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A second study of tensile fatigue properties of human articular cartilage

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SUMMARY The tensile fatigue properties of the collagen fibre meshwork in normal human articular cartilage were measured by subjecting isolated specimens of post-mortem femoral head cartilage to cyclic tensile stress. The results of the study showed (1) that the collagen fibre meshwork is fatigue prone and (2) that its fatigue strength decreases rapidly with age. Extrapolation of the data to physiologically possible stress levels suggests that tensile fatigue failure of the collagen meshwork could occur in life.

In unloaded articular cartilage the swelling tendency of the proteoglycan gel is limited by, and hence induces tensile stresses in, the collagen fibre network. When load is transmitted across a synovial joint the load-bearing regions of the two opposing cartilages are compressed in a direction normal to their surfaces and as a result expand laterally. These deformations are a reflection of the tendency for the proteoglycan gel to be displaced laterally, and it seems clear that it is only the collagen fibre network which prevents the gel from being completely 'squashed off' the bone surfaces. In fulfilling this function the collagen network must experience increased tensile stresses.

In vivo, the position of the load-bearing region within the joint and the magnitude of the transmitted load both vary throughout the range of motion of the joint. It follows that the collagen fibres in articular cartilage experience fluctuating tensile stress. Since the metabolic turnover rate of collagen in adult human cartilage is low (Muir, 1973) the material will experience a large number of stress reversals *in vivo* before being replaced. The possibility therefore exists that articular cartilage may breakdown as a result of tensile fatigue failure in the collagen fibre meshwork. Fatigue failure in the collagen fibre meshwork may even be the primary event in some forms of idiopathic osteoarthrosis (Freeman, 1972; Freeman and Meachim, 1973).

In an effort to study the tensile fatigue characteristics of the collagen fibre meshwork, one of us (Weightman, 1976) conducted tensile fatigue tests on isolated specimens of human articular cartilage. Three dumbbell-shaped specimens, approximately 200 μm thick and aligned parallel to the predominant collagen fibre orientation, were cut from the superior surface of each of more than 30 post-mortem femoral heads. Each specimen was then loaded in tension, in a specially designed piece of apparatus, for 1 second every 20 seconds (essentially a square wave load cycle with a rise time of approximately 0·1 seconds) until it fractured. Different specimens were subjected to different loads and the results were plotted on a fatigue graph of stress magnitude versus number of load cycles to fracture.

Since all the specimens had been cut from normal cartilage the original intention was to 'pool' all the data to obtain the tensile fatigue curve for normal articular cartilage. However, the finding of a wide variation in the fatigue strength of cartilage from different femoral heads made this impossible, and the data from each femoral head had to be analysed separately. This was achieved by assuming (1) that each S *vs* $\log_{10}$ N fatigue curve was a straight line, and (2) that all the fatigue curves had the same slope, the value of which ($-1{\cdot}83$) was given by the mean of the slopes of the individual curves. These assumptions produced a series of parallel fatigue curves such that the intercept with the stress axis (the projected fracture stress) could be taken as a quantitative measure of fatigue strength.

The results of the analysis showed that there was a significant negative correlation ($r=-0{\cdot}54$, $P<0{\cdot}01$) between projected fracture stress/fatigue strength and the age of the cadaver from which the cartilage was obtained. Extrapolation of the experimental

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data to possible physiological stress levels suggested that the fatigue strength of human articular cartilage decreases with age to such an extent that fatigue failure might occur in life. Unfortunately, since the individual fatigue curves in this study were obtained from a maximum of three specimens and the analysis involved two major assumptions, this potentially important finding required substantiation. Thus a second series of tensile fatigue tests, designed to obtain more accurate information about the fatigue strength of cartilage and its relationship to age, was carried out and is now described.

Materials and methods

Tensile fatigue specimens were cut from the superior surface of 20 post-mortem femoral heads in the age range 9 to 82 years. Before specimen preparation the femoral heads were stored at −20°C, a treatment which has been shown not to change the mechanical properties of articular cartilage (Kempson *et al.*, 1971). None of the hips tested showed more than very light staining on the superior surface when washed with Indian ink.

