medial compartment joint space width of a knee decreased by 17% when the x ray beam was lowered by 1 cm below the original alignment of the beam centred at the mid-point of the patella. Furthermore, the selection of anatomical landmarks used to define the boundaries for measurements of radiographic features can vary and depend on the individual investigator's interpretation. Joint space width measurements are taken either across the mid-point or the narrowest part of the joint space,

but more often than not the plane of measurement is never defined. Further, no account is taken of the distance between the centre of the joint and the x ray film. Where this is fairly large, as in an x ray of the hip or knee, it results in magnification of the shadow image and an error in any measurement not corrected by the magnification factor. The radiographic magnification also increases the penumbral blurring and can lead to a further loss in radiographic definition. For these reasons, particularly those relating to joint positioning, Fife *et al*¹⁶ found such a poor correspondence between the radiographic evidence of joint space narrowing and the arthroscopic appearance of articular cartilage damage, in patients with early knee OA, that they state that joint space narrowing in the tibio-femoral compartment does not permit confident prediction of the status of the articular cartilage. Consequently patients with early disease, with minimal joint space loss are unlikely to be detected by standard radiography.

Quantitative standard radiography

Quantitative standard radiography has been applied primarily to joint space width (JSW) measurements in OA of the hip and knee, since assessment of articular cartilage thickness is important in evaluating disease progression²² and the effects of therapy.²³ Two approaches have been used. In the first, joint position is very precisely controlled with the aid of custom built apparatus. This method allowed

standardisation of the position of the hip and knee and reproducible repositioning of the joints on successive examinations.¹²⁻²⁴ However, in these studies JSW measurements were carried out using a simple method such as a ruler. Conversely, the second approach has used an automatic system for increased precision in JSW measurement, employing computerised analysis of digitally stored radiographic images.¹⁸⁻²⁰ In these investigations there has been no standardisation of the joint position.

In the former, Martel's group at Michigan University, undertook to define the precision of hyaline cartilage thickness measurements.²⁴ They used a small sourced x ray tube (0.3 mm focal spot) to obtain magnification radiographs ($\times 1.6$) to facilitate joint space measurement. Hip and knee joints were studied separately and evaluated with collimated views centred on the joint space. The legs were immobilised using a custom built apparatus to stabilise the joints and standardise position for radiography. The radiographs from the initial position were used to align the patient's joint for the follow up examination. Fluoroscopy was used to facilitate reproducible positioning.²⁴ The accuracy of their measurement procedure using a ruler was defined together with the anatomical points at which the measurements were taken.²⁴ The results of their study showed the standard deviation of the mean joint space width measurement in plain film radiographs of the hip and knee gave a variation of $\pm 6.5\%$ for one degree of standard deviation.²⁴ This approach represents a major advance for it defines the significance level at which changes due to the effect of disease should exceed those due to the combination of errors associated with the accuracy of repositioning the patient and the reproducibility of the measurement. It can be estimated that significant changes (that is, greater than two degrees of standard deviation) in JSW are obtained when the loss in joint space width is equal to or greater than 13% of the JSW. With progressive joint destruction the feasibility of detecting significant changes in joint space becomes more difficult. This may well explain the difficulties investigators have found in detecting measurable changes in JSW within a reasonable period of time.²⁶⁻²⁷

The development of microcomputers and image analysis technique has provided the means of obtaining an accurate and reproducible method for measuring changes in joint anatomy and for handling large amounts of numerical data. Browne *et al.*²⁸ developed a method of digital analysis that will readily detect changes in periarticular bone contours. This method could be used for assessing the extent and change in osteophyte number and size, although to date it has only been used for assessing erosions in the rheumatoid hand.²⁹ Most results from this area of technology have come from the method developed by Dacre *et al.*¹⁸⁻²⁵⁻³⁰ providing a rapid, accurate and reproducible means of measuring knee joint width. A video image of a radiograph is digitised and stored within the microcomputer.

