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Rheology of joint fluid in total knee arthroplasty patients

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Abstract

While the properties of joint fluid may affect the tribology of joint replacement prostheses, the flow parameters of joint fluid have not yet been examined in the context of total knee arthroplasty (TKA). The objective of this study was to evaluate the flow properties of joint fluids in patients undergoing index TKA or revision TKA. We hypothesized that an alteration of the properties of joint fluid would result from TKA. The steady-shear viscosity and storage and loss moduli were evaluated in joint fluid from 35 arthritis patients undergoing TKA, 14 patients undergoing revision of a previous TKA, and two patients presenting with joint effusion after TKA. The same properties were also evaluated in two commercially available sodium hyaluronate preparations and bovine serum, which is used as a lubricant in joint simulators. The steady-shear viscosity varied over three orders of magnitude among samples obtained from patients undergoing TKA, spanning previously established "normal" and "diseased" ranges. Fluid obtained at index TKA was more likely to exhibit normal viscous properties than fluid obtained at revision TKA ($p = 0.01$). Other viscous parameters distinguished the two groups, but the difference did not reach statistical significance. Both groups exhibited degenerate flow properties when compared to synovial fluid from healthy individuals. Further examination of the connection between flow properties and the tribology of joint replacement prostheses is warranted.

Introduction

Both boundary and fluid-film lubrication likely contribute to the tribology of the prosthetic joint as they do in the natural joint [7,11,22,24], though the relative contributions of each type of lubrication may differ. Despite the importance of tribology to the function of joint prostheses, very little has been reported regarding the mechanisms of lubrication in these articulations. In the context of fluid-film lubrication, joint fluid flow properties are determinant of tribology. Flow properties of synovial fluid vary substantially among patients with normal and diseased joints [1,5,16,17,20,21]. The variability in joint fluid properties after total knee arthroplasty (TKA) could thus contribute to the widely varying wear rates encountered in vivo.

Understanding the role of joint fluid in fluid-film lubrication requires an assessment of its bulk fluid properties. It must be shown that the variability of synovial fluid flow properties seen among knees in the general population exists in patients undergoing TKA and persists in joint fluid after TKA. In particular, the steady-shear viscosity and linear viscoelastic properties are flow parameters that likely characterize a joint fluid sample's contribution to fluid-film lubrication in TKA, as they do in the natural knee. Both steady-shear viscosity [5,16,17,20,21] and linear viscoelastic properties [1,10,14,15] have been examined previously in both normal and diseased knees. Relatively few data exist, however, evaluating these features for joint fluid in arthroplasty patients.

The objective of this study was to evaluate the flow properties of joint fluids in the context of TKA. Two hypotheses were tested: (1) flow properties vary widely in the joint fluid of patients undergoing revision TKA; and (2) flow properties of joint fluid obtained at revision TKA differ from that of synovial fluid obtained before TKA. The former hypothesis, if verified, might suggest a connection between variability in joint fluid flow properties and wear in TKA. The latter hypothesis, if verified, would provide a rationale for further study into the causes and consequences of the differing compositions. A related aim was to compare the properties of these fluids to those that are or can be used for laboratory wear testing of joint prostheses.

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The steady-shear viscosity and linear viscoelastic properties were evaluated in joint fluid from patients undergoing TKA and patients undergoing revision TKA. These rheological properties were compared to those previously reported in normal and diseased patients. The rheological properties of bovine serum currently used in knee simulators and wear testing were evaluated and compared with the properties of joint fluid. Finally, the flow properties of two commercially available hyaluronic acid preparations were evaluated.

Materials and methods

Fifty-eight synovial fluid samples were obtained from patients during TKA for osteoarthritis. Nineteen samples were obtained during revision TKA in other patients, and two samples were aspirated from effused joints that had previously undergone TKA. All samples came from Brigham and Women's Hospital, New England Baptist Hospital, or Massachusetts General Hospital in accordance with a protocol approved by each hospital's Institutional Review Board. Twenty-two samples from TKA and five samples from revision surgery contained insufficient fluid for mechanical testing. For the remaining samples, patients ranged from 42 to 89 years old, with an average age of 70 years. Of the 14 joint fluids from revision TKA whose properties were successfully measured, seven had undergone revision because of wear-related osteolysis and seven because of mechanical problems not specifically related to wear.