The method of specimen preparation was exactly the same as in the first series of tests (Weightman, 1976) except that up to 10 specimens were cut from each femoral head. This increased number of specimens was achieved by (1) reducing the width of both ends of the specimens while leaving the dimensions of the central section unchanged, (2) reducing the amount of wasted cartilage between each specimen, and (3) extending the area from which the specimens were obtained both anteriorly and posteriorly. The tensile fatigue apparatus (Fig. 1) and the test conditions were the same as those used in the previous study.

Results

Fig. 2 shows the 20 individual cartilage fatigue curves obtained during the present study. Each datum point represents one cartilage specimen and the solid curves are the best fit straight lines (least mean squares, $S = A - B \log_{10} N$). The age and sex of the cadavers from which the cartilage was obtained are indicated. A number of specimens from each femoral head either fractured on the first application of load or had not fractured after 10^5 cycles, and these undefined data points are not shown. The first observation to make is that the data clearly indicate a linear relationship between stress and number of cycles to fracture expressed on a logarithmic scale (see in particular curves *a*, *d*, *i*, *m*, *n*, and *o*). Thus one of the assumptions made in the previous study appears to have been valid.

Although there is some variation in the slopes of the individual best fit straight lines, the data in fact support the hypothesis that fatigue curves for cartilage from different femoral heads have the same slope. That is, the mean slope of all 20 best fit straight lines is −1·65 (SE 0·16) and this value falls within the 95% confidence limits on each of the individual slopes. Thus straight lines of slope −1·65

