ELSEVIER

Journal of Biomechanics 34 (2001) 1031–1037

JOURNAL
OF
BIOMECHANICS

www.elsevier.com/locate/jbiomech
www.JBiomech.com

Constituents and pH changes in protein rich hyaluronan solution affect the biotribological properties of artificial articular joints

Toshio Kitano[a,b,]*, Gerard A Ateshian[a], Van C Mow[a], Yoshinori Kadoya[b], Yoshiki Yamano[b]

[a] *Orthopaedic Research Laboratory, Columbia University, New York, NY, USA*
[b] *Department of Orthopaedic Surgery, Osaka City University, Graduate School of Medicine, Osaka, Japan*

Accepted 18 March 2001

Abstract

The relationship between the coefficient of friction and pH value or protein constituents of lubricating fluid, together with viscosity, were studied within a bearing surface model for artificial joint, ultra-high molecular weight polyethylene (UHMWPE) against stainless steel (SUS), using a mechanical spectrometer. Four lubricants were tested in this study: sodium hyaluronate (HA), HA with γ-globulin, and HA with Lα-dipalmitoyl phosphatidylcholine (Lα-DPPC). The coefficient of friction between UHMWPE and SUS in HA with albumin or HA with γ-globulin varied from 0.035 to 0.070 depending on angular velocity and pH. The coefficient of friction in HA or HA with Lα-DPPC varied from 0.023 to 0.045 depending on angular velocity and pH. The variation in pH for HA with albumin had a large effect on the coefficient of friction at low range of angular velocity with viscosity independence. The variation in pH for HA with γ-globulin had a large effect on the coefficient of friction with viscosity dependence at high angular velocity. The addition of Lα-DPPC showed a small effect on the coefficient of friction at low angular velocity. This study confirms that the presence of albumin in the lubricant promotes pH dependence and viscosity independence of the tribological properties at low speed while the presence of globulin promotes pH and viscosity independence at low speed and promotes pH and viscosity dependence at high speed in the lubrication of UHMWPE against SUS. This study supports the clinical hypothesis that the effect of constituents and pH changes in periprosthetic fluid for the lubrication is a clue toward resolving many complications after total joint replacement. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Artificial joint; Hyaluronic acid; Glycoprotein; Joint lubrication; Ultra-high molecular weight polyethylene

1. Introduction

Osteolysis due to wear debris represents one of the most difficult complications following total joint arthroplasty (Kadoya et al., 1998; Goodman et al., 1990; Howie et al., 1993; Shanbhag et al., 1994). Tribological properties between the surfaces of artificial joints play a role in producing wear particles. Periprosthetic fluid (Mangione et al., 1990) produced after total joint arthroplasty interposes between artificial joint surfaces and acts as a lubricant.

Periprosthetic fluid with biomaterial induced inflammation has been shown to differ from normal synovial fluid in terms of its protein constituents, hyaluronic acid concentration, and pH values. The pH values of periprosthetic fluid, produced after total joint arthroplasties, were reported between 7.5 and 8.5 (Kitano et al., 1998; Mangione et al., 1990), while the pH values of normal synovial fluid are between 7.3 and 7.43 (Cummings and Nordby, 1966; Goldie and Nachemson, 1969; Kofoed, 1986; McCarty, 1989; Ropes et al., 1940). The pH of synovial fluid with OA and RA ranges from 7.4 to 8.1 (Kitano et al., 1998) and from 6.6 to 7.6 (Cummings and Nordby, 1966; Falchuk et al., 1970; Goldie and Nachemson, 1969) respectively. The pH ranges from 6.5 to 8.6 are thought to simulate the pH range of periprosthetic fluid. The protein constituents of periprosthetic fluid were reported in a few papers. The concentration of albumin and γ-globulin in periprosthetic fluid ranges from 20 to 39 and from 4.6 to 15.4 mg/ml respectively (Delecrin et al., 1994; Walker, 1973), while the concentrations of albumin and γ-globulin in normal synovial fluid range from 7 to 18 and from 0.5 to 2.9 mg/ml (McCarty, 1989). Delecrin

---

*Corresponding author. Tel.: +81-6-6645-3851; fax: +81-6-6646-6260.

E-mail address: tkitano@med.osaka-cu.ac.jp (T. Kitano).