The standard lubricant employed for laboratory wear testing, bovine serum, was also tested. All bovine serum samples came from Life Technologies calf serum lot # 1 023 609, with 73 mg/ml total protein, diluted to 40% by volume in distilled water. Additionally, flow properties were measured for two commercially available hyaluronic acid preparations, Supartz (Smith & Nephew, Memphis, TN) and Orthovisc (Anika Therapeutics, Woburn, MA), employed as injectable agents for the treatment of osteoarthritic patients. All Supartz samples came from Artz lot #9Z683A 2002.11 and contained 1% w/v sodium hyaluronate at a molecular weight between 620 000 and 1 170 000. All orthovisc samples came from Anika Therapeutics lot #60 382 000 and contained 1.4% w/v sodium hyaluronate at a mean molecular weight of 1 390 000. Because the flow properties could be measured repeatedly within 10%, only three samples of each fluid were tested.

The flow parameters of each sample were evaluated on a CSL 500 controlled stress rheometer (TA Instruments, New Castle, DE). The rheometer was first calibrated with Cannon Certified Viscosity Standard mineral oil using imposed stresses that varied from 10 to 0.1 Pa. Joint fluid and bovine serum properties were evaluated using the double cylinder Couette flow geometry appropriate for low viscosity fluids. Properties of hyaluronate preparations were evaluated using a cone and plate geometry of radius 3 cm and cone angle 1°.

In order to evaluate the steady-shear viscosity as a function of shear rate, a given shear stress was initially applied, and the steady-state shear rate measured. The shear rate resulting from an imposed shear stress was determined using a stepped ramp sweep decreasing logarithmically over 2 decades of shear stress. For each of 10 steps in the first decade, the mean shear rate was measured over 20 s intervals until the measured mean shear rates within two consecutive intervals agreed to within 1%. For each step in the second decade, the mean shear rate was measured over 40 s until two consecutive intervals agreed to within 3%. The measurements continued in this fashion until reaching the minimum deformation rate measurable on the rheometer. Typically, the deformation rate could be evaluated over 1.5 to 2 decades of shear stress for each joint fluid sample. Steady-shear viscosity could be measured in hyaluronate samples over three orders of magnitude of shear stress.

To compare data from different samples, the viscometric data were fitted to a simplified Cross viscosity model [3]. In this model, the shear rate $\dot{\gamma}$ and viscosity η are related by the equation $\eta = \eta_0/(1 + (c\dot{\gamma})^d)$, where η_0 is the zero-shear-rate viscosity; c is the consistency, which is related to the longest relaxation time of the fluid; and d is the rate index, a dimensionless variable that characterizes the negative slope on a double logarithmic plot of the shear-thinning region, in which $\eta \sim \dot{\gamma}^{-d}$. The data were fit to the simplified Cross model using an iterative χ^2 minimization method on the natural logarithm of the shear rate and viscosity using Igor Pro (WaveMetrics Inc., Lake Oswego, OR). A second method of comparison, the viscosity at 1 Pa shear stress ($\eta_{1\,\mathrm{Pa}}$), was also used as a comparative tool among samples.

A small amplitude oscillatory shear stress test was performed to measure the linear viscoelasticity of joint fluids. During each test, the strain response to a small, sinusoidal shear stress was measured for 25 frequencies between 25 and 0.1 Hz. For sufficiently small strains, the output is a sine wave of different phase and amplitude than the input. The portion of the strain in phase with the stress input is related to the elastic character of the fluid sample and is expressed as the storage modulus, G' (Pa). The portion of the strain out of phase with stress is related to the viscous character of the fluid sample and is expressed as a loss modulus, G'' (Pa), or dynamic viscosity, $\eta' = G''/(2\pi f)$ [8]. These parameters describe the relative importance of elasticity and viscosity in small amplitude oscillatory motion and were measured for five different torque (shear stress) inputs: 25, 50, 100, 200, and 300 μN m. Since the fluid response was linear for small deformations, single plots of the linear storage and loss moduli as functions of frequency were compiled from these curves. Only sinusoidal strain responses with amplitude less than 0.6 were included in the compiled responses.