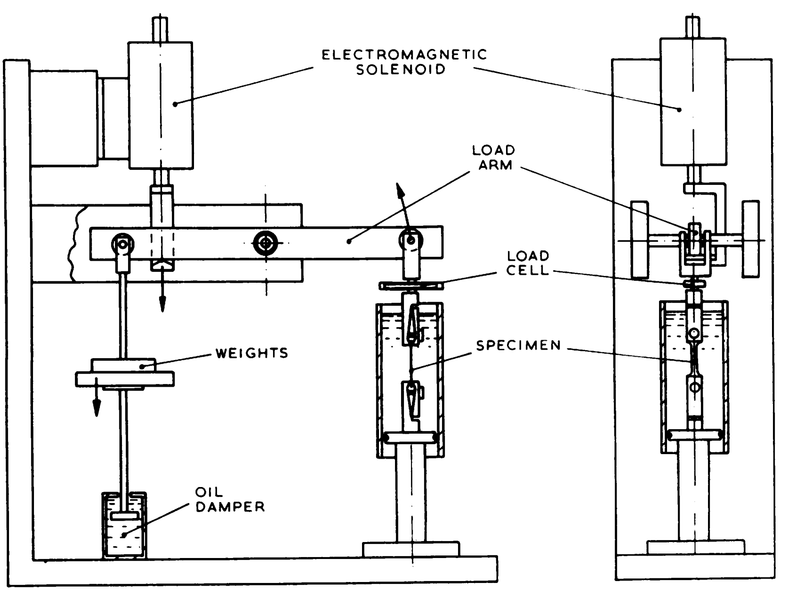
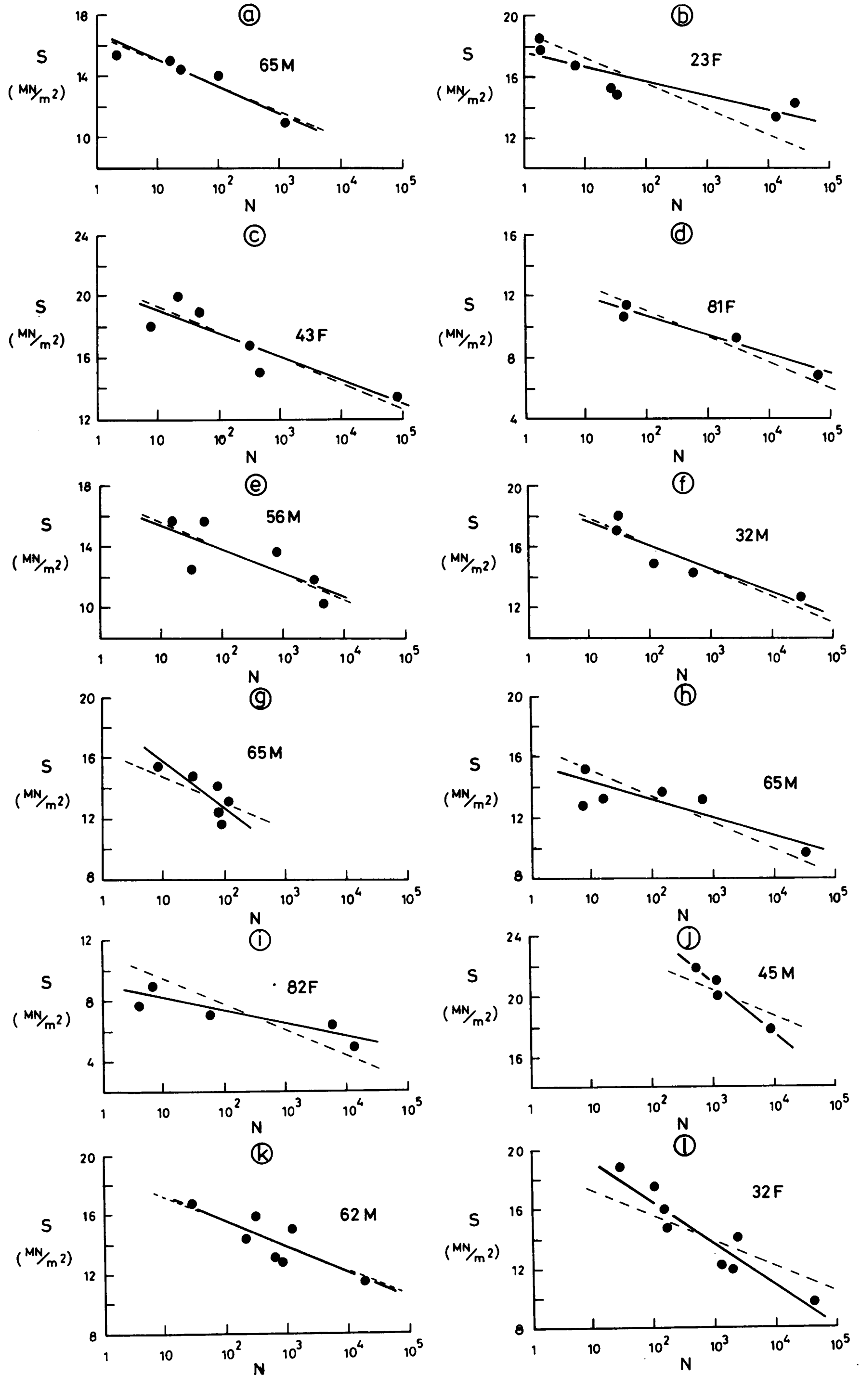


Fig. 1 *Schematic diagram of tensile fatigue apparatus. The specimen is held in perspex clamps in a bath of Ringer's solution plus antibiotics, buffered to pH 7·0–7·5. The whole apparatus was run in a refrigerator at +4°C.*



a
65 M
b
23 F
c
43 F
d
81 F
e
56 M
f
32 M
g
65 M
h
65 M
i
82 F
j
45 M
k
62 M
l
32 F
S
(MN/m2)
N

