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The choice of the femoral center of rotation affects material loss in total knee replacement wear testing – A parametric finite element study of ISO 14243-3

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ABSTRACT

A leading cause of long-term failure of total knee replacements (TKRs) is osteolysis caused by polyethylene wear particles. The current gold standard for preclinical wear testing of TKRs is mechanical knee simulators. The definition of the femoral center of flexion-extension rotation (CoR) has been identified as one possible source of variability within TKR wear tests, since the femoral curvature varies from distal to posterior. The magnitude of the influence on wear due to changes in location of femoral CoR has not been investigated in depth. During this study, a computational framework utilizing finite element analysis for modelling wear of TKRs was developed and used to investigate the influence of the location of femoral CoR on TKR polyethylene wear during standardized displacement controlled testing (ISO 14243-3:2014). The study was carried out using a 40-point Latin Hypercube Design of Experiments approach. Volumetric wear was highly correlated to femoral CoR in both the superior/inferior and anterior/posterior directions, with a stronger relationship in the superior/inferior direction. In addition, wear scars showing linear penetration were examined, with large differences in simulations at the extreme ends of the sampling region. In this study, it was found that variations in the location of the femoral center of rotation can represent a large source of variability in the preclinical testing and evaluation of the wear performance of total knee replacements. This study represents the first attempt at quantifying the effect on wear of different femoral center of rotations across a large sampling space.

1. Introduction

The current standard for treatment of end-stage knee osteoarthritis, a leading cause of disability globally, is a total knee replacement (TKR). The number of TKR surgeries performed annually is rising and is expected to reach 3.48 million in the United States by 2030 (Kurtz et al., 2007, 2014). Aseptic loosening remains a leading cause of TKR failure in the long term, of which much is attributable to osteolysis from the biological consequences of polyethylene wear debris (Fraser et al., 2015; Gallo et al., 2013). Although technological advances in polymer material science, component packaging, and sterilization in nitrogen have drastically reduced wear damage at the articulating surfaces, polyethylene wear debris remains a problem that can limit the lifetime of TKR past the second decade (Chakravarty et al., 2015). TKR design innovations are constant, and preclinical wear testing is performed to ensure that contemporary designs meet the standards set by their predecessors. Preclinical wear testing using mechanical knee simulators of new designs typically happens once the new design is far along in the process due to the time and expense of testing.

During mechanical testing, experimental error and variations in testing methodology can lead to variability in wear outcome. Some of the sources of experimental variability include the choice of displacement vs force control (Schwenke et al., 2009), differences in the lubricant (Brandt et al., 2010; Schwenke et al., 2005; Wang et al., 2004), the component starting position (Cheng et al., 2003; Zietz et al., 2015), and the effect of fluid absorption by the polyethylene, which can mask low wear rates (Schwenke et al., 2005). Another source of variability within TKR wear tests that has been identified is the definition of the femoral flexion/extension center of rotation (CoR) (Brockett et al., 2016; DesJardins and Rusly, 2011; Jennings et al., 2007; McEwen et al., 2005; Zietz et al., 2015). The location of femoral CoR location is also clinically relevant, as its position can vary surgically (Abdel et al., 2014; Rivière et al., 2017).