To compare differences between samples, the viscoelastic crossover frequency f_c and modulus at crossover $G_c = G'(f_c) = G''(f_c)$ were calculated when possible. Since crossover did not always occur within the range of frequencies measured, especially in fluids with lower moduli, other parameters were used to compare samples. In particular, the moduli at 2.5 Hz (denoted by subscripts) were used to compare samples. Other investigators [2] reported values for $G'_{2.5\,\mathrm{Hz}}$ and $G''_{2.5\,\mathrm{Hz}}$ in healthy and diseased knees.

Results

Viscometric parameters

The joint fluid samples generally displayed characteristic shear-thinning behavior reflected in a decrease in viscosity with increasing shear rate (Fig. 1). In contrast, bovine serum remained Newtonian (i.e., with a constant viscosity) throughout the test range. Although each joint fluid curve exhibited the same characteristic shape, the magnitude of the steady-shear viscosity varied over three orders of magnitude.

In 44 cases, the joint fluid exhibited evidence of a viscosity plateau at low shear rates. In these cases, the data fit the Cross model well. A fit was considered good if the standard deviation of two parameters was less than 10% of their calculated value. In the five remaining cases (three index and two revision), data could not be obtained at low enough shear rates to fit a low shear plateau. These cases could be fit to the Cross model, but only the rate index, d, could be determined with certainty. In each case, η_0 and c had standard deviations as large as their calculated values, indicating that these parameters were not uniquely defined by the data. Consequently, η_0 and c were used to compare only those data that fit the Cross model. The rate index, d, was used to compare all samples. The use of the simplified Cross model is justified both by the experience of previous work and the goodness-of-fit of most of the samples.

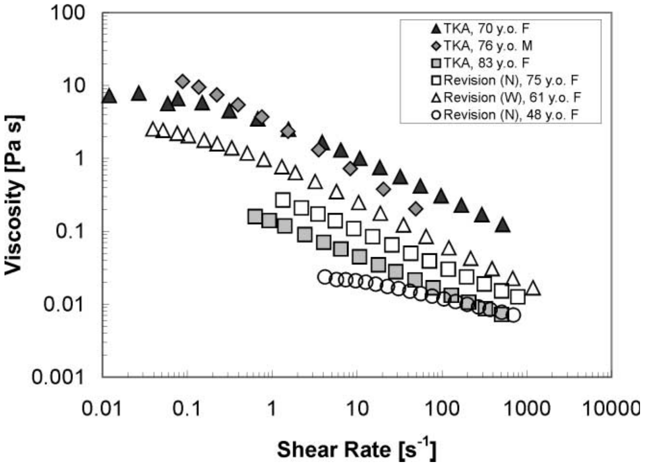

Fig. 1. Rheogram showing a characteristic decrease in the viscosity with increased shear rate for several samples of joint fluid from patients undergoing TKA and revision TKA. All samples exhibited shear thinning, and all but the squares demonstrated some measure of low-shear plateau and could be fit to the simplified Cross model. N = revision for reasons unrelated to wear. W = revision due to wear-related reasons.

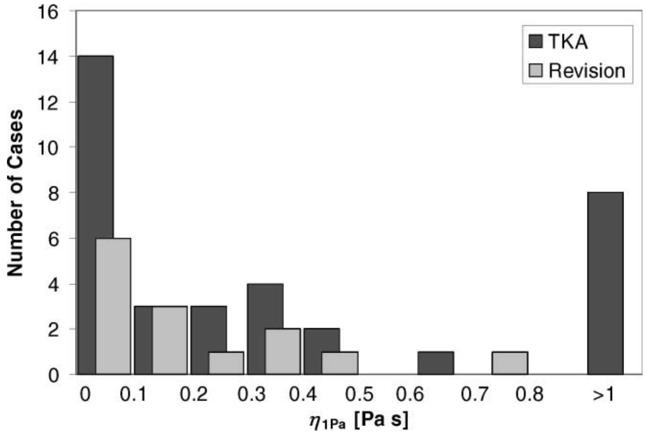

Fig. 2. Histogram demonstrating the sample frequency distribution for the steady-shear viscosity at 1 Pa.

