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## Impact of degeneration and material pairings on cartilage friction: Cartilage versus glass

de Roy, Luisa ; Schlickerieder, Klaus ; Rüger, Matthias ; Faschingbauer, Martin ; Ignatius, Anita ; Seitz, Andreas M

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## RESEARCH ARTICLE

# Impact of degeneration and material pairings on cartilage friction: Cartilage versus glass

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## Abstract

The association of knee joint osteoarthritis and altered frictional properties of the degenerated cartilage remains ambiguous, because previous in vitro studies did not consider the characteristic loads and velocities during gait. Therefore, the aim of this study was to quantify the friction behavior of degenerated human cartilage under characteristic stance and swing phase conditions. A dynamic pin-on-plate tribometer was used to test the tribological systems of cartilage against cartilage and cartilage against glass, both with synthetic synovial fluid as lubricant. Using the International Cartilage Repair Society classification, the cartilage samples were assigned to a mildly or a severely degenerated group before testing. Friction coefficients were calculated under stance and swing phase conditions at the beginning of the test and after 600 s of testing. The most important finding of this study is that cartilage against glass couplings displayed significantly higher friction for the severely degenerated samples compared to the mildly degenerated ones, whereas cartilage against cartilage couplings only indicated slight tendencies under the observed test conditions. Consequently, care should be taken when transferring in vitro findings from cartilage against cartilage couplings to predict the friction behavior in vivo. Therefore, we recommend in vitro tribological testing methods which account for gait-like loading conditions and to replicate physiological material pairings, particularly in preclinical medical device validation studies.

## KEYWORDS

aging areas of expertise: friction, tribology, interfaces; biomechanics; cartilage; knee; osteoarthritis

## 1 | INTRODUCTION

In knee osteoarthritis (OA), all anatomic joint components are affected, including articular cartilage (AC), menisci, and synovial fluid (SF). As OA progresses, substantial changes in AC composition

disturb its protective function, which makes it more vulnerable to damage.<sup>1</sup> Most in vitro studies focus on how degenerative changes affect tissue biomechanical properties.<sup>2,3</sup> Arthroscopically, the severity of cartilage degeneration can be evaluated by the arising damage patterns, as characterized by initial roughening of its

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surface, followed by progressive fibrillation, and ending in total tissue loss. Accordingly, joint degeneration is frequently referred to as joint wear.<sup>4</sup> From an engineering perspective, wear is defined as a material degradation caused by mechanical interaction of two sliding surfaces which are exposed to friction forces.<sup>5</sup> If the physical principle of wear is applied to the articulating surfaces in the knee joint, it could be hypothesized that friction contribute to cartilage wear in OA. From a biological perspective altered friction might be involved in OA progression by causing an increased production of cartilage-degrading enzymes via cell mechanotransduction in chondrocytes.<sup>1</sup> However, studies focusing on the tribology of human knee AC are underrepresented in OA research. Only a few in vitro studies investigated the friction properties of degenerated human cartilage samples on the tissue level, and these indicated contradictory results.<sup>5,6</sup> Caligaris et al. did not find a difference in the coefficient of friction (CoF) of cartilage samples with different OA severity.<sup>6</sup> By contrast, Neu et al. reported that the CoF of femoral cartilage samples correlated positively with OA severity.<sup>5</sup> The different outcome of these studies might be attributed to the different testing conditions which were applied. Both studies did not consider that during normal gait, the knee joint tissues are exposed to varying loads and velocities. There is a continuous transition between a high-loaded stance phase with a low relative velocity, followed by low-loaded swing phase with high relative velocity.<sup>7</sup> It is known that the friction properties of cartilage tissue strongly depend on the magnitude of the applied force and testing velocity.<sup>8,9</sup> Because friction of degenerated cartilage was, to date, examined only under constant loads and velocities, it remains unknown whether its friction properties are affected when accounting for characteristic swing and stance phase conditions. On the basis of this knowledge gap, the aim of the present study was to quantify the friction behavior of degenerated human cartilage under gait-like loading conditions.