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It is challenging to define the femoral CoR as a fixed location because the curvature of the femoral component of a TKR can vary from distal to posterior. The International Standards Organization (ISO) standard for displacement-controlled knee wear simulation specifies the CoR as the intersection of the two lines perpendicular to the contact plane (contact normals) of the femoral condyle at 30° and 60° of flexion (Fig. 1) (ISO 14243-3, 2014). Other groups, including our own, have adopted different femoral CoRs. For example, the protocol developed at the University of Leeds takes the femoral distal radius as the CoR (Fig. 1) (Barnett et al., 2002, 2001; Brockett et al., 2016; McEwen et al., 2005, 2001). In our group, we take the centroid of the triangle formed by the contact normals of the femoral condyles at 0°, 30°, and 60° of flexion as the CoR (Fig. 1). This is done to approximate an average of the femoral radii in components such as the NexGen Cruciate-Retaining (CR) TKR (Zimmer-Biomet, Warsaw, IN) which have a changing radius along the entire range of flexion, and to better account for the various activities which engage both the distal and posterior part of the femoral condyles during load transfer. This has the effect of reducing the mechanical burden on the simulator by keeping the tibial component relatively level during flexion. In addition, to accommodate high flexion angles during tests such as stair ascent, it may be necessary to relocate the CoR farther posterior and inferior due to the specialized fixtures required to perform these tests. Furthermore, as the location of the CoR is identified manually for mechanical testing, additional sources of error are introduced during this step. The ISO standard itself acknowledges this by stating "The axis of rotation of the femoral component in the test will not exactly match the theoretical flexion/extension axis. The coincidence of the flexion/extension axis and the axis of rotation of the test machine should be as close as possible within reasonable laboratory practice" (ISO 14243-3, 2014). This may be a greater contributor to experimental error than previously realized.

Despite the research suggesting that the femoral CoR location may be a significant contributor to variability in wear of TKRs during simulator testing, the magnitude of the influence on wear due to changes in location of femoral CoR alone has not been investigated in depth. A study by Brockett et al compared femoral CoRs as defined by the Leeds protocol and the ISO displacement control standard, and showed little difference in wear between the two locations under identical input conditions (Brockett et al., 2016). It was found however, that in order to keep the femoral component in contact with the tibial insert, they had to reverse the direction of the anterior/posterior (AP) translation input. It was concluded that the location of the femoral CoR was an important factor influencing wear of TKRs during simulator testing. Pal et al incorporated the location of the femoral CoR into a larger probabilistic study under force control and showed a minor effect on wear from the superior/inferior (SI) location of the femoral flexion/extension axis (Pal et al., 2008). As the study by Pal et al was done under force control, it is difficult to extrapolate their results to displacement control. However, a change in femoral CoR may have more of an effect on wear under the fixed kinematics of displacement control, as opposed to force control where an implant would respond to a change in testing conditions with a change in kinematics. In addition, the displacement controlled ISO Standard and other displacement control testing protocols are widely used (Abdelgaied et al., 2017; Abdel-Jaber et al., 2016, 2015; Ash et al., 2000; Barnett et al., 2002, 2001; Brandt et al., 2011; Brockett et al., 2016, 2012; Galvin et al., 2009; McEwen et al., 2005; Mell et al., 2018; O'Brien et al., 2014; Okazaki et al., 2019; Popoola et al., 2010), making investigations into how the choice of CoR affects wear testing under displacement control all the more necessary.

It was therefore the motivation of this study to investigate the influence of the location of femoral CoR on TKR polyethylene wear, during displacement controlled testing. To perform a large parametric study in a timely and cost-efficient manner, a computational framework utilizing finite element analysis (FEA) for modelling wear of TKRs was developed and employed. During this investigation, we varied the AP and SI location of the femoral CoR in a FEA model of TKR wear using a Latin Hypercube Design of Experiments (DOE) approach. Linear regression was performed on the results from the DOE to generate a statistical model of wear based on the location of the femoral CoR, enabling wear prediction without running further FEA simulations.

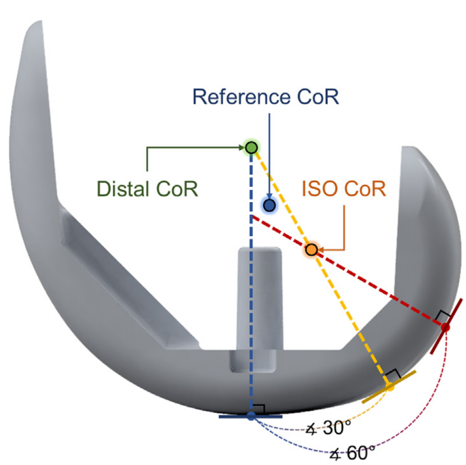


Fig. 1. Schematic showing the locations of various definitions of femoral center of rotation (CoR) used. The ISO Standard CoR is defined as intersection of the two lines perpendicular to the contact plane (contact normals) of the femoral condyle at 30° and 60° of flexion. The distal CoR is used in the protocol developed at the University of Leeds and uses the intersection of the contact normal for 0° and 30° of flexion (Brockett et al., 2016). The reference CoR is defined as the centroid of the triangle formed by the contact normals of the femoral condyles at 0°, 30°, and 60° of flexion.