Joint space is assessed automatically using an edge detection technique and is expressed either as the mean width of several repeat measures or as the joint space area. The reproducibility of the computerised JSW measurement technique is good, giving a coefficient of variation for repeat measures of 1.4%.²⁵ Results obtained with this method have shown that men have larger joint spaces than women and that there was a progressive decline in joint space size with age from 27.9 to 69.5 years.³⁰ Preliminary reports on the quantitative assessment of radiological changes occurring in patients with osteoarthritis of the knee²⁷ showed that very little change in joint space was detected within an 11 year period. These findings indicate that in spite of the accuracy and reproducibility of the image analysis methods, it is mandatory to control the accuracy and reproducibility of the radiographic procedure and patient position, in order to detect changes in the size of x ray features, such as JSW, within a reasonably short period of time. Otherwise, the statement that standard radiographs are not sensitive to minor changes in OA, and therefore are not precise measures for short-term longitudinal studies,²³ may prove to be true.

Microfocal radiography

Microfocal x ray units are characterised by an extremely small x ray source ($<15\ \mu\text{m}$ in diameter) which allows radiographs to be taken at high magnification with very fine detail recorded in the film.³¹⁻³⁴ These macrographs are obtained by placing the object close to the source (20–30 cm) and the shadow image is projected onto the film placed at some distance away (1.5–2 m). The radiographic magnification obtained is the ratio of the source to film over the source to object distances.

Advantages of microfocal radiography are those characteristic of an extremely small x ray source. Large object magnifications are obtained ranging from $\times 2$ to $\times 20$, although, macroradiographs are more usually taken between $\times 4$ and $\times 10$. High spatial resolution within the film: the size of the smallest object recorded in the film is between $25\ \mu\text{m}$ and $50\ \mu\text{m}$ depending on the thickness of the joint under examination. The large air gap of at least one metre between the object and x ray film removes nearly all of the secondary x ray scatter, resulting in a significant improvement in film contrast and in the ability to detect detail within the film. The minimal penumbral blurring results in all planes of the object being in focus. A three dimensional assessment of bones in the joint can be achieved by the accurate displacement of the object between succeeding x ray exposures and examining the stereopair macroradiographs obtained under a large format stereoscopic unit.³¹⁻³³ This technique enables the observer to determine the precise location, within the tissues of the joint, of a lesion in three dimensions and to more accurately define its boundary. The combination of all these advantages and more particularly of high magnification and spatial

Figure 2 Part of the macro-radiographs of osteoarthritic knee joints with medial compartment involvement, in the weight bearing standing A) and loaded tunnel B) views. In the medial compartment the anterior and posterior margins of the joint are superimposed, the floor of the tibial plateau is the superior margin of the bright radiodense band of the subchondral cortex (original radiographic magnification $\times 5$, reproduced $\times 1.2$).

resolution, makes it possible to detect structural detail virtually at the histological level³⁴ and to carry out direct accurate measurement of the x ray features characteristic of arthritis with a high degree of precision.^{35 36}

Limitations are also a function of the small x ray source size. The smallness of the source limits the output of an x ray tube and results in longer exposure times. This restriction has been largely overcome with the use of rare-earth film screen combinations³³ permitting x ray exposures of less than a second.

Care and accuracy are needed in positioning the patient in relation to the source. This requires specially developed apparatus enabling the patient to keep still and to maintain the position of their joints. The radiation dose, although higher than in standard radiography, due to the patients proximity to the tube, is none the less well within radiation safety requirements.³⁴ Contrary to the notion held by some,³⁷ this equipment, although not widely accessible at present, is relatively inexpensive at a cost similar to that of a conventional x ray unit.

Standardisation of macro-radiographic procedure

Stereotaxic devices are used to position each patient accurately and reproducibly. The centre of the joint under examination (the middle phalanx in the hand, the joint space in the knee and the femoral head in the hip joint) is aligned with the central ray of the x ray beam by means of a cross-optic laser. For

knee radiography an image intensifier and camera are used to screen the joint to ensure that the tibial plateau is flat and parallel to the central ray of the x ray beam and perpendicular to the x ray film, and that the tibial spines appear centrally placed relative to the femoral notch (fig 2). Precise repositioning of the hip and knee on successive x ray visits, plus the control of any rotational displacement in these joints, is achieved by outlining the position of the feet, at first visit, on a large sheet of paper located on the platform of the stereotaxic unit. Macro-radiographs from the initial examination are used to assist in positioning the patient for the follow up examinations. The radiographic magnification of the joint recorded in the macro-radiograph, required for computing the size of x ray features within the joint, is established by placing either fine wire meshes or small metal spheres on the anterior and posterior surfaces of the joint before radiography.