## 2 | MATERIALS AND METHODS

### 2.1 | Study design

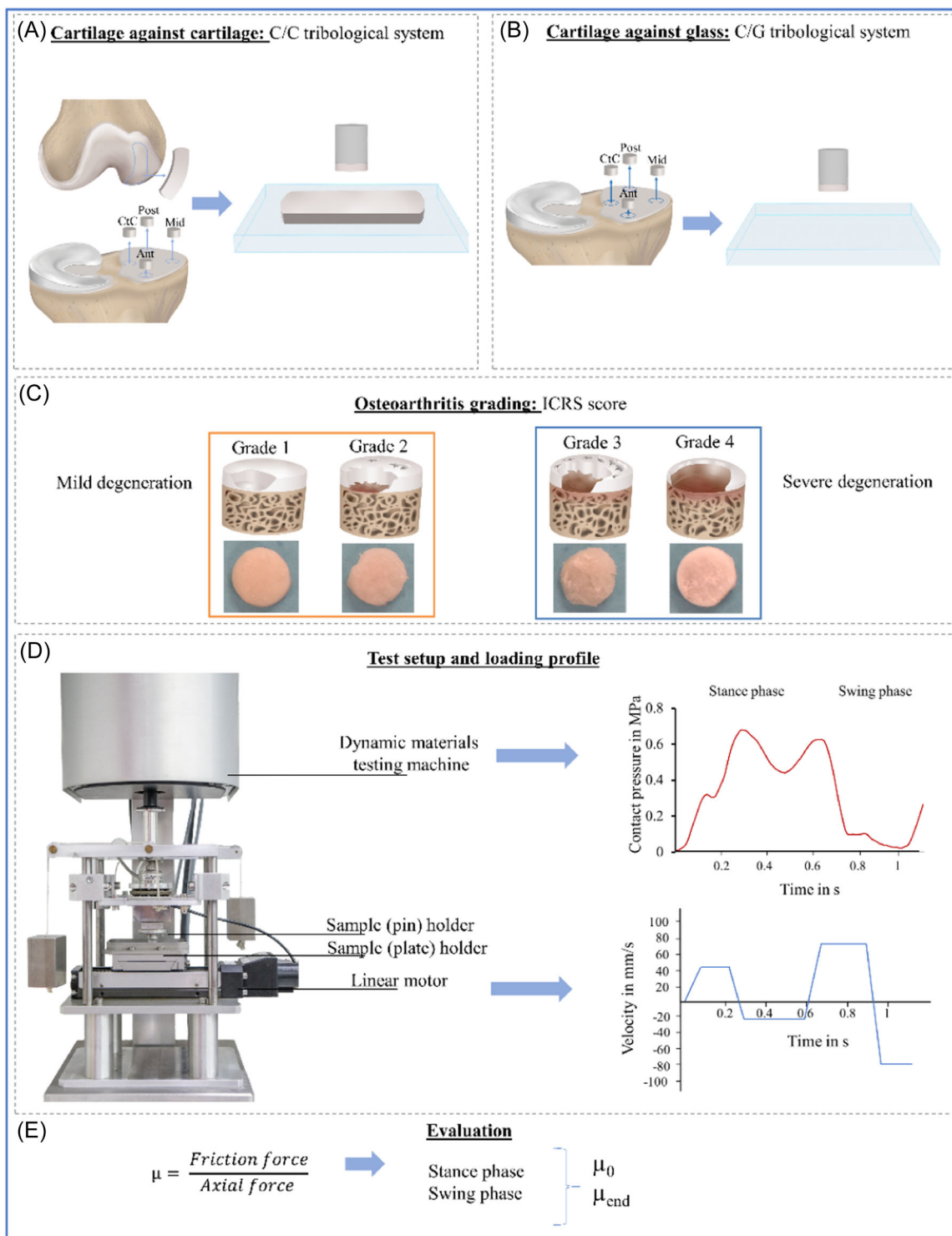
The friction properties of degenerated human cartilage samples were assessed on a tribological system, consisting of human cartilage contact partners (C/C tribosystem) and another consisting of human tibial cartilage pins and a glass plate (C/G tribosystem) using a dynamic pin-on-plate tribometer (Figure 1). The cartilage samples were assigned to a mildly or a severely degenerated group using the International Cartilage Repair Society (ICRS) classification<sup>10</sup> to consider the influence of the degeneration state on the friction properties. All samples were tested under gait-like loading conditions,<sup>9</sup> while synthetic SF was used as lubricant. The CoF were calculated under stance phase and swing phase conditions in accordance with the literature<sup>9</sup> at the beginning of the test ( $\mu_0$ ) and after 600 s of testing ( $\mu_{end}$ ).