2. Methods

We used a previously published and validated FEA model of TKR wear to estimate wear of the ultra-high molecular weight polyethylene (UHMWPE) tibial insert (Mell et al., 2018). The FEA model was created using CAD models of a NexGen Cruciate-Retaining TKR (Zimmer-Biomet, Warsaw, IN) and solved using Abaqus v2017/Standard. The cobalt-chromium-molybdenum (CoCrMo) component was modeled using 2nd order rigid surface elements. The UHMWPE tibial insert was modeled as a deformable body using 1st order hexahedral elements. The J2-plasticity model (Bergstrom et al., 2003; Bergström et al., 2002) was applied to the tibial insert and the elastic modulus was set to 1051 MPa (Bergström et al., 2002). The friction coefficient between the two articulating surfaces was set to 0.04 (Godest et al., 2002; Halloran et al., 2005; O'Brien et al., 2014). Contact was modeled using penalty contact and the surface-to-surface contact formulation. The wear model (Eq. (1), symbols in Table 1) is based on

Table 1
List of symbols used in the wear model (Eq. (1)).

SD	Sliding Direction (anterior direction is 0°)
V	Relative Sliding Velocity
F_f	Tangential (Friction) Force
θ	Initial Fibril Orientation
A	Element Area
t	Time
$\delta Work_x$	Unit work parallel to fibril direction
$\delta Work_y$	Unit work perpendicular to fibril direction

the concept of energy loss due to friction (Schwenke and Wimmer, 2013) and incorporated cross shear. Wear is determined according to unit work values where more unit work is required to remove material when translating along (parallel to) a polyethylene fibril than translating against (perpendicular to) a polyethylene fibril. Unit work values were set as: $\delta Work_x$ = 3.547E07 (perpendicular to fibril direction), $\delta Work_y$ = 3.855E08 (parallel to fibril direction). As in the previous publication (Mell et al., 2018), initial polyethylene fibril direction was determined for each contact node as the angle between the total work done in each direction, or the resultant direction of total frictional work.

$$WearDepth_{cycle} = \sum_{Starttime}^{Endtime} \frac{F_f(t) * V(t) * cos^2(|\theta - SD|)}{\delta Work_x} \times \frac{F_f(t) * V(t) * sin^2(|\theta - SD|)}{\delta Work_y} * \frac{\Delta t}{\Delta A} \quad (1)$$

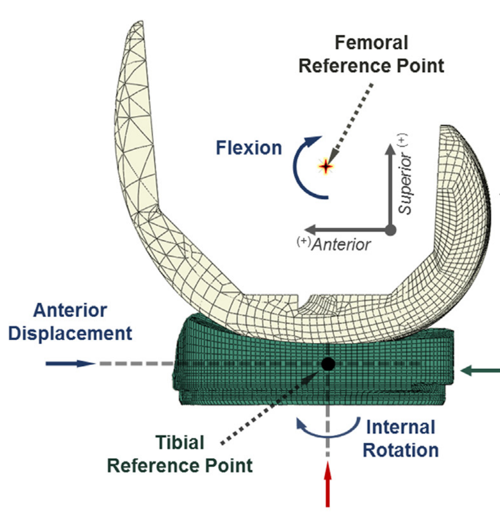
Model boundary conditions, kinematics, and loading were defined as described by the ISO standard for displacement control knee wear simulation (ISO 14243-3, 2014) (Fig. 2), with the femoral CoR positioned based on simulator testing done at our lab and hereafter referred to as the 'reference CoR' (Fig. 1). Flexion was applied through a reference axis located on the femur passing through this femoral CoR. AP translation and internal/external rotation were applied through a reference point located on the tibial insert. Adduction/abduction and medial/lateral translation of the tibial insert were left free. All other degrees of freedom were fixed. Axial loading was applied through the tibial component reference point.