0021-9290/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0021-9290(01)00058-6

et al. (1994) studied quantitative and time dependent changes of periprosthetic fluid from rabbit knee joints and found that total protein concentration had increased during the acute phase and decreased to near the control level in the chronic phase, while the concentration of γ-globulin maintained an increased level in the chronic phase. They also found that the concentrations of sodium hyaluronate (HA) in chronic inflammation conditions increased to concentrations similar to normal levels. The concentration 3 mg/ml for HA, 12 mg/ml for albumin, and 8 mg/ml for γ-globulin are thought to simulate periprosthetic fluid in chronic inflammatory conditions for the reason described above.

Despite some studies about periprosthetic fluid were reported, information about the relationship between the coefficient of friction and pH value or protein constituents of periprosthetic lubricating fluid, in relation to viscosity, may not be sufficient to elucidate the mechanism of lubrication in artificial joints under inflammatory conditions. Hydrodynamic lubrication, boundary lubrication, or the combination thereof (mixed lubrication) have been suggested as mechanisms for reducing friction between the surfaces of artificial joints (Jin et al., 1998; Unsworth, 1978; Weightman et al., 1972). Viscosity of the lubricant plays an important role under the conditions of hydrodynamic lubrication (O'Kelly et al. 1979; Unsworth, 1978), while the dose and substance of adsorbed boundary lubricant may govern boundary lubrication conditions. Glycoproteins and phosphatidyl choline are thought to be candidate boundary lubricants for cartilage (Hills, 1989; Williams et al., 1995). A recent frictional study between artificial cartilage and stainless steel reported that the addition of γ-globulin or Lα-dipalmitoyl phosphatidylcholine (Lα-DPPC) to HA solutions reduced the coefficient of friction under boundary lubrication conditions (Murakami et al., 1998). It has been hypothesized that the most important factor that influences lubrication between artificial joint surfaces, when boundary lubrication is dominant, is not the viscoelasticity of the fluid, but the protein constituents of and pH changes in protein-rich periprosthetic fluid. The purpose of this study is to test this hypothesis, assessing the coefficient of friction of ultra-high molecular weight polyethylene (UHMWPE) against stainless steel (SUS) using a mechanical spectrometer with changes in pH and constituents of synthetic protein-rich periprosthetic fluids, and also clarifying the situation under which boundary lubrication may dominant.

2. Materials and methods

2.1. Lubricant (synthetic protein-rich periprosthetic fluid)

Four lubricants were tested in this study:

- Lubricant 1 (L01); 0.033 M Tris hydroxymethyl aminomethane (Tris buffer) + HA 3 mg/ml.
- Lubricant 2 (L02); L01 + bovine albumin 12 mg/ml.
- Lubricant 3 (L03); L01 + bovine γ-globulin 8 mg/ml.
- Lubricant 4 (L04); L01 + Lα-DPPC 3 mg/ml.

HA, bovine albumin, bovine γ-globulin, and Lα-DPPC were commercially obtained: HA; Sigma H-5388, from rooster comb, MW = approximately 2×10^6. Bovine albumin; Sigma A-0281, fatty acid and globulin free, MW = 6.6×10^4, Bovine γ-globulin; Sigma G-5009, from Cohn fraction II & III, MW = 1.5×10^5, Lα-DPPC; Sigma P-0763, synthetic, MW = 7.3×10^2.

Lα-DPPC was suspended in 0.033 M Tris buffer to give a concentration of 3 mg/ml and ultrasonicated for 15 min and then HA was dissolved in this Lα-DPPC dispersed medium. To prevent destroying HA molecules and decreasing the viscosity of HA, Lα-DPPC was dispersed in a manner different from the method described by Hills (1989).

2.2. Mechanical spectrometer

The coefficient of friction of UHMWPE against SUS was measured with a mechanical spectrometer (Rheometrics Model RMS-800, Rheometrics Inc., Piscataway, NJ) using plate on plate geometry. The cylindrical UHMWPE plug (2.5 mm in radius and 2.0 mm thick) was glued onto a compliant polyurethane foam pad (7 mm in diameter and 2 mm thick, 'foam rubber') on the bottom plate to facilitate application of a prescribed constant compressive load under displacement control. The sample and plates were submerged in a chamber containing synthetic lubricating fluid (Fig. 1). The cylindrical UHMWPE plug was obtained from Kyocera Co., Ltd. (Kyoto Japan). No wear was observed during the experiments. This geometry was maintained throughout the series of experiments, with only the polyurethane foam pad changed when a different lubricant was tested.

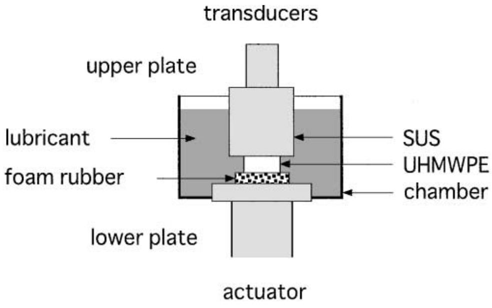

Fig. 1. A measurement apparatus for coefficient of friction. The sample and plates were submerged in a chamber containing synthetic lubricating fluid.