### 2.2 | Specimen preparation

An a priori sample size calculation revealed a sample size of 12 knee joints for each tribosystem. For the C/C tribosystem, 12 human knee joints from body donors (male:  $n = 7$ , female:  $n = 5$ , mean age: 65 (range: 41–85 years, restriction criterion: without prior knee surgery) were obtained from an official tissue bank (Science Care Inc.) after Institutional Review Board (IRB) approval (approval no. 228/20 Ulm University). The knee joints were stored at  $-20^{\circ}\text{C}$  and thawed for 36 h at  $4^{\circ}\text{C}$  for the sample preparation. A flat cartilage sample (approximately 40 mm length, 15 mm width, 1.8 mm height) was harvested from the lateral femoral condyle using a peeler.<sup>11</sup> Four cylindrical samples were extracted from standardized locations on the lateral compartment of the tibial plateau (anterior, posterior, middle, cartilage-to-cartilage contact area) using a trephine drill ( $\varnothing$  6 mm) (Figure 1B). The subchondral bone was removed using a custom-made cutting device.<sup>12</sup> Measurements using a digital caliper revealed a height of the cartilage pins between 1.9 and 2.8 mm, depending on the OA severity and location. For the C/G tribosystem, 12 degenerated human tibial plateaus (IRB approval no. 146/21 Ulm University) were collected from patients undergoing total knee replacement arthroplasty (TKA). Tibial plateaus were collected at the time of surgery and stored at  $-20^{\circ}\text{C}$  until the day before testing. Following thawing at  $4^{\circ}\text{C}$  for 24 h, four cylindrical samples were similarly harvested as described above from the lateral compartment of the tibial plateaus (Figure 1B). An uncoated, smooth glass microscope slide was used as the friction contact plate.<sup>11</sup> To investigate whether the different tissue origins (body donors vs. TKA patients) influenced the friction behavior, the pins of the C/C tribosystem were additionally tested against glass in a second test run. The extraction of four cartilage pins out of each tibial plateau resulted in a total sample number of  $n = 48$  per tribological system (Table 1). Immediately after extraction, the degeneration state of each cartilage pin was macroscopically evaluated according to the ICRS classification system (Figure 1C),<sup>10</sup> ranging from Grade 0 (healthy cartilage) to 4 (absence of cartilage with exposed subchondral bone). For the experiments, Grades 1–2 were assigned to a mildly degenerated group and Grades 3–4 to a severely degenerated group. In the C/C tribosystem, the tibial pins and the femoral plate were classified according to the ICRS classification system.<sup>10</sup> The higher value of the two samples was used as the grade of the material pairing and thus for the group assignment.

### 2.3 | Friction tests

An established custom-made dynamic pin-on-plate friction testing device was used for the experiments which was described in detail previously.<sup>9</sup> In brief, a dynamic material testing machine (Electro-Force 5500, with a 200 N load cell, accuracy class  $\leq 1\%$ , WMC-50-456; both BOSE/TA Instruments) was coupled with an external linear motor (linear stage VT-75; PI miCos GmbH). This setup



**FIGURE 1** Study design overview. (A) Cartilage against glass (C/G) and (B) cartilage against cartilage (C/C) tribosystems were used to assess the friction properties of degenerated cartilage samples. In both systems, cylindrical samples were extracted from standardized locations on the lateral compartment of the tibial plateau (anterior [ant], posterior [post], middle [mid], and cartilage-to-cartilage contact area [CtC]). (C) In accordance with the International Cartilage Research Society (ICRS) classification,<sup>10</sup> all samples were grouped into mildly or severely degenerated before testing. Representative images of the samples. (D) An established tribometer was used to apply a gait-like load profile with characteristic stance and swing phase conditions.<sup>9</sup> (E) The coefficient of friction was determined at the beginning ( $\mu_0$ ) and end ( $\mu_{\text{end}}$ ) of the test.