To efficiently determine the effect of multiple parameters and their interactions in computational analyses, the Latin Hypercube design of experiments (DOE) technique is often employed (Dar et al., 2002; Dopico-González et al., 2010; Fitzpatrick et al., 2011; Rohlmann et al., 2010a, 2010b). The Latin Hypercube approach divides each parameter into n-evenly spaced increments, and then randomly combines them to generate n-unique combinations (Fig. 3). In this study, a 40-point Latin Hypercube DOE was used to investigate the effect of femoral CoR on volumetric wear. First, a sample space was defined to represent the variability of the femoral CoR. Using the reference CoR as the origin, the sample space was defined as a square spanning −10 mm to 10 mm in the AP direction and −10 mm to 10 mm in the SI direction. Here, negative is posterior and inferior, and positive is anterior and superior. The location of the sample points can be seen in (Fig. 3). A simulation was also run at the reference point (reference CoR). Wear simulations were scaled to one million cycles. The Isight Execution Engine (Dassault Systèmes, Waltham, MA) was used to control and run the DOE. The framework developed within Isight (Fig. 4) first runs an Abaqus model to determine the initial conditions of the model (initial fibril direction and plastic deformation). Next an Abaqus FEA model runs in parallel with the wear model to simulate one million wear cycles. Finally, the results from the wear step are output to Matlab to calculate wear scar parameters. The wear scar parameters calculated are the area, length (in the AP and medial/lateral direction), and perimeter of the worn regions on both the medial and lateral side of the tibial insert (Fig. 5). The angle between the medial and lateral wear scar centroids is also calculated (Fig. 5).

Pearson correlation coefficients are reported by Isight for all parameters to assess sensitivity of volumetric wear to the location of femoral CoR. Further analysis of volumetric wear was carried out using the Statistics and Machine Learning Toolbox of Matlab v2017a (The Mathworks Inc., Natick, MA). Linear regression was performed, and a model was fit to predict volumetric wear as a function of femoral CoR location. Stepwise linear regression up to second order terms and the interaction coefficient were used, with terms eliminated that did not contribute to the explained variance of the model. Statistical model coefficient of determination (R^2) value, root mean squared error (RMSE), and Analysis of Variance (ANOVA) are reported and used to evaluate the predictive capability of the regression model.

To test the robustness of the linear regression and the computational framework as a whole, the sample space was expanded to include the entire area inside the femoral component, −20 mm to 10 mm in the SI direction and −17 mm to 13 mm in the AP direction, and the entire analysis was performed again. The resulting linear regression was compared to that from the smaller and more clinically relevant sample space.

The wear model was previously validated by comparing FEA predicted wear rates for ISO 14243-3:2004 displacement control standard using a mechanical simulator, as reported in Mell et al. (2018). Additional validation of the computational framework for predicting wear was carried out in this study by comparing FEA predicted wear rates for two additional simulator tests: a wear test using the newest displacement control standard ISO 14243-3:2014 (ISO 14243-3, 2014), and a wear test using the average of 20 patient stair ascent waveforms reported in Freed et al (Freed



Component	Degree of Freedom	Constraint
Femoral Component Rigid Body Quadratic Surface Elements (4627)	Abduction Internal Rotation Anterior Displacement Medial Displacement Superior Displacement	Fixed
	Flexion	Applied Velocity
UHMWPE Tibial Insert Deformable Body Linear Hexahedral Elements (78108)	Flexion	Fixed
	Abduction Medial Displacement	Free
	Superior Displacement	Loaded
	Anterior Displacement Internal Rotation	Applied Velocity

Fig. 2. Finite element model loading and boundary conditions for a left-sided cruciate retaining TKR.