The anatomical sites within the macro-radiograph used in defining the boundaries for the measurement of a feature are described precisely. Steroscopic examination of the macro-radiographs identified the following bony margins used for measuring the interbone distance in the standing view of the medial tibio-femoral compartment:

Femur: the distal convex margin of the condyle (fig 2).

Tibia, medial compartment: a line extending from near the tibial spine to the medial or outer margin, across the centre of the floor of the articular fossa in the mid-coronal plane of the joint. This line is defined by the superior margin of the bright radiodense band of the subchondral cortex, and appears below the anterior and posterior articular margins of the tibial plateau (fig 2). JSW is the space occupied by apposing articular cartilages separated by a thin synovial fluid layer. Joint space narrowing is the reduction in the interbone distance that follows the destructive loss of articular cartilage. Measurements, in fractions of a millimetre, are taken across the narrowest part of the joint, where the space was uneven, and across the joint midline, where it was even.³⁸ An equally careful approach has been adopted for each of the remaining features, of subchondral sclerosis, osteophytes and juxta-articular radiolucencies.³⁸

A detailed description of the method of measuring radiographic features and the accuracy in recording them is reported elsewhere.^{35 36 38 39} This showed that the precision repositioning and test-retest reliability for the same observer was found to give coefficients of variation for length measurement of 2.1%.³⁶ This represents a three fold increase in sensitivity for linear measurements compared with standard radiography.²³ Real changes in the dimension of x ray features, representing either disease progression or the response to therapy, are greater than that of the coefficient of variation for errors of measurement. Changes in the dimension of features that are twice the coefficient of variation represent a significant alteration.

Quantitative microfocal radiography

Measurement of the radiographic features of OA of the hand and their change over an 18 month study period³⁸⁻⁴² determined the distribution, extent and progression of the different x ray features across the hand joints, and that significant changes in the dimension of these features were detected within as short a period as 18 months. The results of this study showed that the radiographic features of OA were found not only at the classic site of hand involvement at the distal and proximal interphalangeal and first carpo-metacarpal joints,¹ but also at the metacarpo-phalangeal and wrist joints, showing that the disease is far more widespread than is generally accepted.⁴³⁻⁴⁴ Preliminary results of similar analyses of knee OA⁴⁵⁻⁴⁷ confirm, that in a larger joint, significant changes in radiographic features were measured within an 18 month period.

Joint space width

Joint space narrowing is considered the most important radiological feature of OA but its accuracy in measuring true cartilage loss has been questioned.¹⁶ To overcome this problem we carried out a study in 20 patients with OA of the knee in which measurements of interbone distance, representing radiological JSW, were compared with true cartilage thickness visualised using double contrast arthrography and found there was such a close agreement between the two measures that the observations⁴⁸ leave few grounds for concern regarding the reliability of this radiographic measurement.

In patients with early, but definite OA of the hand, JSW measurements showed that 56% of the patients had an increase in the interbone distance compared with the reference value obtained from healthy non-arthritic joints.³⁸ The increase in JSW, although not statistically significant within the global assessment of the

wrist and hand joints, showed a significant increase at the first carpo-metacarpal joint of the wrist and in the proximal interphalangeal joints of these patients.³⁹ This feature appears to represent an increase in cartilage thickness due to overhydration associated with early disease,⁴⁹⁻⁵⁰ a phenomenon previously reported in animals with experimentally induced OA.⁵¹ The joint space narrowing, observed in the remaining 44% of patients, represents either a loss in the substance of the cartilage, or in some, an apparent loss due to the advance of the subchondral mineralised cartilage zone into the cartilage³⁴ (fig 3).