2.3. Measuring conditions

All measurements were performed at 25°C. A compressive strain was first applied on the sample for about an hour until the normal stress reached equilibrium at 30 ± 0.6 g (15.0 ± 0.3 kPa). A shear rate sweep was then applied to the bottom plate, with an initial value of $\dot{\gamma} = 0.003$ 1/s ($\omega = 0.024$ rad/s) and a final value of $\dot{\gamma} = 11.9$ 1/s ($\omega = 9.55$ rad/s), using logarithmic increments of 5 pts/decade. To minimize the influence of the polyurethane foam pad, equilibration time and measurement time was set up to 30 and 50 s, respectively. The normal force (N) and frictional shear torque (T), measured from a biaxial load cell, were collected with a microcomputer after the response equilibrated.

Under the measuring condition we used, low range of angular velocity (from 0.024 to 0.955 rad/s) corresponds to the sliding speed representative of standing situation, middle range of angular velocity (from 1.51 to 3.81 rad/s) to slow walk or slow rise up situation, and high range of angular velocity (from 6.03 to 9.55 rad/s) to fast walk situation.

2.4. Preparation for testing

Each lubricant was tested with eight different pH values varying from 6.5 to 8.6. The pH value of the lubricant was adjusted in a beaker on a magnetic agitator using 1.0–0.1 M HCl while monitoring the solution with a pH meter (at 25°C). The pH value was checked before and after testing and the average of these two pH values was calculated to minimize the influence of oxygenation.

2.5. Measurement of normal force and frictional shear torque

A measurement was performed for the first L01 sample at one of the prepared pH values. After the lubricant was taken out of the chamber, the surfaces of both UHMWPE and SUS were cleaned with water and wiping paper. The next measurement for a second L01 sample of the same pH value was performed. After six consecutive samples with the same pH value were tested, the next series of measurements were performed for the next prepared pH value. When a type of lubricant was changed after measurements at all pH values, the surfaces were cleaned with acetone and wiping paper. For each of the four lubricants, six samples were tested at each of eight pH values, in the same manner as described above.

2.6. Calculation of the coefficient of friction

The following protocol follows the study of Wang and Ateshian (1997). The coefficient of friction (μ) was calculated using the equation:

$$\mu = F/N, \tag{1}$$

where N is the measured normal contact force between UHMWPE and SUS plates. An average frictional force (F) was calculated using the following equation by assuming that the frictional shear stress at the sliding surface increases linearly along the radial direction of the cylindrical plug:

$$F = 4T/3r. \tag{2}$$

T is the measured frictional shear torque and r is the radius of the cylindrical UHMWPE plug. The coefficient μ was subsequently obtained from Eq. (1). Note that the average sliding speed for this testing configuration is given by $V = 3\omega r/4$ from power considerations ($FV = T\omega$). The mean values from six coefficients of friction for each kind of lubricant at each pH value were calculated and plotted against angular velocity.

2.7. Measurement of lubricant viscosity

The viscosity of each lubricant was also measured as a function of shear rate, for all pH values, on the same apparatus, using a parallel plate configuration. These measurements were obtained to compare the difference between the coefficient of friction and the viscosity of the lubricant at different pH values.

2.8. Statistical analysis

Statistical analysis was performed with one way ANOVA to evaluate the effect of pH value on coefficient of friction at each angular velocity. Coefficient of determination (r^2) for standard linear regression analysis was used to determine whether a correlation exists between coefficient of friction and lubricant viscosity at the corresponding angular velocities to five selected shear rates, for all four lubricants. Statistical analysis was also performed with one way ANOVA to evaluate the effect of pH value on lubricant viscosity at each shear rate. Mann–Whitney test was used to evaluate the effect of constituents of lubricant.

3. Results

The friction coefficient versus angular velocity curves for L01, L02, L03, and L04 are presented in Figs. 2, 3, 4, and 5, respectively. The coefficient of friction ranged from 0.024 ± 0.003 (mean ± SD) to 0.040 ± 0.002 in L01, from 0.035 ± 0.002 to 0.070 ± 0.008 in L02, from 0.039 ± 0.001 to 0.059 ± 0.002 in L03, and from 0.023 ± 0.001 to 0.045 ± 0.003 in L04.