In part to compare the data in a manner that more fully included the data that did not exhibit a zero-shear plateau, $\eta_{1\,\mathrm{Pa}}$ was also used to compare samples. In contrast to the other parameters, which were calculated by fitting a curve to a set of data, $\eta_{1\,\mathrm{Pa}}$ enabled direct data comparison, and could be measured for all samples. As was the case with the viscosity–stress curves, $\eta_{1\,\mathrm{Pa}}$ varied over a wide range. In the group of revision TKA, $\eta_{1\,\mathrm{Pa}}$ was less than 0.8 Pa s for all samples, whereas 23% of samples obtained at index TKA had viscosities greater than 1 Pa s (Fig. 2).

The distributions of $\eta_{1\,\mathrm{Pa}}$, η_0 and c were highly skewed toward the low end of their range and did not form a Gaussian distribution. Consequently, median and range, rather than mean and standard deviation, were used to compare these parameters (Table 1). Stratifying the joint fluid samples obtained at revision TKA into wear-related revision ($n = 7$) and revision for reasons other than wear ($n = 7$) revealed no differences in any of the measured or calculated parameters. However, because no direct wear measure was made, no conclusions can be drawn from this observation.

Joint fluid obtained at revision TKA displayed a lower viscosity compared to the index TKA samples (Table 1), albeit not statistically significant by the Mann–Whitney test ($\eta_{1\,\mathrm{Pa}}$, $p = 0.08$; η_0, $p = 0.12$; c, $p = 0.09$) [12]. There was a stronger indication of the difference between these two groups in shear rate dependence, with the revision TKA samples having a smaller rate index, d, indicating a lower shear rate dependence (Student's t-test, $p = 0.07$).

Others have evaluated the viscosity of synovial fluid obtained from individuals who were categorized as "normal," "degenerative," or "chronically inflamed" [5, 16,17,20,21]. In these studies, synovial fluid from asymptomatic patients consistently exhibited higher viscosity than synovial fluid from patients with degenerative or

Table 1
Flow properties of different groups of joint fluids

Group	$\eta_{1\,\mathrm{Pa}}$ (Pa s)	η_0 (Pa s)^a	c (s)^a	d^b
TKA ($n = 35$)	0.26 (0.0094–11)	1.3 (0.087–25)	4.2 (0.047–35)	0.54 ± 0.10
Revision ($n = 14$)	0.13 (0.0043–0.77)	1.0 (0.0087–4.0)	2.6 (0.0043–10.8)	0.48 ± 0.11
Effusion after	0.0096^c	0.12	45	0.29
TKA ($n = 2$)	0.18^d	2.7	37	0.47
Supartz^e	3.0	3.1	0.056	0.78
Orthovisc^e	37	39	1.0	0.71
Bovine serum^e	0.0015	N/A	N/A	N/A

All joint fluid data are presented as median (range) except where noted.
[a] Values include only samples which fit the Cross model.
[b] Mean ± standard deviation.
[c] 75 year old male, traumatic aspiration.
[d] 69 year old male, hemarthrosis.
[e] Mean values only.

Table 2
Joint fluid parameters in the context of previous work on normal and diseased fluid

Group	Parameter	Normal	Diseased	Chronically inflamed	Total patients
Established range	$\eta_{1\,\mathrm{Pa}}$	2–10	0.05–2	0.003–0.02	
	η_0	6–12	0.1–1	0.005–0.05	
TKA (% of patients)	$\eta_{1\,\mathrm{Pa}}$	14%	74%	11%	35
	η_0	29%	71%	0%	
Revision (% of patients)	$\eta_{1\,\mathrm{Pa}}$	0%	71%	29%	14
	η_0	14%	64%	21%	

inflammatory disease. The samples studied here were fit to these established ranges (Table 2). Both groups of joint fluids were most likely to fit in the diseased range, rather than the normal or inflamed range. A notable finding was that joint fluid obtained at index TKA was more likely to exhibit normal viscous parameters than fluid obtained at revision TKA (Fisher's exact test, $p = 0.01$ for η_0).