Relationship between changes in joint space, subchondral sclerosis and osteophytes

The results of the studies of OA of the hand³⁸⁻³⁹ and knee⁴⁵⁻⁴⁶ showed that the extent of subchondral sclerosis and osteophytosis was significantly advanced in these joints in over half of the OA patients, all of whom possessed a joint space width within the range of the non-arthritic healthy reference group. Thus bony changes appear to advance ahead of articular cartilage changes measured as joint space narrowing. This has led to our working hypothesis,³⁸ together with that proposed by Mow *et al*,⁵¹ suggesting that the bony changes occur in association with the earliest changes in articular cartilage which are biochemical,⁵⁴⁻⁵⁵ leading to overhydration⁴⁹⁻⁵⁰ and cartilage softening and that this is followed by the histological appearance of cartilage fibrillation and fissuring.⁵⁶ Under these conditions of altered mechanical status of the cartilage, bone responds to the increase in applied load.⁵⁷ Subchondral bone increases in thickness, and osteophytes form as a result of either the changing biochemical and histological conditions of the joint⁵⁸ or an increase in joint instability.⁵⁹ The destructive loss of articular

Figure 3 Part of a macroradiograph of the metacarpo-phalangeal joints of a patient with hand OA, showing the mineralised cartilage zone extending into the existing articular cartilage space, contributing to joint space narrowing (original magnification $\times 5$, reproduced $\times 3.2$).

cartilage, measured as joint space narrowing, is a late stage phenomenon of osteoarthritis.

In the OA hand, the pattern of increased sclerosis and osteophytosis³⁹ at the joints of the wrist and hand was found to coincide with that attributed to the distribution of mechanical forces in this extremity.⁶⁰⁻⁶³ The presence of these bony features appears not to be due to abnormal forces in the joints⁶⁴ but to existing forces exerting a greater stress on the subjacent bone due to the altered properties of the cartilage.^{39, 42} This further confirms that subchondral cortical sclerosis and osteophyte formation are part of the bone's response to increased mechanical load^{59, 65, 66} associated with cartilage degeneration.

Evaluation of the pattern of joint space narrowing in the OA hand patients, during the study, showed no association between this feature and the pattern of normal force distribution in the hand, described in previous reports.⁶⁰⁻⁶³ Narrowing of the joint space was generalised, involving the joints of both the wrist and hand.³⁹ Measurements showed that there was symmetrical narrowing of joint space in both the right and left extremities and that there was sequential narrowing of JSW starting at the distal interphalangeal and extending proximally through the proximal interphalangeal, to the metacarpo-phalangeal and wrist joints.³⁹ These findings support the hypothesis that changes in the articular cartilage of patients with OA of the hand are determined by genetic or other constitutional^{43, 67, 68} rather than mechanical factors. Observations which, together with those described above for OA of the hand and knee, support the suggestion that cartilage is the primary site of the disease.

The results of these investigations show that by using accurate and precise radiographic procedures and methods of measurement, it is possible to detect early OA and to evaluate its severity and progression quantitatively. This has provided a better understanding of the natural history of OA of the hand and the correlation between its progression and the radiographic findings. It is anticipated that comparable results will be obtained with the completion of similar studies in OA of the knee and hip.

The greater sensitivity of this technique, compared with standard radiography, has improved the chances of measuring the effect of a 'disease modifying' agent, particularly in patients with radiologically mild OA, since this group is the more suitable for investigation,¹⁶ rather than those with more severe changes. Preliminary results of a study of 33 patients with early knee OA in a randomised, double blind, placebo-controlled trial of 100 mg diclofenac daily, lasting 18 months showed that quantitative microfocal radiography could detect statistically significant differences in the extent of joint space narrowing between the active and placebo treated groups over the study period.⁴⁷ Evaluation of this data (in preparation), has led to a number of observations: such studies should include the radiographic assessment of both knees and not

just the signal or most painful knee, but also the contra-lateral since nearly all of these joints were found to be painful with clear radiopathological evidence of early OA; patients with marked joint space loss (JSW < 1.5 mm) should be excluded from studies since the destructive changes in the joint precluded the detection of a therapeutic effect; and studies should be continued for at least two years or longer to determine whether any detected effect is sustained.