**TABLE 1** Summary of the group assignment of the cartilage pins based on their degeneration grade classified according to the International Cartilage Repair Society (ICRS) classification system.<sup>10</sup>

ICRS grade	C/C tribosystem				C/G tribosystem			
	1	2	3	4	1	2	3	4
<i>n</i>	17	20	11	0	15	17	11	5
$\Sigma$ <i>n</i> per group	Mild: 37		Severe: 11		Mild: 32		Severe: 16	

Abbreviations: C/C, cartilage against cartilage; C/G, cartilage against glass.

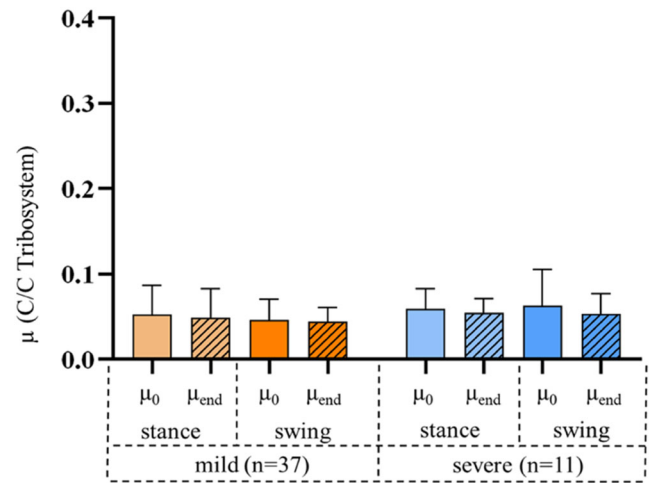
enabled both tribological systems to be tested under gait-like loading conditions derived from a human gait cycle (Figure 1D). Thereby, stance and swing phase conditions were simulated by a loading regime with a double-peak load followed by a lower load plateau applied by the dynamic material testing machine. The relative velocities associated with the stance and swing phase were derived from a walking speed of 5 km/h<sup>9</sup> (Figure 1D) and implemented in a synchronized manner by the linear motor. The testing duration was set to 600 s to account for viscoelastic effects on the friction properties.<sup>9,13</sup> The axial force ( $F_N$ ) and the resulting friction force ( $F_f$ ) were recorded by a load cell (sample rate 100 Hz, accuracy class: 0.5%; ME-Messsysteme GmbH). To lubricate the cartilage and to prevent sample dehydration during testing, 0.3 mL synthetic SF<sup>14</sup> was used. Because four cartilage pins were tested against the same cartilage plate in the C/C tribosystem, the order of the pins was randomized. Between the test runs, the flat cartilage plate was maintained in phosphate-buffered solution for 600 s to allow for full cartilage thickness recovery.<sup>15</sup>

Friction was quantified by calculating the Coulomb's CoF ( $\mu$  = friction force/axial force) at the onset ( $\mu_0$ ) and the end ( $\mu_{end}$ ) of each test using a custom-made MATLAB script (MATLAB R2021; The Math Works Inc.) (Figure 1E). According to the literature, the first three and last three coefficients were averaged, respectively.<sup>9</sup> This was performed separately for the stance and swing phases.

## 2.4 | Statistical analysis

The statistical analysis was performed using a statistics software package (GraphPad Prism 7.03; GraphPad Software Inc.). Gaussian distribution of the results was checked using Shapiro–Wilk testing, resulting in normal distribution of only  $\mu_{end}$  of the C/G tribosystem of the patient's samples. Consequently, nonparametric statistical tests were applied. Three comparisons were made per tribosystem:

- *Level of degeneration:* Mann–Whitney testing was applied to examine differences between the mildly and severely degenerated samples.
- *Gait phase:* Differences in the CoF between the stance and swing phase condition were analyzed using Wilcoxon testing.
- *Time of testing:* Differences between  $\mu_0$  and  $\mu_{end}$  were elaborated using Wilcoxon testing.