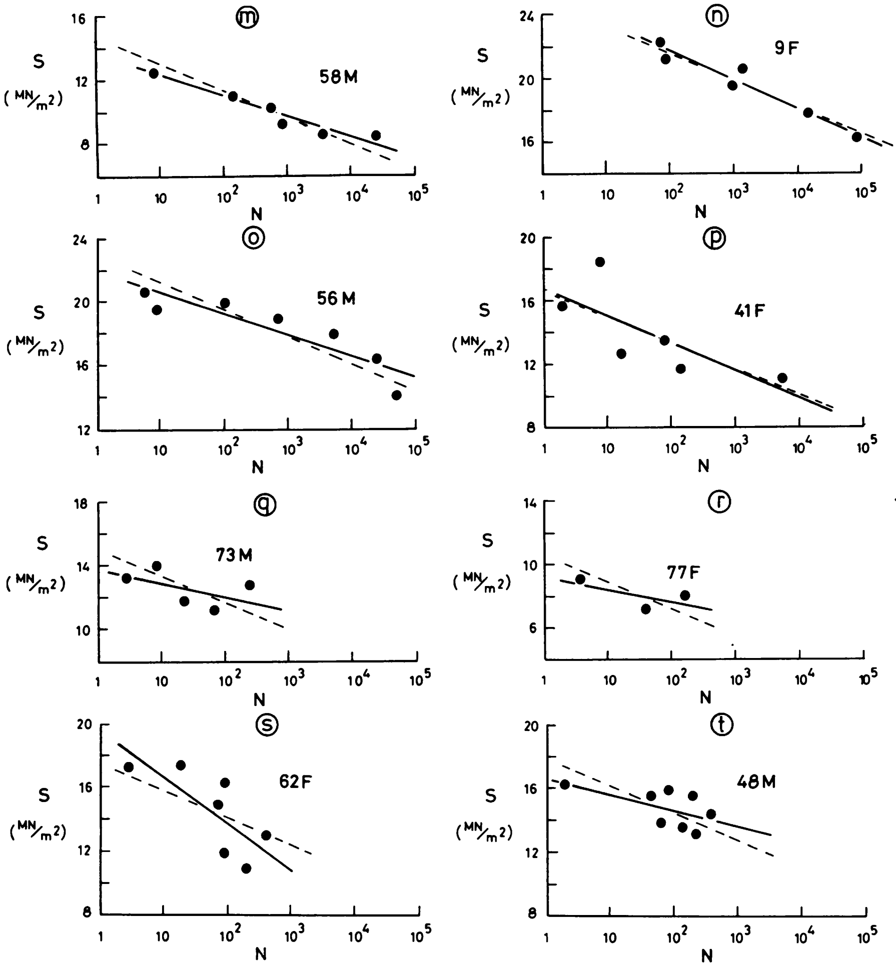


Fig. 2 *Individual fatigue curves for cartilage from different femoral heads. S=stress magnitude; N=no. of load cycles to fracture; M=male; F=female.*

(the broken lines in Fig. 2) fit the data from each femoral head well, and the intercepts of these lines with the stress axis (the projected fracture stress, i.e. the stress to produce fracture on a single application) can be used as a quantitative measure of fatigue strength.

Fig. 3 is a graph of fatigue strength obtained in this way versus the age of the cadaver from which the cartilage was obtained. The correlation between fatigue strength and age (correlation coefficient $-0{\cdot}73$) is highly significant ($P>0{\cdot}001$). The equation of the best fit straight line (least mean squares) is

$$FS=25{\cdot}4-0{\cdot}15a, \quad (1)$$

where *FS* is fracture stress/fatigue strength in MN/m^2, and *a* is age in years. The standard error of the slope ($-0{\cdot}15$) is 0·03.

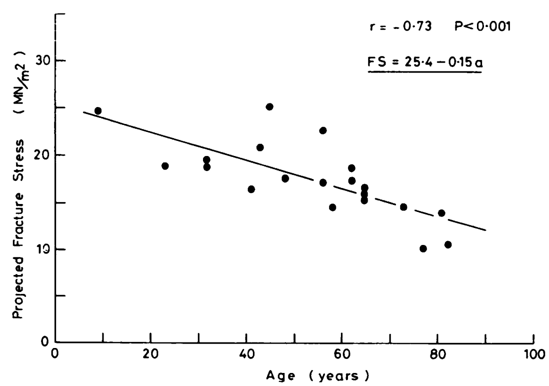


Fig. 3 *Relationship between projected fracture stress/ fatigue strength (FS) and age.*

Discussion

These data suggest that the fatigue behaviour of the superficial layer of femoral head cartilage, when loaded parallel to the predominant collagen fibre orientation, can be represented by the equation

$$S = 25{\cdot}4 - 0{\cdot}15a - 1{\cdot}65 \log_{10}N \qquad (2)$$

where S is the tensile stress in the cartilage in MN/m^2, a is age in years, and N is the number of cycles to fracture.