Increasing the accuracy and reproducibility in standard radiography

As described above, quantitative microfocal radiography can measure progression, in hand and knee OA, within a reasonably short period of time, providing information on the natural history of the disease and its outcome. This has been achieved, not only through the advantages of this x ray technique, but more particularly by controlling the accuracy and reproducibility of both the radiographic procedure and methods of measurement. For standard radiography different groups have applied such an approach separately to the radiographic procedures^{11-13, 24} and to measurement from radiographs.^{18, 25, 30} Where both these two procedures are not controlled there will be little or no progress in accurately quantifying changes from standard radiographs. Three factors, those relating to the equipment, the positioning of the patient and the method of measurement, need to be optimised and standardised for improving quantitative standard radiography.

Equipment: Accurate measurement within the plain film radiograph is dependent on good spatial resolution. This is determined by the smallness of the x ray source, the use of fine grain film or a high resolution film/screen combination, precise radiographic exposures, since the accuracy of measurement can suffer from any loss or change in the appearance of boundaries due to under or over exposure, and the alignment of the centre of the joint with the central ray of the x ray beam.

Patients: Standardisation of the radio-anatomical position of the joint is necessary so that the appearance of the joint is the same both within and between patients on successive x ray visits. This is helped by using a stereotaxic or custom built apparatus for stabilising the joint and image intensifier screening has been recommended for larger joints.^{25, 69} The degree of radiographic magnification, resulting from the object being placed at a distance from the film, must be determined to correct the dimensions of features measured from the radiograph.

Measurement: The boundaries or limits of the radiographic feature to be measured must be defined precisely. Computerised measurement systems which reduce inter-observer variation either through increased accuracy of measurement^{30, 34} or semi-automated procedures^{17, 24, 70} should be considered. These systems are linked to microcomputers for ease of handling and storing numerical data. They permit statistical

analysis and overall reduce the time taken for the mensural procedures.

Conclusion

To measure OA progression, it is necessary to establish a universally acceptable method for accurate and reproducible and quantitative assessment of changes in joint structure. This will require more stringent controls on the reproducibility of standard radiological procedures. Accurate measurement demands technical and mensural precision. The greater the precision required, the more time taken in acquiring data. The time can be reduced by the use of the new image analysis techniques. These methods eliminate inter-observer variation and would help standardise mensural procedures for multicentre trials. The therapeutic effects of 'chondroprotective drugs' on disease progression in OA have not been proven using conventional imaging techniques. These changes can be detected through the application of accurate and reproducible radiographs and mensural techniques illustrated by the results of studies using microfocal radiography.