Using regression analysis, η_0 was correlated to d by a power law relationship for all samples ($r^2 = 0.67$ for all data, 0.82 for data which fit the Cross model well). Consistency could not be correlated with either η_0 or d. No correlation could be found between any viscous parameter and age, gender, or involved limb. Moreover, no correlation was found between the viscosity and the volume of joint fluid.

In two cases, fluid was taken from each knee during bilateral TKA. For these two cases, right and left knees were compared. In both cases, the two knees had very different viscometric parameters (Table 3).

Viscoelastic parameters

The linear viscoelastic curves for joint fluid samples displayed a characteristic shape (Fig. 3). At low frequencies, the loss modulus dominated over the storage modulus. As the imposed frequency was increased, the storage modulus and loss modulus both increased, but in many cases the storage modulus increased more rapidly than the loss modulus, so that at high frequencies ($f > f_c$), the storage modulus dominated the response. The crossover frequency (f_c), at which the storage and loss moduli were equal, has been used to characterize the relative importance of elastic and viscous effects in fluids for which crossover existed. This frequency corresponds to the frequency at which the phase angle δ between the imposed stress and resulting strain is 45°; i.e., $\tan\delta = G''/G' = 1$.

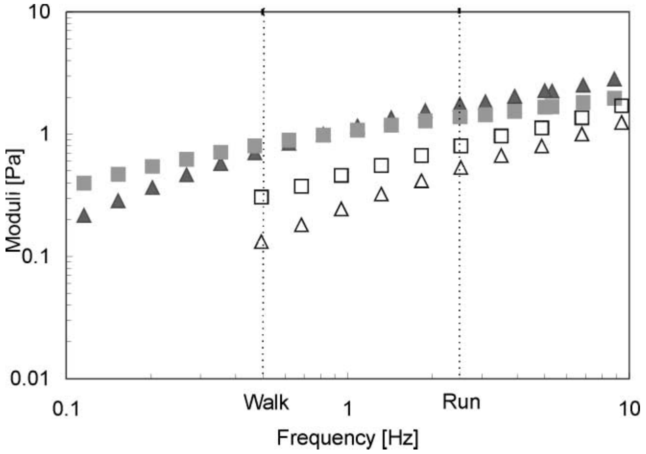

Fig. 3. Typical curves representing the change in storage modulus (triangles) and loss modulus (squares) with frequency of oscillation. A sample obtained from an 88 year old female at index TKA (solid shapes) exhibited viscoelastic crossover at 0.87 Hz; hollow shapes are data collected for a 72 year old male undergoing revision TKA for wear-related osteolysis. This sample did not exhibit viscoelastic crossover within the range tested. Crossover in the first sample occurred within the range of frequencies encountered in vivo (dotted lines). The amplitude of the shear stress used to measure G' and G'' was, for the closed shapes: 1.6 Pa at 8.8 Hz; 0.78 Pa at 6.9 and 5.3 Hz; 0.39 Pa at 5.0 to 3.1 Hz; 0.19 Pa at 2.5 Hz and below; for the open shapes: 0.78 Pa at 9.4 and 6.8 Hz; 0.39 Pa at 4.9 Hz; 0.19 Pa at 3.5 Hz and below. These shear stresses corresponded to 200, 100, 50, and 25 μN m, respectively. The strain was, in all cases, less than 0.6.