On a graph of stress versus logarithm to the base ten of the number of cycles to fracture this is the equation of a straight line, of slope $-1{\cdot}65$, which moves vertically down the graph with increasing age. For comparison the previous study (Weightman, 1976) yielded the equation

$$S = 23{\cdot}0 - 0{\cdot}10a - 1{\cdot}83 \log_{10}N.$$

Thus the present, more accurate, study indicates that the fatigue strength of young cartilage is greater than was originally thought (the tensile fracture strength at zero age is greater, 25·4 MN/m^2 compared with 23·0, and the slope of fatigue curves is less, $-1{\cdot}65$ compared with $-1{\cdot}83$), but that fatigue strength decreases more rapidly with age ($-0{\cdot}15a$ compared with $-0{\cdot}10a$). Combining these two factors indicates that the fatigue strength of older cartilage is less than was previously thought.

The fact that increasing osteoarthrotic fibrillation and decreasing fatigue resistance both occur with advancing age suggests the possibility of a causal connection between these phenomena. However, it may be that the stresses experienced *in vivo* could not produce fatigue failure in even old cartilage within a sensible period of time, and this possibility requires investigation.

Before attempting such an assessment of the physiological relevance of the experimental data a distinction must be made between the tensile fatigue properties of cartilage and the tensile fatigue properties of the collagen fibre meshwork. The laboratory experiments were designed to study the tensile fatigue characteristics of the collagen fibre meshwork (by producing tensile stresses in the network by the direct application of a tensile load, instead of by way of the application of a compressive load as *in vivo*), but the stress values plotted in Figs. 2 and 3 are the tensile stresses produced in the specimens of cartilage and not the tensile stresses produced in the collagen fibres. That is, the stress values were calculated by dividing the applied load by the cross-sectional area of the cartilage specimen and not by the total cross-sectional area of the collagen fibres. Thus equation (2) describes the tensile fatigue characteristics of cartilage, not the tensile fatigue characteristics of collagen. However, assuming that the tensile load applied to specimens of cartilage is carried entirely by the collagen fibres, the tensile stresses produced in the fibres must be greater than the quoted values by a factor (say t) equal to the ratio of cartilage cross-sectional area to total cross-sectional area of the collagen. It follows that a description of the tensile fatigue characteristics of collagen can be obtained by multiplying each term on the right hand side of the equation (2) by t, to give

$$S_{coll} = 25{\cdot}4t - 0{\cdot}15at - 1{\cdot}65\, t \log_{10}N \qquad (3)$$

where S_{coll} is the tensile stress in the collagen fibres in MN/m^2.

In order to relate this behaviour to physiological conditions it is necessary to know the magnitude of the tensile stresses produced in collagen fibres *in vivo*. This information does not exist at present and only a rough approximation can be made. Clearly the tensile stresses produced in the collagen fibres of young cartilage by normal activity are less than the tensile fracture stress of collagen. Since equation (3) shows a maximum tensile strength of $25{\cdot}4t$ MN/m^2 (at age zero) the tensile stresses experienced by collagen fibres *in vivo* must therefore be less than $25{\cdot}4t$ MN/m^2. Since cartilage can normally withstand the stresses induced by occasional activity considerably more severe than walking, it follows that the stresses induced by walking are likely to be a factor of *at least* 2 or 3 less than the tensile fracture stress. Thus an absolute upper limit of, say, $8t$ MN/m^2 can be put on the tensile stress experienced by collagen fibres *in vivo* during normal activity.