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- Resnick D, Niwayama G. Degenerative diseases of extra-spinal locations. In: Resnick D, Niwayama G, eds. *Diagnosis of bone and joint disorders*, 2nd ed. Philadelphia: Saunders, 1988: 1365-479.
- Altman R, Asch E, Block D, et al. Development of criteria for the classification and reporting of osteoarthritis. *Arthritis Rheum* 1986; 29: 1039-49.
- Altman R, Fries J F, Bloch D A, et al. Radiographic assessment of progression in osteoarthritis. *Arthritis Rheum* 1987; 30: 1214-25.
- Kallman D A, Wigley F M, Scott W W, Hochberg M C, Tobin J D. New radiographic grading scales for osteoarthritis of the hand. *Arthritis Rheum* 1989; 32: 1584-91.
- Larsen A. Radiographic evaluation of osteoarthritis in therapeutic trials. In: Verbruggen G, Veys E M, eds. *Degenerative joints, test tubes, tissues, models, man*. Amsterdam: Excerpta Medica, 1982: 179-81.
- Pearson J R, Ridell D M. Idiopathic osteo-arthritis of the hip. *Ann Rheum Dis* 1962; 21: 31-9.
- Ahlback S. Osteoarthritis of the knee: a radiographic investigation. *Acta Radiol* 1968; (suppl): 1-277.
- Lequesne M. Clinical features, diagnostic criteria, functional assessments and radiological classifications of osteoarthritis (excluding the spine). *Baillieres Clin Rheumatol* 1982; 7: 1-10.
- Schouten J S A G, van den Ouweland F A, Valkenburg H A. A 12 year follow up study in the general population on prognostic factors of cartilage loss in osteoarthritis of the knee. *Ann Rheum Dis* 1992; 51: 932-7.
- Dieppe P, Cushnaghan J, McAlindon T. Epidemiology, clinical course and outcome of knee osteoarthritis. In: Kuettner K, Schleyerbach R, Peyron J G, Hascall V C, eds. *Articular cartilage and osteoarthritis*. New York: Raven Press, 1992: 617-27.
- Wevers H W, Siu D, Cooke T D V. A quantitative method of assessing malalignment and joint space loss of the human knee. *J Biomed Eng* 1982; 4: 319-24.
- Siu D, Cooke T D V, Broekhoven L D, et al. A standardized technique for lower limb radiography, practice, applications and error analysis. *Invest Radiol* 1991; 26: 71-7.
- Jonson H, Karholm J, Elmquist L-G. Kinematics of active knee extension after tear of the anterior cruciate ligament. *Am J Sports Med* 1989; 17: 796-802.
- Leach R E, Gregg T, Siber F J. Weight bearing radiography in osteoarthritis of the knee. *Radiology* 1970; 97: 265-8.
- Menkes C J. Radiographic criteria for classification of OA. *J Rheumatol* 1991; 18 (suppl 27): 13-5.
- Fife R S, Brant K D, Braunstein E M, et al. Relationship between arthroscopic evidence of cartilage damage and radiographic evidence of joint space narrowing in early osteoarthritis of the knee. *Arthritis Rheum* 1991; 34: 377-82.
- Brandt K D, Fife R S, Braunstein E M, Katz B. Radiographic grading of the severity of knee osteoarthritis: relation of the Kellgren and Lawrence grade to a grade based on joint space narrowing, and correlation with arthroscopic evidence of articular cartilage degeneration. *Arthritis Rheum* 1991; 34: 1381-6.
- Dacre J E, Huskisson E C. The automatic assessment of knee radiographs in osteoarthritis using digital image analysis. *Br J Rheumatol* 1989; 28: 506-10.
- Dougados M, Gueguen A, Nguyen M, et al. Longitudinal radiologic evaluation of osteoarthritis of the knee. *J Rheumatol* 1992; 19: 378-84.
- Messieh S S, Fowler P J, Munro T. Anteroposterior radiographs of the osteoarthritic knee. *J Bone Joint Surg* 1990; 72-B: 639-40.
- Resnick D, Vint V. The 'tunnel' view in assessment of cartilage loss in osteoarthritis of the knee. *Radiology* 1980; 137: 547-8.
- Altman R, Fries J F, Block D A, et al. Radiological assessment of progression in osteoarthritis. *Arthritis Rheum* 1987; 30: 1214-25.
- Adams M E, Wallace C J. Quantitative imaging of osteoarthritis. *Semin Arthritis Rheum* 1991; 20: 26-39.