The dependence of the coefficient of friction on angular velocity for L01 followed the same trend at all

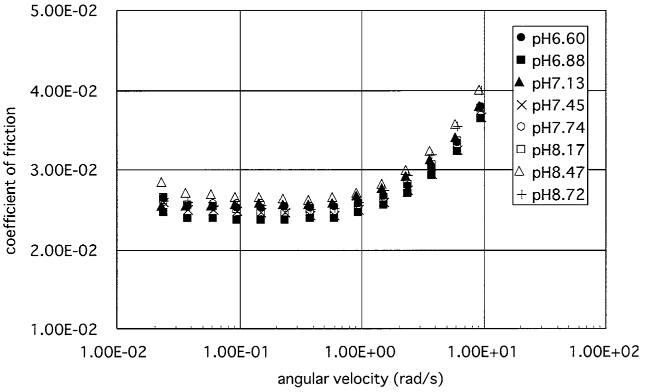

Fig. 2. The coefficient of friction versus angular velocity curves for L01. The dependence of the coefficient of friction on angular velocity for L01 followed the same trend at all pH values over the entire range of angular velocities, showing an increase at higher velocities.

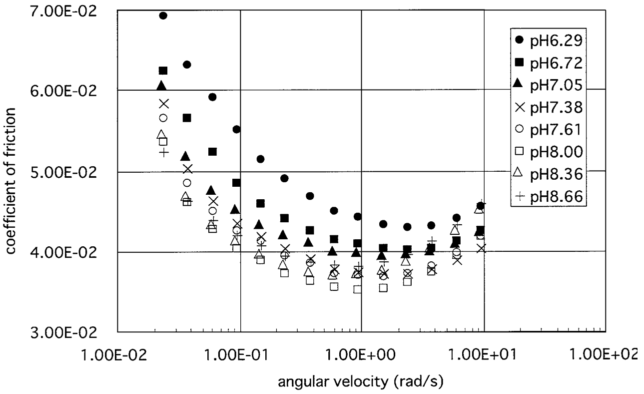

Fig. 3. The coefficient of friction versus angular velocity curves for L02. The variation in pH for L02 had a large effect on the coefficient of friction in the low ranges of angular velocity (ANOVA, $p<0.001$, $\omega<1.51$ rad/s).

pH values over the entire range of angular velocities, showing an increase at higher angular velocities. The addition of albumin (L02) or γ-globulin (L03) showed a large effect on the coefficient of friction over the entire range of angular velocity compared with HA solution (L01) (Mann–Whitney test, $p<0.0001$), i.e., the addition of albumin or γ-globulin increased the coefficient of friction over the entire range of angular velocity, showing some differences according to angular velocity. On the other hand, the addition of Lα-DPPC (L04) showed a small effect at low angular velocity compared with L01 (Mann-Whitney test, $p>0.43$, $\omega<0.24$ rad/s)

The variation in pH for L01 had an effect on the coefficient of friction in the high range of angular velocity (ANOVA, $P<0.001$, $\omega>6.03$ rad/s) (Fig. 2). The variation in pH for L02 had a large effect on the coefficient of friction in the low ranges of angular velocity (ANOVA, $p<0.001$, $\omega<1.51$ rad/s). The lowest coefficient of friction in L02 was obtained at pH 8.00 ($\omega=0.955$ rad/s), and the highest coefficient of friction was obtained at pH 6.29 ($\omega=0.024$ rad/s) (Fig. 3). The variation in pH for L03 had a small effect on the coefficient of friction at low range of angular velocity, but a larger effect at middle and high angular velocity (ANOVA, $p<0.001$, $\omega>1.51$ rad/s). The highest coefficient of friction in L03 occurred at pH 6.31 ($\omega=0.024$ rad/s) or pH 8.76 ($\omega=9.55$ rad/s) and the lowest at pH 7.00 ($\omega=3.80$ rad/s) (Fig. 4). The variation in pH for L04 had an effect almost over the entire range of angular velocity (ANOVA, $p<0.001$, $\omega>0.151$ rad/s) (Fig. 5).