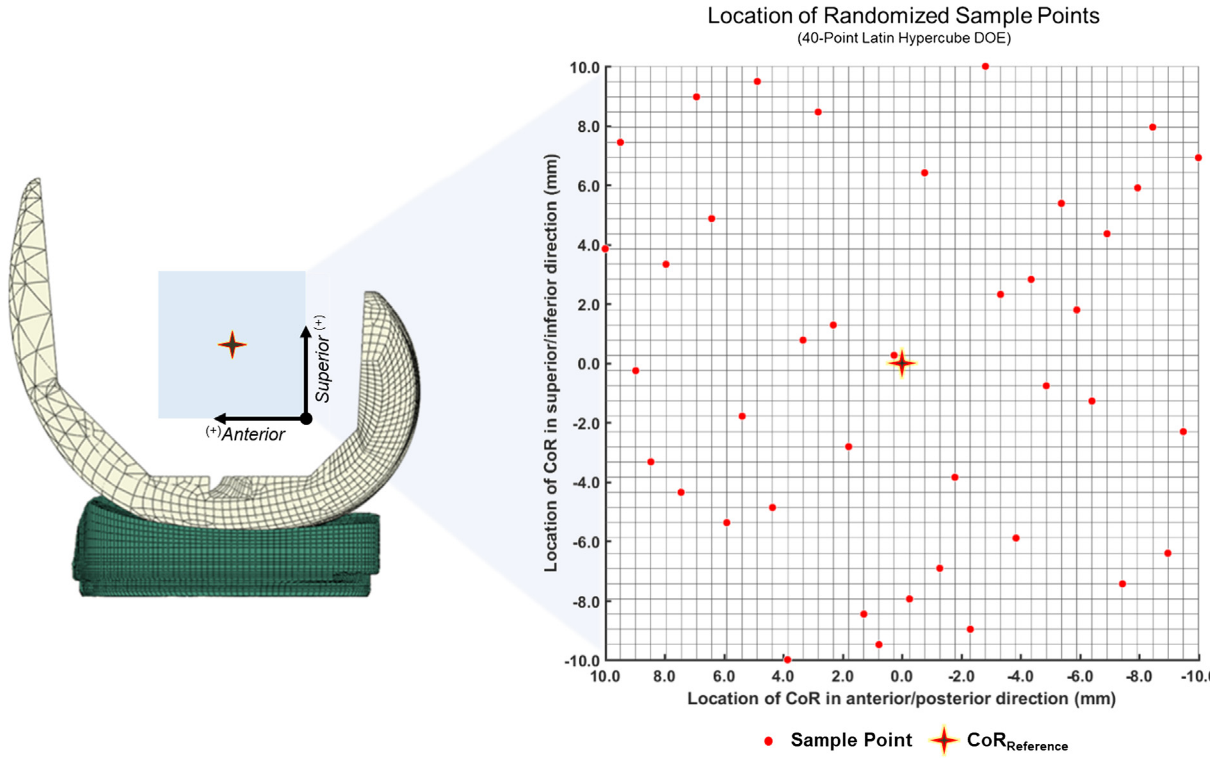


Fig. 3. Definition of sample region and location of ISO CoR and sample points generated by the 40-point Latin Hypercube DOE.