The crossover could be measured in 13 of 19 joint fluid samples obtained at arthroplasty and 7 of 11 joint fluid samples obtained at revision (Table 4). In the other six samples, the storage modulus was too small, even at

Table 3
Two examples of properties of joint fluid contrasted between contralateral knees during bilateral TKA

	Leg	$\eta_{1\,\mathrm{Pa}}$ (Pa s)	η_0 (Pa s)	c (s)	d
52 year old female	Right	0.44	1.8	2.8	0.61
	Left	1.7	6.0	7.2	0.67
68 year old female	Right	0.052	0.13	0.13	0.48
	Left	0.41	1.9	3.9	0.58

Table 4
Crossover frequency and modulus at crossover for joint fluid samples

Group	Number exhibiting crossover	f_c (Hz)	G_c (Pa)	$G'_{2.5\,\mathrm{Hz}}$ (Pa)	$G''_{2.5\,\mathrm{Hz}}$ (Pa)
TKA	13/19	1.8 ± 0.5	1.1 ± 0.2	1.9 ± 0.5	1.4 ± 0.3
Revision	7/11	3.1 ± 0.6	1.4 ± 0.2	1.0 ± 0.2	1.1 ± 0.2
Supartz	All	11	39	12	20
Orthovisc	All	0.83	38	60	46
Normal 52–78 year old[a]		0.41 ± 0.12	6.1 ± 0.7	19 ± 3	10 ± 1

Data are presented as mean ± standard error, except joint supplements, which are presented as means only.

[a] Ref. [2, p. 183].

high frequency, to directly measure a crossover. Crossover could also be measured for the hyaluronate preparations. Bovine serum exhibited no storage modulus, being Newtonian at the frequencies studied.

Using Fisher's exact test, viscosity range correlated with the existence of a viscoelastic crossover within the measured range ($p < 0.04$ for both η_0 and $\eta_{1\,\mathrm{Pa}}$) with more viscous samples being more likely to exhibit crossover. Among those samples for which crossover between G' and G'' could be measured, crossover occurred within the range of frequencies encountered by the knee in vivo, 0.7 Hz (walking) to 3 Hz (running). Although crossover did not occur within this range for all samples, both storage and loss moduli were of the same order of magnitude throughout this range in many samples.

The data suggested a difference in crossover frequency between samples obtained at index TKA and samples obtained at revision TKA (Table 4). However, the difference was not statistically significant (Student's *t*-test, $p = 0.11$). Normal joint fluid for patients in the age group likely to have TKA was previously found to crossover from viscous to elastic at frequencies an order of magnitude lower than either group presently studied [2].

Discussion

Flow properties of joint fluid

The viscous properties of synovial fluid obtained at index TKA and revision TKA varied widely and were degenerated with respect to synovial fluid from healthy patients as previously published. A comprehensive study of viscoelastic properties of normal and diseased synovial fluid has not previously been conducted. However, viscous and elastic moduli at 2.5 Hz as well as the crossover frequency and the modulus in normal synovial fluid have been reported [2]. Compared to normal, all modulus parameters were markedly decreased in patients undergoing index and revision TKA. Moreover, crossover frequency was increased in these arthroplasty fluids compared to normal, indicating that viscosity is more likely to dominate over elasticity at frequencies encountered in vivo.

Of particular note, the hypothesis that viscous properties of joint fluid at revision TKA would be altered with respect to properties of fluid obtained at index TKA was supported by certain data. Viscosity when compared to expected ranges, showed fluid from revision TKA to be degenerate with respect to fluid obtained at index TKA. Direct comparison of viscous parameters (η_0, $\eta_{1\,\mathrm{Pa}}$, c, and d) yielded only the suggestion of a difference between the two groups due to the wide range of the data.

The viscoelastic moduli did not show a difference between the two groups. Modulus at crossover was actually slightly higher at revision, but this parameter was skewed by the higher frequency of crossover in the group. Loss modulus was not different between the two groups at any frequency in the range studied. Storage modulus was somewhat lower at 2.5 Hz, but not enough to be statistically significant ($p = 0.17$). At lower frequencies, the difference between the two groups was sufficiently large to reach statistical significance ($p < 0.04$ at 0.5 Hz).

The differences between viscous and viscoelastic parameters at index and revision TKA further suggested that the joint fluid in TKA patients was different from the synovial fluid present before TKA. This finding supports the work in a rabbit model that hyaluronic acid concentration did not return to normal values after arthroplasty [6]. These results warrant an examination of the composition of joint fluid after TKA.