**FIGURE 2** Mean  $\pm$  SD values of the coefficient of friction ( $\mu$ ) assessed in the cartilage against cartilage (C/C) tribosystem for the mildly (orange) and severely (blue) degenerated samples. Friction was quantified by averaging the first three cycles ( $\mu_0$ ) and last three cycles ( $\mu_{end}$ ) of a total test time of 600 s. This was performed for the simulated stance and swing phases. Nonparametric statistical tests: \* $p < 0.05$ .

## 3 | RESULTS

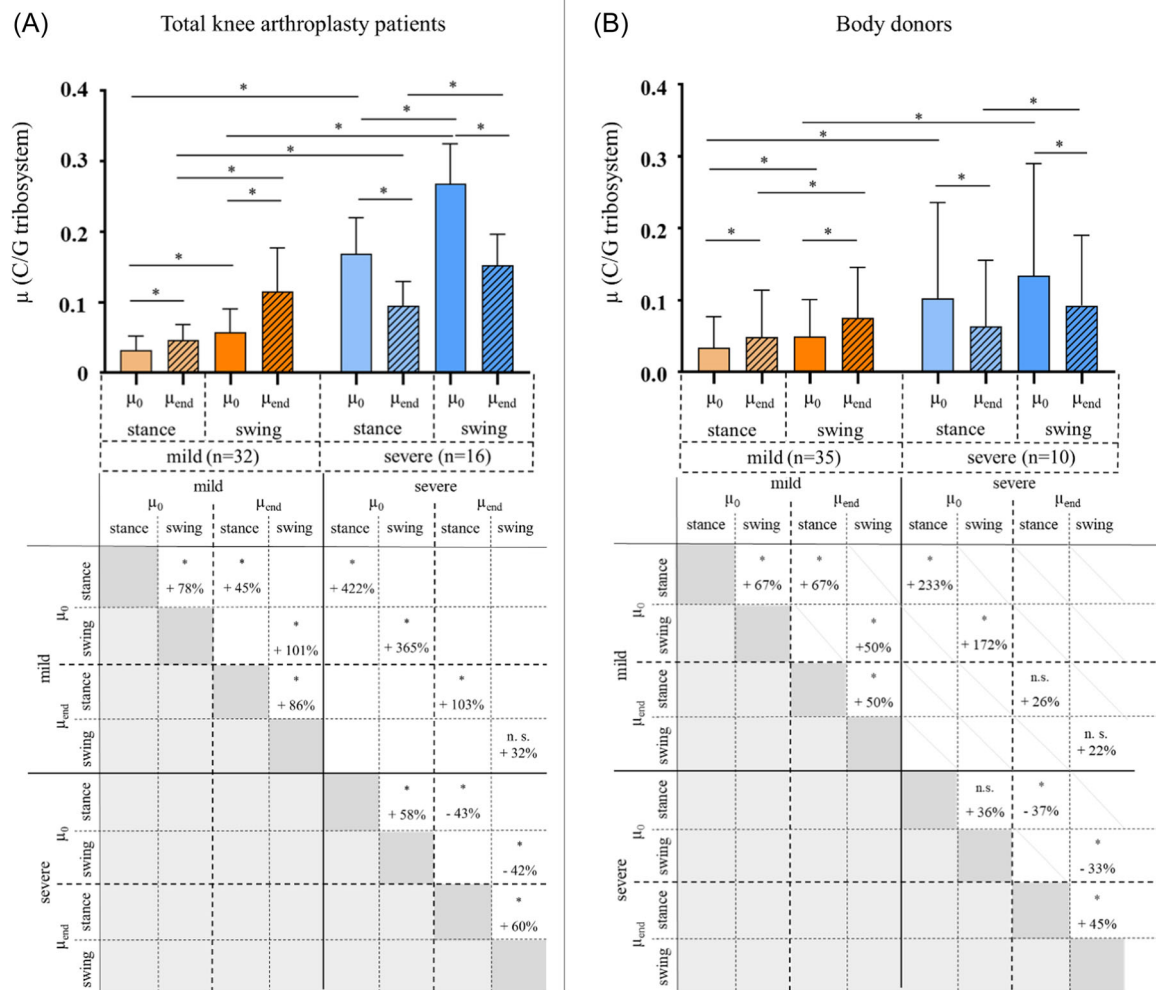
### 3.1 | C/C tribosystem

When testing cartilage against cartilage, the comparison of  $\mu_0$  and  $\mu_{end}$  using nonparametric statistical analyses revealed no significant differences ( $p > 0.05$ ) (Figure 2). There were no CoF differences ( $p > 0.05$ ) for the comparison between the stance phase and swing phase conditions, neither for  $\mu_0$  nor  $\mu_{end}$ . Using Wilcoxon testing, no statistical differences ( $p > 0.05$ ) were found between the CoF of the mildly and severely degenerated groups. Descriptive statistics showed that friction in the severely degenerated group was nonsignificantly higher than in the mildly degenerated group.

### 3.2 | C/G tribosystem

In the mildly degenerated group, Wilcoxon testing revealed significantly higher  $\mu_{end}$  values than  $\mu_0$  values under stance phase and swing phase conditions for both, the patients' samples (Figure 3A) and body donor samples (Figure 3B). Under swing phase conditions, the CoF was always statistically higher than under stance phase conditions, both, for  $\mu_0$  and  $\mu_{end}$ . This was evident for both, the patients' and body donor samples. In the severely degenerated group of the patient's samples, nonparametric statistical analyses revealed that  $\mu_{end}$  was significantly lower compared to  $\mu_0$ , for both, the stance and swing phase conditions, respectively. In the severely degenerated group of the body donor samples,  $\mu_{end}$  was also statistically lower under stance phase and swing phase conditions. When comparing the CoF under swing phase and stance phase conditions,