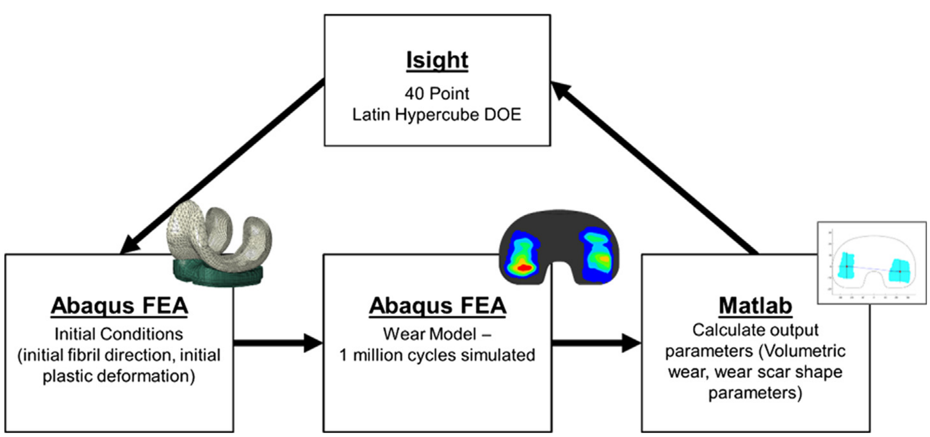
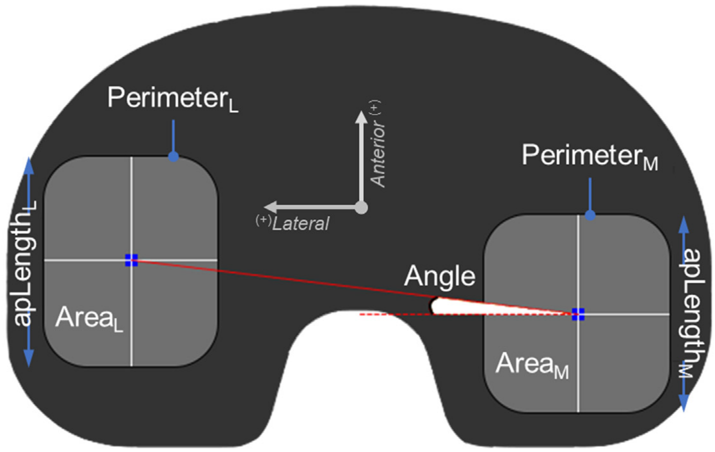


Fig. 4. Computational workflow. Isight generates the 40-point Latin Hypercube DOE and executes it. First, an FEA model is run in Abaqus to determine the initial conditions. Next, a wear step is performed and scaled to simulate one million gait cycles. Finally output parameters are calculated by a custom Matlab script. This process is repeated for each point generated by the DOE.

et al., 2017). A four-station knee wear simulator (Endolab, Rosenheim, Germany) was used to test polyethylene tibial liners (NexGen CR, Zimmer-Biomet, Warsaw, IN) under the two different kinematic conditions. All tests were performed in displacement control mode with one tibial liner acting as a soak control. Kinematics, loading, and degrees of freedom fixed and left free were identical to the FEA model described above (Fig. 2). Lubricant consisted of bovine serum (Life Technologies Corporation, Carlsbad, California) diluted with saline to a protein content of 30 g/L and pH of 7.6. Ethylenediaminetetraacetic acid (EDTA) was added at 200 mg/L. Testing was performed at 37° C. Tests were conducted at 1.0 Hz frequency. Testing was stopped every 0.5 million cycles for cleaning and weighing of the tibial liners. Gravimetric wear was compared between simulator-tested components and the wear predicted by the FEA model after 3 million cycles. The simulator-produced gravimetric wear was compared to FEA wear by examining the change in volume of the entire mesh over the course of the FEA simulation and converted to gravimetric wear using a density of 9.4E-7 kg/mm^3 (O'Brien et al., 2013).

3. Results

Volumetric wear and wear scar appearances varied depending on the location of the femoral CoR. Wear for the reference CoR was 4.45 mm^3/million cycles (MC). Wear reported from the Latin Hypercube DOE was as high as 6.00 mm^3/MC and as low as 4.07 mm^3/MC depending on the location of the femoral CoR. Volumetric wear was highly correlated to changes in the femoral CoR in the SI direction (r = 0.91), with more superior CoR locations



Parameter	Description
Angle	Angle between medial and lateral wear scar centroids (blue squares)
$apLength_L$	Length of the wear scar on the lateral side, in the AP direction
$apLength_M$	Length of the wear scar on the medial side, in the AP direction
$Area_L$	Area of the wear scar on the lateral side
$Area_M$	Area of the wear scar on the medial side
$Perimeter_L$	Perimeter of the wear scar on the lateral side
$Perimeter_M$	Perimeter of the wear scar on the medial side
$Area_{total}$*	Total area of the wear scar
VolumeChange*	Total volume change due to volumetric wear

**Not shown in reference figure*

Fig. 5. Definition of wear scar shape parameters. Note, a counter-clockwise angle is defined as positive.