The lubricant viscosity versus shear rate curves for L01, L02, L03, and L04 are presented in Figs. 6, 7, 8, and 9 respectively. The variation in pH for L01 had an effect on the lubricant viscosity in the middle and high ranges of shear rate (ANOVA, $p<0.005$, $\dot{\gamma}>0.754$ 1/s). The viscosity of L02 decreased with increasing shear rate for all values of pH (Fig. 7). The variation in pH for L02 had an effect on the lubricant viscosity in the high ranges of shear rate (ANOVA, $p<0.005$, $\dot{\gamma}>7.54$ 1/s). The affects of pH on viscosity of L03 varied with the shear rate. At shear rates lower than 0.30 1/s, viscosity decreased with increasing pH, while viscosity increased with decreasing pH at shear rates higher than 3.00 1/s (ANOVA, $p<0.005$, $\dot{\gamma}<0.30$ 1/s; $p<0.005$, $\dot{\gamma}>3.00$ 1/s) (Fig. 8). The variation in pH for L04 had an effect on the lubricant viscosity in the high ranges of shear rate (ANOVA, $p<0.005$, $\dot{\gamma}>7.54$ 1/s) (Fig. 9).

Coefficient of determination for regression analysis between friction coefficient and lubricant viscosity at the corresponding angular velocities to five-selected shear rates is presented in Table 1. Coefficient of determination for regression analysis shows that there is significant correlation between coefficient of friction and lubricant viscosity at high angular velocity (9.55 rad/s) for L01 ($p<0.01$), L03 ($p<0.001$), and L04 ($p<0.01$). There is no significant correlation between coefficient of friction and lubricant viscosity at corresponding angular velocities for L02.

4. Discussion

Not a few investigations measuring the coefficient of friction between the surfaces of artificial joints have been performed in the last quarter of this century. These studies reported coefficients of friction between 0.03 and 0.1 (Fisher and Dowson, 1991; Weightman et al., 1972). The coefficient of friction obtained in this study, ranging from 0.023 to 0.070, is similar to the results of previous studies.

The coefficient of friction between SUS and UHMWPE differs with the addition of albumin or γ-globulin or Lα-DPPC to HA solution with concomitant changes in pH and angular velocity. The pH variation

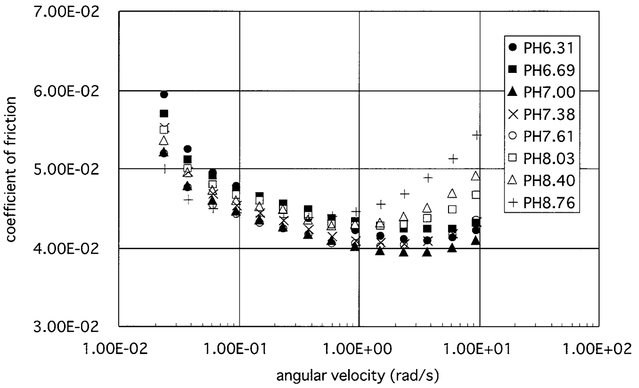

Fig. 4. The coefficient of friction versus angular velocity curves for L03. The variation in pH for L03 had a small effect on the coefficient of friction at low ranges of angular velocity, but a larger effect at middle and high angular velocity (ANOVA, $p = 0.005$, $\omega = 0.024$ rad/s; $p < 0.001$, $\omega > 1.51$ rad/s).

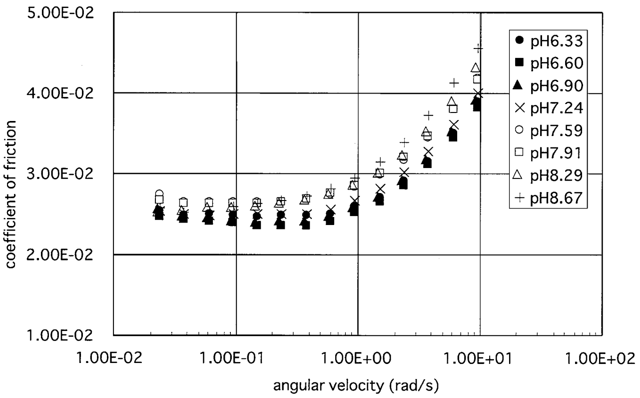

Fig. 5. The coefficient of friction versus angular velocity curves for L04. The variation in pH for L04 had a larger effect almost over the entire range of angular velocity (ANOVA, $p < 0.001$, $\omega > 0.151$ rad/s).

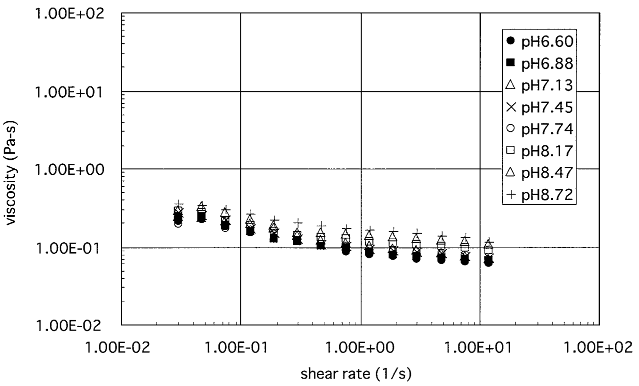

Fig. 6. The lubricant viscosity versus shear rate curves for L01. The variation in pH for L01 had an effect on the lubricant viscosity in the middle and high ranges of shear rate (ANOVA, $p < 0.005$, $\dot{\gamma} > 0.754$ 1/s).