**FIGURE 3** Mean  $\pm$  SD values of the coefficient of friction ( $\mu$ ) assessed in the cartilage against glass (C/G) tribosystem for the mildly (orange) and severely (blue) degenerated samples. (A) Results of the total knee arthroplasty patients' samples and (B) results of the body donor samples, which were tested against cartilage in a first test run. Friction was quantified at the beginning of the test ( $\mu_0$ ) and at the end of the test after 600 s ( $\mu_{end}$ ) both, for the stance and swing phases. The tables show the percentage change for the performed statistical comparisons. Nonparametric statistical tests with  $*p < 0.05$ . ns, not significant.

significantly higher values were found under swing phase conditions for both,  $\mu_0$  and  $\mu_{end}$ . This was evident for the patients' and body donor samples. In the patients' sample group, the severely degenerated samples indicated a significantly higher  $\mu_0$  and  $\mu_{end}$  in comparison to the mildly degenerated ones, except  $\mu_{end}$  under swing phase conditions. For the body donor samples, the CoF of the severely degenerated group was statistically higher for  $\mu_0$  under stance phase and swing phase conditions compared to the corresponding mildly degenerated samples.

## 4 | DISCUSSION

In healthy cartilage, the friction properties of AC are attributed to two predominant lubrication regimes: interstitial fluid pressurization (IFP) and boundary lubrication.<sup>6</sup> It is believed that an increased surface

roughness of samples with a high OA score promote the dominance of friction mechanisms like asperity deformation and adhesion.<sup>5</sup> These are characterized by higher friction compared to energy dissipation caused by shearing of a boundary lubrication layer.<sup>5</sup> In tribological in vitro tests, the different lubrication regimes applied can be guided by the used articulating friction partners. Boundary lubrication can be achieved by testing cartilage against glass, whereby testing cartilage against cartilage promotes sustained IFP.<sup>6</sup> In vivo, friction is correlated with hydrodynamic phenomena that are determined by the relative velocity between the articulating surfaces in the knee, which can readily exceed 100 mm/s.<sup>13</sup> Consequently, testing velocity, contact pressure, and lubricant are key factors for tribological testing of cartilage in vitro.<sup>9,13</sup> Previous studies are limited by not establishing gait-like loading conditions (Table 2) and most notably, applying a low sliding velocity of 1 mm/s.<sup>5,6</sup> To the best of the authors' knowledge, this is the first study that applied a

**TABLE 2** Overview of the different testing conditions used in the present study and other friction studies on degenerated knee joint cartilage against glass.