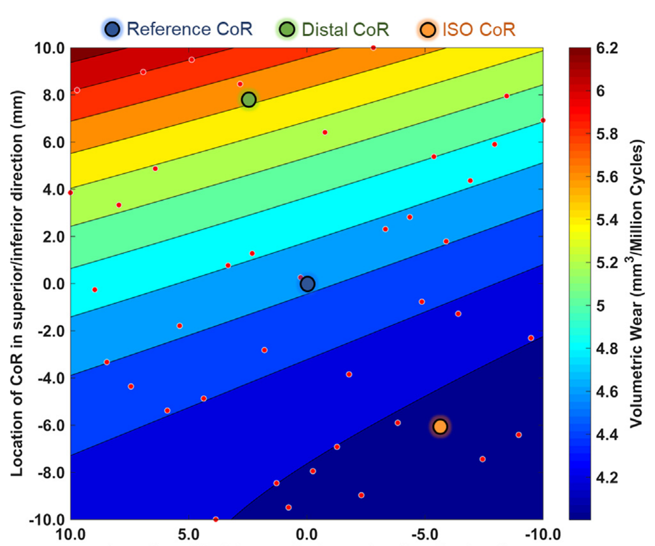


Fig. 6. Polynomial approximation of volumetric wear as a function of femoral center of rotation (CoR) location. Red dots represent sample points generated by the Latin Hypercube DOE, the results of which are used to determine the polynomial coefficients. The reference center of rotation is located at 0 mm anterior and 0 mm superior. The distal CoR is located at 2.4 mm anterior and 7.8 mm superior. The ISO Standard CoR is located 5.7 mm posterior and 6.0 mm inferior. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

producing more wear (Fig. 6). AP location of femoral CoR was weakly correlated with volumetric wear ($r = 0.35$), with more anterior CoR locations producing more wear (Table 2). Several wear scar parameters were strongly correlated with changes in femoral CoR as well. For example, the SI direction CoR location was highly correlated with wear scar area on the medial side ($r = -0.82$) and wear scar length in the AP direction on the medial side ($r = -0.81$). The location of the femoral CoR in the SI direction had stronger correlations with wear scar parameters than the AP direction. There was a large amount of variability seen in wear scar appearance including in location and areas of localized wear at the extreme ends of the sample space (Fig. 7).

The linear regression analysis produced a second order polynomial approximation (Eq. (2), Fig. 6) with $R^2 = 0.987$, an $RMSE = 0.0685$, and $p < 0.001$. Due to the lack of contribution to the explained variance in the statistical model, the second order term corresponding to the location of the femoral CoR in the AP direction was excluded from the model by the stepwise algorithm (Table 3). All terms included in the model, including the interaction term, were strongly significant (Table 3). The ANOVA results can be found in (Table 4).

$$VolumetricWear = 4.638 + 0.030 * CoR_{AP} + 0.086 * CoR_{SI} + 0.0015 * CoR_{AP} * CoR_{SI} + 0.0037 * CoR_{SI}^2 \quad (2)$$

The model predicted the mechanical simulator results within a reasonable degree of accuracy (Fig. 8). ISO 14243-3:2014 wear rates were 3.42 ± 0.814 mg/MC vs model prediction of 4.52 mg/MC. For the patient average stair ascent test, mechanical knee sim-

Table 2
Pearson Correlation Coefficients of wear scar shape parameters (Fig. 5) and total volumetric wear. Darker colors represent stronger correlations. Blue is a positive correlation and red is negative. CoR AP refers to the anterior/posterior direction while CoR SI refers to the superior/inferior direction of the femoral center of rotation.