- Jonsson K, Buckwalter K, Helvie M, Niklason L, Martel W. Precision of hyaline cartilage thickness measurements. *Acta Radiol* 1992; 33: 234-9.
- Dacre J E, Coppock J S, Herbert K E, Perrett D, Huskisson E C. Development of a new radiographic scoring system using digital image analysis. *Ann Rheum Dis* 1989; 48: 194-200.
- Jasani M K. Diclofenac and the osteoarthritis disease process in cartilage. In: Moskowitz R, Hirohata K, eds. *Diclofenac (Voltaren) and cartilage in osteoarthritis*. Toronto: Hogrefe and Huber, 1989: 46-52.
- Spector T D, Dacre J E, Harris P A, Huskisson E C. Radiological progression of osteoarthritis: an 11 year follow up study of the knee. *Ann Rheum Dis* 1992; 51: 1107-10.
- Browne M A, Gaydecki P A, Gough R F, Grennan D M, Khalil S I, Mamtara H. Radiographic image analysis in the study of bone morphology. *Clin Phys Physiol Meas* 1987; 8: 105-21.
- Gaydecki P A, Browne M, Mamtara H, Grennan D M. Measurement of radiographic changes occurring in rheumatoid arthritis by image analysis techniques. *Ann Rheum Dis* 1987; 46: 296-301.
- Dacre J E, Scott D L, Da Silva J A P, Welsh G, Huskisson E C. Joint space in radiologically normal knees. *Br J Rheumatol* 1991; 30: 426-8.
- Buckland-Wright J C. X-ray assessment of activity in rheumatoid disease. *Br J Rheumatol* 1983; 22: 3-10.
- Buckland-Wright J C. Microfocal radiographic examination of erosions in the wrist and hand of patients with rheumatoid arthritis. *Ann Rheum Dis* 1984; 43: 160-71.
- Buckland-Wright J C. A new high-definition microfocal x-ray unit. *Br J Radiol* 1989; 62: 201-8.
- Buckland-Wright J C, Bradshaw C R. Clinical applications of high definition microfocal radiography. *Br J Radiol* 1989; 62: 209-17.
- Buckland-Wright J C, Carmichael I, Walker S R. Quantitative microfocal radiography accurately detects joint changes in rheumatoid arthritis. *Ann Rheum Dis* 1986; 45: 463-7.
- Clarke G S. *Quantitative microfocal radiographic assessment of changes in the joint structure of the rheumatoid wrist and hand*. PhD Thesis, University of London, 1991.
- Foley-Nolan D, Stack J P, Ryan M, et al. Magnetic resonance imaging in the assessment of rheumatoid arthritis—a comparison with plain film radiographs. *Br J Rheumatol* 1991; 30: 101-6.
- Buckland-Wright J C, Macfarlane D G, Lynch J A, Clark B. Quantitative microfocal radiographic assessment of progression osteoarthritis of the hand. *Arthritis Rheum* 1990; 33: 57-65.
- Buckland-Wright J C, Macfarlane D G, Lynch J. Relationship between joint space width and subchondral sclerosis in the osteoarthritic hand: a quantitative microfocal radiographic study. *J Rheumatol* 1992; 19: 788-95.
- Buckland-Wright J C, Macfarlane D G, Fogelman I, Emery P, Lynch J A. Technetium 99mm methylene diphosphonate bone scanning in osteoarthritic hands. *Euro J Nuclear Med* 1991; 18: 12-16.
- Macfarlane D G, Buckland-Wright J C, Emery P, Fogelman I, Lynch J. Comparison of clinical, radionuclide, and radiographic features in osteoarthritis of the hands. *Ann Rheum Dis* 1991; 50: 623-6.
- Buckland-Wright J C, Macfarlane D G, Lynch J A. Osteophytes in the arthritic hand: their incidence, size, distribution and progression. *Ann Rheum Dis* 1991; 50: 627-30.
- Kellgren J H, Lawrence J S. Radiological assessment of osteoarthritis. *Ann Rheum Dis* 1957; 16: 494-501.
- Moll J M H. Investigation of osteoarthritis. *Clin Rheum Dis* 1977; 2: 587-613.
- Buckland-Wright J C, Macfarlane D G, Lynch J A, Jasani M K. Measurement of joint space loss in osteoarthritic knees using high definition macroradiography: comparison of standing and loaded views. *Trans Combined Orthop Res Soc USA, Japan, Canada, Banff*; 1991: 163.
- Buckland-Wright J C, Macfarlane D G, Jasani M K, Lynch J A. Quantitative microfocal radiographic assessment of osteoarthritis of the knee from weight-bearing tunnel and semi-flexed standing views. *J Rheumatol* 1994; 21 (in press).