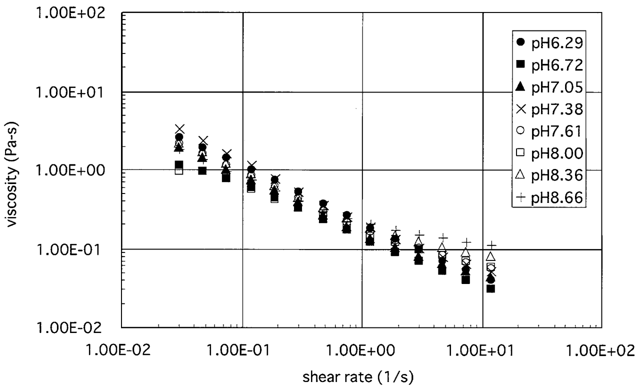

Fig. 7. The lubricant viscosity versus shear rate curves for L02. The viscosity of L02 decreased with increasing shear rate for all values of pH.

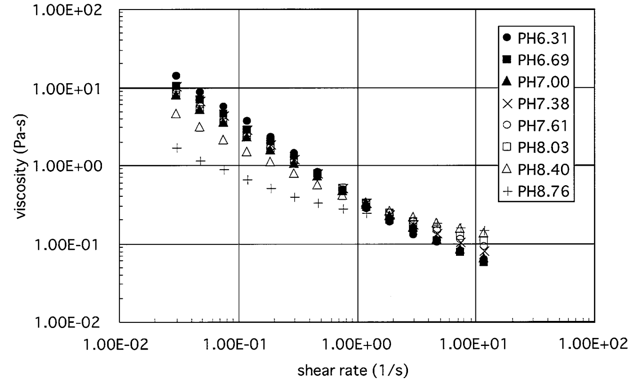

Fig. 8. The lubricant viscosity versus shear rate curves for L03. The affects of pH on viscosity of L03 varied with the shear rate. At shear rates lower than 0.30 1/s, viscosity decreased with increasing pH, while viscosity increased with decreasing pH at shear rates higher than 3.00 1/s (ANOVA, $p < 0.005$, $\gamma < 0.30$ 1/s; $p < 0.005$, $\dot{\gamma} > 3.00$ 1/s).

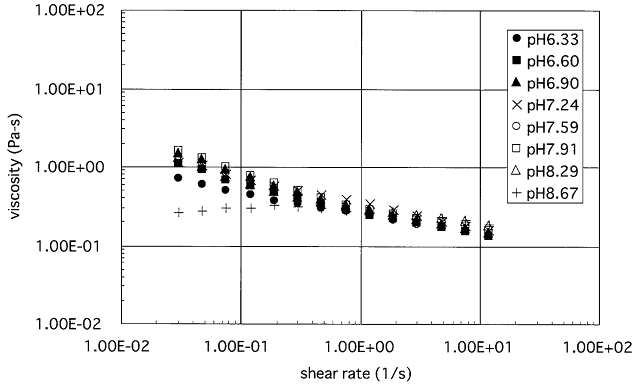

Fig. 9. The lubricant viscosity versus shear rate curves for L04. The variation in pH for L04 had an effect on the lubricant viscosity in the high ranges of shear rate (ANOVA, $p < 0.005$, $\dot{\gamma} > 7.54$ 1/s).

and the addition of albumin or γ-globulin or Lα-DPPC to HA solution also produced differences in viscosity. The coefficient of friction showed pH dependence for HA solution at high angular velocity. There was a significant correlation between lubricant viscosity and coefficient of friction for HA solution at the corresponding range of high angular velocity. The lubricant viscosity was dependent on pH value for HA solution at the corresponding range of middle and high angular velocity. These results suggest that the dependence of pH on friction coefficient for HA solution at high angular velocity may be mediated by lubricant viscosity. According to the same consideration, the dependence of pH on the coefficient of friction may be mediated by lubricant viscosity at high angular velocity for HA with γ-globulin or Lα-DPPC.