The viscous parameters of synovial fluid taken at revision TKA spanned a wide range, η_0 covering almost three orders of magnitude. The confirmation of this hypothesis, coupled with variation in prosthetic wear rates observed in vivo [19], raises the question of the importance of fluid-film lubrication in the tribology of prosthetic joints and, in particular, the connection between viscosity and wear. This issue warrants the additional study of wear test lubricants with different rheological properties to determine the effect of the shear viscosity on wear rates in TKA.

One limitation of this study was that the flow properties were not measured under the specific conditions that are likely to exist in the replacement knee joint (viz., the gap between the surfaces and the shear rate). The minimum gap between the cartilage surfaces in the loaded knee joint has been estimated at 0.1 μm in the natural knee [4], much smaller than the 300 μm gap employed by the CSL 500 rheometer. Flow properties of fluid films on the order of hundreds of nanometers in thickness have been shown to differ from flow properties of a bulk fluid [18]. Furthermore, the estimated maximum shear rates in the natural knee are at least an order of magnitude higher than the range in which we have measured [7]. The shear rate dependence of the viscosity of joint fluid has been demonstrated in this work. Since it is likely that the maximum shear rate and minimum gap present in the replacement knee are different from the conditions extant during analysis, the properties measured do not completely describe the relevant behavior of joint fluid. Nonetheless, it was necessary to measure the properties in the chosen range in order to compare our samples with those measurements previously made.

Interestingly, even within a single patient, the viscosity of synovial fluid was found to differ substantially between the left and right legs. This result suggests that local alterations, rather than a systemic disorder, control the properties of the joint fluid in these cases. A possible source of local control of joint fluid properties is the synovial membrane, whose role in TKA has not been fully examined.

Notably, in 22 of 58 patients undergoing TKA, less than 2.5 ml of joint fluid could be removed for evaluation. Although this problem was recorded in only 5 of 19 cases at revision, there were many other cases in which there was not a sufficient amount of fluid for the surgeon to obtain. This raises the question of the role of joint fluid volume in the wear of total knee replacement prostheses. Even though all fluid present in the knee could not be removed, the volumes recorded represent a reasonable estimate of the amount of fluid present in the joint. Furthermore, the quantities obtained are consistent with the observations of others regarding the quantity of synovial fluid in symptomatic and asymptomatic joints [13]. No work has been conducted to correlate fluid volume to the tribology of TKA, though a strong connection is recognized in other (non-biological) articulations.

Bovine serum and hyaluronic acid preparations

All prosthetic joint fluids were at least an order of magnitude more viscous than bovine serum, the lubricant currently used in most laboratory wear tests. If viscosity affects wear at the shear rates encountered in the replacement joint, then bovine serum cannot mimic the in vivo environment in lubricating metal on polyethylene articulation. This would suggest that a lubricant should be used that has all relevant tribological properties and components in common with joint fluid. This finding warrants further study into the relative importance of fluid-film lubrication on tribology of these components, and specifically the effect of viscosity and viscoelasticity on wear. In order to truly represent joint fluid, however, a test fluid must mimic the properties of joint fluid throughout the range of parameters relevant to TKA, including boundary lubricating properties and small gap rheological properties.

The hyaluronate preparations were more viscous than the joint fluid samples. Orthovisc was 10 times more viscous than Supartz, primarily due to its higher molecular weight and concentration. That the consistency of Orthovisc and Supartz was less than that of normal joint fluid samples correlates well with their molecular weights, which are smaller than that of the hyaluronic acid in normal synovial fluid. These findings were consistent with other rheological properties of hyaluronic acid [9]. Since the joint fluid supplements tended to be more viscous than the joint fluid samples, the addition of hyaluronic acid to bovine serum could provide a mixture whose bulk flow properties more closely mimic the in vivo environment over the range of frequencies and deformation rates measured. Since endogenous hyaluronic acid imparts to joint fluid its viscosity [23], these supplements would mimic the in vivo environment chemically as well as rheologically and may therefore be a more appropriate mixture for use in wear tests.

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