- 47 Buckland-Wright J C, Macfarlane D G, Jasani M K, Lynch J A. Changes in OA knee joint space width loss in patients on diclofenac sodium vs placebo measured from high resolution macroradiographs. *Trans Orthop Res Soc* 1992; 17: 232.
- 48 Buckland-Wright J C, Macfarlane D G, Jasani M K, Lynch J A. Joint space width measures cartilage thickness in knee OA: plain film and double contrast macroradiographic investigation. *Trans Orth Res Soc* 1993; 18: 352.
- 49 Maroudas A. Balance between swelling pressure and collagen tension in normal and degenerative cartilage. *Nature* 1976; 260: 808-9.
- 50 Mankin H J, Thrasher A Z. Water content and binding in normal and osteoarthritic human cartilage. *J Bone Joint Surg* 1975; 57A: 76-80.
- 51 Mow V C, Setton L A, Ratcliff A, Howell D S, Buckwalter J A. Structure-function relationships of articular cartilage and the effects of joint instability and trauma on cartilage function. In: Brandt K D, ed. *Cartilage changes in osteoarthritis*. Indianapolis: Indiana University School of Medicine, 1990: 22-42.
- 52 Lane L B, Villacin A, Bullough P G. The vascularity and remodelling of subchondral bone and calcified cartilage in adult human femoral and humeral heads. *J Bone Joint Surg* 1977; 59B: 272-8.
- 53 Bullough P G, Goodfellow J W. Incongruent surfaces in the hip joint. *Nature* 1968; 217: 1290.
- 54 McDevitt C A, Gilbertson E, Muir H. An experimental model of osteoarthritis: early morphological and biochemical changes. *J Bone Joint Surg* 1977; 59B: 24-35.
- 55 Mankin H J, Brant K D. Biochemistry and metabolism of cartilage in osteoarthritis. In: Moskowitz R W, Howell D S, Goldberg V M, Mankin H J eds. *Osteoarthritis: diagnosis and management*. Philadelphia: W B Saunders, 1984: 43-80.
- 56 Fassbender H G. Significance of endogenous and exogenous mechanisms in the development of osteoarthritis. In: Helminen H J, Kiviranta I, Tammi M, Saamanen A-M, Paukkonen K, Jurvelin J, eds. *Joint loading: biology and health of articular structure*. Bristol: Wright, 1987: 352-74.
- 57 Lanyon C E. Functional strain as a determinant for bone remodelling. *Calc Tissue Int* 1984; 36: S56-61.
- 58 Williams J M, Brandt K D. Exercise increases osteophyte formation and diminishes fibrillation following chemically induced articular cartilage injury. *J Anat* 1984; 139: 599-611.
- 59 Gilbertson E M. Development of periarticular osteophytes in experimentally induced osteoarthritis of the dog. *Ann Rheum Dis* 1975; 34: 12-25.
- 60 Napier J R. The form and function of the carpo-metacarpal joint of the thumb. *J Anat* 1955; 89: 362-9.
- 61 Backhouse K M, Hutchings R T. *A colour atlas of surface anatomy, clinical and applied*. Netherlands: Wolfe Medical Publications, 1986: 144-69.
- 62 Tubiana R, Thomine J-M, Mackin E. *Examination of hand and upper limb*. Philadelphia: Saunders, 1984: 1-97.
- 63 Jones A R, Unsworth A, Haslock I. A microcomputer controlled hand assessment system used for clinical measurement. *Engineer Med* 1985; 14: 191-8.
- 64 Moskowitz R W. Experimental models of osteoarthritis. In: Moskowitz R W, Howell D S, Goldberg V M, eds. *Osteoarthritis, diagnosis and management*. Philadelphia: Saunders, 1984: 109-28.
- 65 Radin E L, Paul I L, Rose R M. Role of mechanical factors in pathogenesis of primary osteoarthritis. *Lancet* 1972; 1: 519-22.
- 66 Buckland-Wright J C. The early lesion in subchondral bone in osteoarthritis: a microfocal radiographic study. In: Thould A K, Dixon A S T J, Dieppe P F, eds. *The role of the osteophyte and subchondral bone*. Pendragon Papers No 2. Nottingham: Boots Publications, 1986: 75-8.
- 67 Sokoloff L. Loading and motion in relation to ageing and degeneration of joints: implications for prevention and treatment of osteoarthritis. In: Helminen H J, Kiviranta I, Saamanen A-M, Tammi M, Paukkonen K, Jurvelin J, eds. *Joint loading. Biology and health of articular structures*. Bristol: Wright, 1987: 412-24.
- 68 Stecher R M. Heberden's nodes. A clinical description of osteoarthritis of the finger joints. *Ann Rheum Dis* 1955; 14: 1-10.
- 69 Buckland-Wright J C. Imaging and measurement of change in osteoarthritis. In: Barrowclough D, ed. *Proc Second Geigy Rheumatol Symp, Gold Coast, October 1989*. Sydney: Adis Int Pty, 1991: 29-38.
- 70 Lynch J A, Buckland-Wright J C, Hawkes D J. Automated measurement of interbone distance on macroradiographs of osteoarthritic knees using the symmetric axis transformation. *Br J Radiol* 1992; 65: 23-4.