The coefficient of friction shows pH dependence and viscosity independence at low range of angular velocity for HA with albumin. The addition of albumin to the HA solution extremely increased the coefficient of friction at low angular velocity in our model, while viscosity of the lubricant did not affect the coefficient of friction. Furthermore, the variation of pH affected the coefficient of friction in lubricant containing albumin in the low range of angular velocity, i.e., the lower the pH value of the lubricant, the higher the coefficient of friction. These results suggest that albumin regulates the pH dependence of the frictional response without viscosity dependence at low angular velocity. With regard to pH dependence, pH changes of lubricant are thought to act on lubrication properties through the surface charge of protein and the conformational changes of glycoproteins. Isoelectric pH, at which a protein has no net charge, ranges from 4.7 to 5.2 for albumin and from 5.8 to 7.3 for γ-globulin. The higher the pH of lubricant, the higher the absolute value of protein negative charge. The variation of pH may affect the adherence of albumin to the artificial joint surfaces as well as the repulsive force produced by its net charge, potentially altering its tribological properties as a boundary lubricant. This consideration accords with our result, showing that the lowest coefficient of friction in HA with albumin was obtained at pH 8.00 and the highest coefficient of friction was at pH 6.29 at low angular velocity. These results suggest that the presence of albumin in the lubricant may promote boundary lubrication mode in artificial joint at low speed.

On the other hand, the highest coefficient of friction in HA with γ-globulin occurred at pH 6.31 (at low angular velocity), pH 8.76 (at high angular velocity) and the lowest at pH 7.00 (at middle angular velocity). At close to isometric pH range, the addition of γ-globulin decreased coefficient of friction through the change of viscosity at high angular velocity. It has been suggested that conformational changes of large molecular globulin in hyarulonan glycoprotein complex might act on decreasing the coefficient of friction through the change of viscosity at high angular velocity. Furthermore, the addition of globulin to HA solution increased the coefficient of friction at low angular velocity without pH dependence while viscosity of the lubricant did not affect the coefficient of friction. These results suggest that the presence of globulin in the lubricant may work as a pH-independent boundary lubricant at low speed and may produce hydrodynamic lubrication or mixed lubrication with pH dependence at high speed.

The addition of Lα-DPPC showed a small effect on the coefficient of friction at low range of angular velocity. This result may be related to the fact that Lα-DPPC was only dispersed in this study. It has been suggested that when Lα-DPPC adsorbs to the artificial joint surface, rather than being dispersed in the lubricant, the coefficient of friction between UHMWPE and SUS is reduced at low angular velocity, as reported in a previous study (Williams et al., 1995).

This study confirms that the presence of albumin in the lubricant promotes pH dependence and viscosity independence of the tribological properties at low speed while the presence of globulin promotes pH and viscosity independence at low angular velocity and promotes pH and viscosity dependence at low and high speed in the lubrication of UHMWPE against SUS. The findings obtained from this work are not yet sufficient to resolutely conclude that albumin in periprosthetic fluid works as a pH-dependent boundary lubricant and globulin works as a pH-independent boundary lubricant at low speed or that globulin in periprosthetic fluid promotes pH- and viscosity-dependent hydrodynamic or mixed lubrication at high speed. However, it may be concluded that there are two pH-dependent components in the lubrication of UHMWPE against SUS, i.e., a component independent of viscosity (which may favor

Table 1
Coefficient of determination (r^2) for regression analysis between friction coefficient and lubricant viscosity at corresponding angular velocity to five selected shear rates, for all four lubricants. In each cell, the regression is performed over data points for all eight pH values

Lubricant	Angular velocity (rad/s)				
	0.038	0.151	0.603	2.400	9.550
L01	0.003	0.312	0.162	0.549	0.711[a]
L02	0.032	0.097	0.013	0.006	0.277
L03	0.588	0.178	0.268	0.308	0.885[b]
L04	0.108	0.009	0.001	0.342	0.785[a]

[a] $p < 0.01$.

[b] $p < 0.001$.

boundary lubrication), and another component related to viscosity (which may favor hydrodynamic lubrication). This study supports the clinical hypothesis that the pH and constituent dependence of the lubrication of UHMWPE against SUS is a clue toward resolving many complications after total joint replacement. The elucidation of biotribological phenomena of artificial joint surfaces in vivo awaits further studies to simulate the artificial joint in clinical use.

Acknowledgements

This work was supported by the Fund of Osaka City University Medical School Orthopaedic Surgery Alumni Association. We thank Dr. Laura H Wang for the help and suggestions.

References

Cummings, N.A., Nordby, G.L., 1966. Measurement of synovial fluid pH in normal and arthritic knees. Arthritis Rheumatism 9, 47–56.