	Present study		Neu et al. <sup>5</sup>	Caligaris et al. <sup>6</sup>	
Velocity (mm/s)	Stance phase: Max: 50	Swing phase: Max: 80	1	1	
Contact pressure (MPa)	Stance phase: 0.9	Swing phase: 0.2	0.1	0.5	
Sample Lubricant	Tibial cartilage Synthetic SF	Femoral cartilage PBS	Tibial cartilage Bovine SF	PBS	
CoF	Stance phase	Swing phase			
	Mild: 0.05	Mild: 0.12	Lowest OA score: ~0.12 <sup>a</sup>	Less OA: ~0.04 <sup>a</sup>	Less OA: ~0.14 <sup>a</sup>
	Severel: 0.1	Severe: 0.17	Highest OA score: ~0.28 <sup>a</sup>	More OA: ~0.04 <sup>a</sup>	More OA: ~0.10 <sup>a</sup>

Abbreviations: CoF, coefficient of friction; OA, osteoarthritis; PBS, phosphate-buffered solution; SF, synovial fluid.

<sup>a</sup>Values derived from results graph.

dynamic pin-on-plate friction tester to objectively assess the CoF of two different tribosystems under gait-like loading conditions.

The most significant finding of our study is that the C/G tribosystem indicated a significantly higher CoF for the severely degenerated samples compared to the mildly degenerated ones, whereas the C/C tribosystem indicated nonsignificant effects under the same test conditions. In our C/C tribosystem tests, no differences between  $\mu_0$  and  $\mu_{end}$  were found. It is likely that the continuous migration of the cartilage pin over the cartilage plate sustained the friction-minimizing IFP.<sup>16</sup> In addition, no differences between the CoF under stance phase and swing phase conditions were detected. This is in contrast with findings from Warnecke et al., who investigated healthy bovine cartilage in a C/C tribosystem using the same gait-like loading conditions.<sup>9</sup> Under swing phase conditions, our CoFs were comparable with those of the healthy bovine samples. However, under stance phase conditions, our degenerated human samples indicated a higher CoF.<sup>9</sup> This suggested that the degeneration mainly affects friction under stance phase conditions. This finding might be a critical determinant for predicting disease progression,<sup>17</sup> because cartilage is exposed to particularly high loads during the stance phase.<sup>7</sup> In the C/C tribosystem, the comparison of the mildly and severely degenerated groups revealed no differences in the CoF. Similar findings were reported by Caligaris et al. when testing tibial cartilage against femoral cartilage from osteoarthritic human knee joints. According to the authors, the CoF is strongly regulated by the IFP.<sup>6</sup> They analyzed the effect of degeneration on the IFP by estimating the Peclet number:  $P_e = V \times h / H_A \times k$  ( $V$  = migration speed,  $h$  = cartilage thickness,  $H_A$  = aggregate modulus,  $k$  = hydraulic permeability). Here, the friction coefficient of cartilage tissue remains low if  $P_e$  is sufficiently greater than unity.<sup>6</sup> The resulting high IFP results from the interstitial fluid inertia, caused by trapping the fluid in the cartilage matrix while the joint contact progresses during knee joint motion. Deterioration of the cartilage matrix during OA progression increases  $k$  while HA decreases, thus, resulting in an altered fluid flow behavior. Nevertheless, the  $P_e$  calculated by Caligaris et al. ( $V = 1$  mm/s and  $h \sim 2$  mm) was still much greater than unity, thus, resulting in a constant CoF, even during cartilage degeneration. Using the same values for  $k$  ( $k = 3.5 \times 10^{-4}$  mm<sup>4</sup>/N × s<sup>6</sup>),  $H_A$  (mild OA:

$H_A = 1.12$  MPa, severe OA:  $H_A = 0.24$  MPa<sup>6</sup>) and  $h$  ( $h \sim 2$  mm), but a higher migration speed ( $V = 80$  mm/s) in the current study resulted in  $P_e$  values much greater than unity (mild OA:  $P \sim 408,000$ , severe OA:  $P \sim 1,900,000$ ). Consequently, we concur that degenerated human C/C tribosystems can still maintain the friction-reducing IFP.<sup>6</sup>