The collagen in articular cartilage will protect itself from fatigue if it is replaced before it experiences the number of load cycles required to produce fracture. After reviewing the data on collagen synthesis, Muir (1973) concluded that 'the collagenous framework of cartilage is mainly laid down prior to maturity'. Thus a conservative approach would be to consider a fatigue process taking longer than 5 years to be physiologically irrelevant. It has been estimated that the average man takes approximately 2×10^6 walking steps per year and hence each femoral head will experience approximately half this number of steps. Since the variation of the hip joint force with time during the load carrying phase of a walking cycle shows two distinct peaks (Paul, 1976), there are effectively two loading cycles in every walking step. Thus an order of magnitude approximation suggests that if the number of cycles to fatigue failure is greater than 10×10^6, fatigue is unlikely to be a factor in human osteoarthrosis.

Fig. 4 shows the age at which a given tensile stress in the collagen fibres is predicted to produce fatigue failure within 5 years. The graph was obtained from

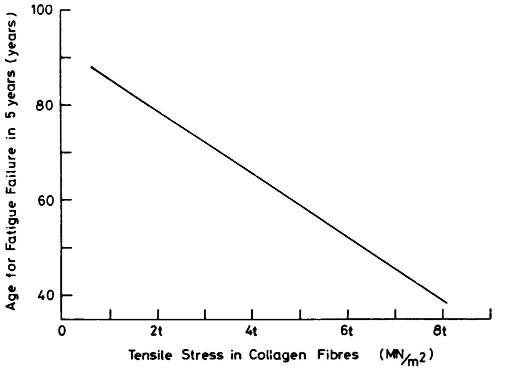


Fig. 4 *Relationship between stress in collagen fibres and age at which fatigue fracture is predicted to occur after 5 years.*

equation (3) by setting N equal to 10×10^6 and calculating the value of a for different values of S_{coll} in the range 0 to $8t$ MN/m^2. Bearing in mind the approximations which were made in obtaining this relationship, it is perhaps surprising that the age scale of Fig. 4 is at all relevant to the human lifespan. Even if the analysis indicated that the maximum conceivable tensile stress in the collagen fibres would not produce fatigue failure in cartilage less than 200 years of age, its accuracy is such that the possibility of fatigue occurring in life could not be ruled out. In fact the results suggest that a stress of $8t$ MN/m^2 will produce fatigue fracture in 39-year-old cartilage after 5 years, and that the stress would have to be lower than, say, $2t$ MN/m^2 (i.e. a factor of more than 10 less than the maximum tensile stress) for fatigue to be physiologically irrelevant. It follows that the tensile fatigue properties of the collagen fibre meshwork in adult human articular cartilage are such that fatigue failure in life is a possibility.

If the tensile fatigue of collagen is an important factor in osteoarthrosis it should be possible to explain the limited incidence of the disease in terms of fatigue. In a study of the contact pressures in loaded human hips, Day *et al.* (1975) found that in two-thirds of the hips tested the maximum contact pressure was up to 1·5 times greater than the average contact pressure in the hip. In contrast, in one hip in three the peak pressure was approximately 3 times greater than the average pressure. Although it is not possible to calculate the tensile stresses produced in collagen fibres by a given contact pressure higher contact pressures must produce higher stresses in the collagen fibres and it therefore seems reasonable to speculate that in a certain proportion of human hip joints the stresses in the collagen fibres are twice those in 'normal' hips. As Fig. 4 shows, a doubling of the tensile stress in the collagen fibres could have a significant effect on the likelihood of fatigue failure occurring in life.

Equation (3) and the relationship shown in Fig. 4 are based on results from 20 femoral heads and therefore describe the 'average' properties of the collagen fibre meshwork. As Fig. 3 shows, there is considerable variation in the fatigue strength of cartilage from different femoral heads of the same age. It is therefore possible that fatigue failure could occur in life in those hips (and perhaps other load-bearing joints) which have abnormally high contact pressures and collagen of below average fatigue strength, but not in those hips which have normal contact pressures and collagen of average or above average fatigue strength. It is worth noting that the abnormally high contact pressures referred to above are found at the zenith of the femoral head, the site at which progressive osteoarthrotic changes occur (Byers *et al.*, 1970).

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