Delecrin, J., Oka, M., Takahashi, S., Yamamuro, T., Nakamura, T., 1994. Changes in joint fluid after total arthroplasty. Clinical Orthopaedics and Related Research 307, 240–249.

Falchuk, K.H., Goetzl, E.J., Kulka, J.P., 1970. Respiratory gases of synovial fluids. An approach to synovial tissue circulatory–metabolic imbalance in rheumatoid arthritis. American Journal of Medicine 49, 223–231.

Fisher, J., Dowson, D., 1991. Tribology of total artificial joints. Proceedings of the Institution of Mechanical Engineers 205, 173–179.

Goldie, I., Nachemson, A., 1969. Synovial pH in rheumatoid knee-joints. I. The effect of synovectomy. Acta Orthopedica Scandinavica 40, 634–641.

Goodman, S.B., Fornasier, V.L., Lee, L., Kei, J., 1990. The histological effects of the implantation of different size of polyethylene particles in the rabbit tibia. Journal of Biomedical Material Research 24, 517–524.

Hills, B.A, 1989. Oligolamellar lubrication of joints by surface active phospholipid. Journal of Rheumatology 16, 82–91.

Howie, D.W., Haynes, D.R., Rogens, S.D., McGee, M.A., Dearcy, M.J., 1993. The response to particulate debris Orthopedic Clinics of North America 24, 571–581.

Jin, Z.M., Dowson, D., Fisher, J., Ohtsuki, N., Higaki, H., Moriyama, S., 1998. Prediction of transient lubricating film thickness in knee prostheses with compliant layers. Proceedings of the Institution of Mechanical Engineers 212, 157–164.

Kadoya, Y., Kobayashi, A., Ohashi, H., 1998. Wear and osteolysis in total joint replacements. Acta Orthopedica Scandinavica Supplementum 278, 1–16.

Kitano, T., Ohashi, H., Kadoya, Y., Kobayashii, A., Yutani, Y., Yamano, 1998. Measurement of ζ-potentials of particulate biomaterials in protein-rich hyaluronan solution with changes in pH and protein constituents. Journal of Biomedical Material Research 42, 453–457.

Kofoed, H., 1986. Synovitis causes hypoxia and acidity in synovial fluid and subchondral bone. Injury 17, 391–394.

Mangione, P., Chauveaux, D., Baquey, C., Honton, L.L., 1990. Caracterisation chimique, biochimique, et dosage des metaux du liquide <periprothetique>. International Orthopaedics 14, 393–397.

McCarty, D.J., 1989. Synovial Fluid in Arthritis and Applied Conditions. In: McCarty, D.J. (Ed.), Arthritis and Allied Condition—A Textbook of Rheumatology. Lea and Febiger, Philadelphia, pp. 69–90.

Murakami, T., Higaki, H., Sawae, Y., Ohtsuki, N., Moriyama, S., Nakanishi, Y., 1998. Adaptive multimode lubrication in natural synovial joint and artificial joints. Proceedings of the Institution of Mechanical Engineers 212, 23–35.

O'Kelly, J., Unsworth, A., Dowson, D., Wright, V., 1979. An experimental study of friction and lubrication in hip prostheses. Engineering in Medicine 8, 153–159.

Ropes, M.W., Rossmeisl, E.C., Bauer, W., 1940. The origin and nature of normal human synovial fluid. Journal of Clinical Investigation 19, 795–799.

Shanbhag, A.S., Jacobs, J.J., Blach, J., Galante, J.O., Glant, T.T., 1994. Macrophage/particle interactions: effect of size, composition and surface area. Journal of Biomedical Materials Research 28, 81–90.

Unsworth, A., 1978. The effects of lubrication in hip joint prosthesis. Physics in Medicine and Biology 23, 253–268.

Walker, P.S., 1973. A comparison of normal and artificial human joints. Acta Orthopedica Belgica Supplementum 39, 43–54.

Wang, L.H., Ateshian, G.A., 1997. The normal stress effect and equilibrium friction coefficient of articular cartilage under steady frictional shear. Journal of Biomechanics 30, 771–776.

Weightman, B., Simon, S., Paul, I., Rose, R., Radin, E., 1972. Lubrication mechanism of hip joint replacement prosthesis. Journal of Lubrication Technology 72, 131–135.

Williams III, P.F., Powell, G.L., Love, B., Ishihara, K., Johnson, R., LaBerge, M., 1995. Fabrication and characterization of dipalmitoylphosphatidylcholine attracting elastomeric material for joint replacement. Biomaterials 16, 1169–1174.