In our C/G tribosystem, we found an increase of friction over time for the mildly degenerated samples, because the CoF at the end of the test ( $\mu_{end}$ ) was higher than at the beginning ( $\mu_0$ ). Other authors also previously agreed that loading of a cartilage pin against a glass plate drives unmitigated IFP loss during motion, leading to increased friction.<sup>5,18</sup> Interestingly, the opposite finding was observed in our tests with the severely degenerated group. Here, reduced friction might be attributable to an increased fluid exudation-aided lubrication between the cartilage pin and the glass surface.<sup>19</sup> Additionally, the permeability of degenerated cartilage as well as its water content increases with OA severity, which is associated with a higher fluid flow.<sup>2,20</sup> Overall, we found that severely degenerated samples exhibited higher friction compared to the mildly degenerated ones in our C/G tribosystem. Our gait-like loading profile replicated the sliding environment in the joint in a more physiologic way than in previous studies.

This study is not without limitations. First, we sourced the biosamples for the C/C tribosystem and C/G tribosystems both from body donors and TKA patients, respectively, which could introduce systematic error. Second, no SF was extracted from the knee joints, neither from the TKA patients by the surgeon, nor from the body donor knees by the researchers. For this reason, synthetic SF based on the composition of healthy SF was used in all experiments.<sup>14</sup> Nevertheless, in OA knees the composition of the SF is different from healthy SF.<sup>1</sup> In detail, the hyaluronic acid concentration and molecular weight decreases, the total protein concentration increases, while the lubricin content is controversial.<sup>14</sup> Therefore, the use of the synthetic SF in the current study might have resulted in slightly improved friction coefficients compared to the real in-vivo situation.<sup>21</sup> To simulate conditions as closely as possible to the in vivo situation, we recommend to develop a synthetic SF that mirrors the properties of degenerated human SF for future in vitro friction studies on OA samples. We are aware of the fact that cartilage against glass reflects a

nonphysiological material pairing.<sup>11</sup> By investigating both the C/G and C/C tribosystems, we were able to directly compare the respective friction outcome. On the basis of our results, care should be taken when transferring findings from C/G tribosystems to the in vivo friction behavior.

By testing the cartilage pins of the C/C tribosystem against glass in a second test run, we demonstrated that cartilage pins extracted from the body donor knee joints exhibited comparable friction behavior to the patients' samples. Overall, using a pin-on-plate tribometer requires the extraction of the cartilage out of the tissue composite and is, therefore, a simplification of the complex in vitro knee joint tribomechanics.<sup>19</sup> Therefore, it remains unknown whether knee joint friction alters with degeneration and should be investigated in future studies.

OA has a multifactorial etiology which is still not fully understood.<sup>22</sup> Investigating whether friction is one of the contributing factors in the curse of OA can help to better understand the progression of this disease. This understanding is necessary for the development and improvement of therapeutic approaches. Currently, OA can be treated with therapeutics that target joint friction/lubrication, like intra-articular injection of hyaluronic acid.<sup>23</sup> However, the tribological efficacy of injectable hyaluronic acids are frequently investigated in cartilage against glass tribosystems and/or under very simplified testing conditions.<sup>23–25</sup> On the basis of our findings, we recommend further research of such therapies and their presumed friction-minimizing effects in vitro. This can only be reliably assessed if gait-like loading conditions as well as physiological material pairings are considered in such tribological in vitro tests.

## 5 | CONCLUSIONS AND OUTLOOK

The findings of the present in vitro tribological tests indicated no degeneration impact on cartilage-to-cartilage friction under gait-like loading simulations, which might be, from a tribological point of view, a possible explanation for “the relatively slow progression of the disease.”<sup>6</sup> However, complementary studies are required to fully understand the complex structure-tribomechanical-relationship of knee joint tissues during OA progression.

### AUTHOR CONTRIBUTIONS

Luisa de Roy and Andreas M. Seitz conceived the study. Luisa de Roy performed the sample preparation, tribological testing, data analysis, and statistics. Martin Faschingbauer collected the tissue. Anita Ignatius provided expert opinion and helped in study design. Luisa de Roy drafted the manuscript. Klaus Schlickerrieder, Matthias Ruger, and Andreas M. Seitz helped in drafting the manuscript. All authors read and approved the final manuscript.

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### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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