	CoR AP Position	*CoR SI Position*
Angle	-0.32	-0.49
Lateral wear scar AP length	0.41	0.56
Medial wear scar AP length	0.073	-0.81
Lateral wear scar area	0.47	0.30
Medial wear scar area	0.10	-0.82
Lateral wear scar perimeter	0.18	0.89
Medial wear scar perimeter	0.34	-0.25
Total wear scar area	0.28	-0.55
Volumetric Wear	0.35	0.91

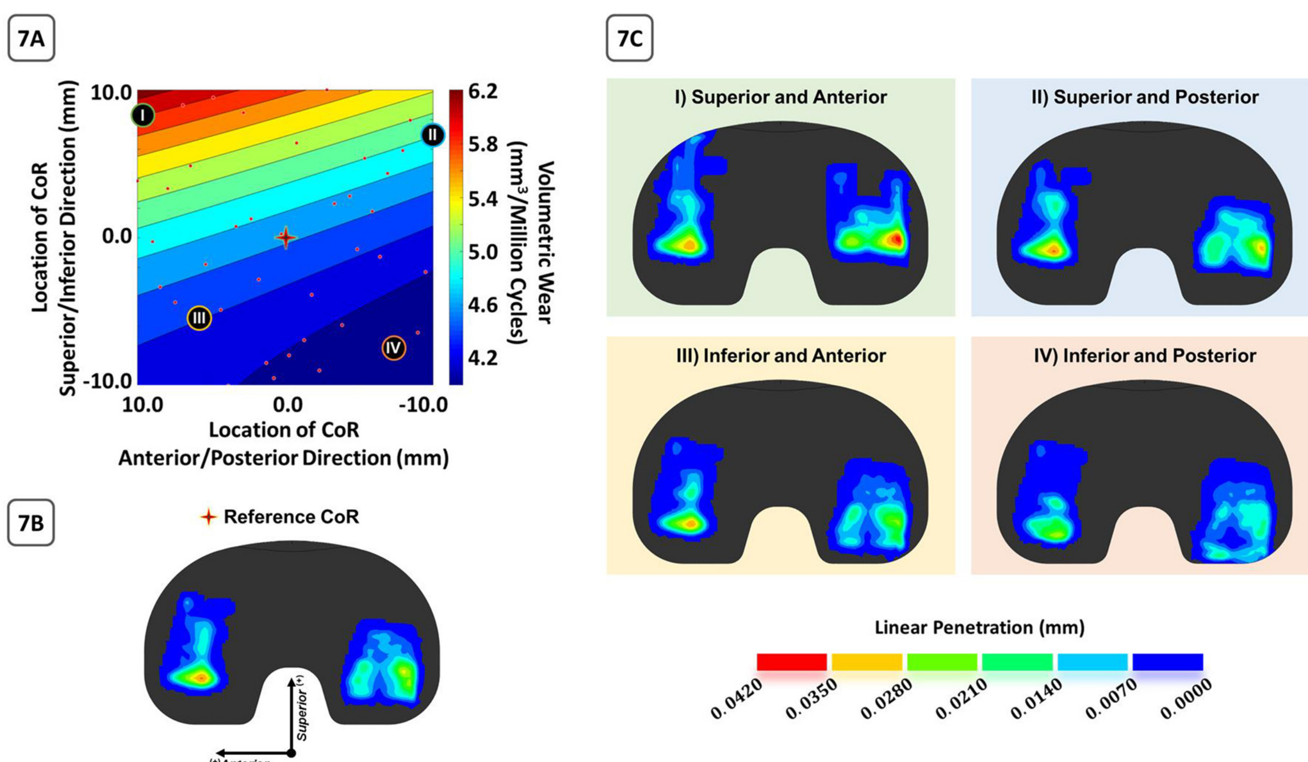


Fig. 7. Comparison of wear scars and linear penetration at the extreme ends of the sample space. Sample points examined are shown in (A). The wear scar for the Reference CoR is shown in (B), and the wear scar for locations I-IV in (C). Differences can be seen in both location and distribution of wear, particularly in the position of wear scars in the AP direction and location of maximum penetration.

ulator wear rates were 15.24 ± 0.79 mg/MC vs model prediction of 12.24 mg/MC. The R^2 of the wear model was 0.84. For the purpose of comparison, simulator and FEA model results for ISO 14243-3:2004 from Mell et al., 2018 are also shown in Fig. 8 (simulator-produced wear rate of 5.14 ± 2.18 mg/MC vs. a FEA model prediction of 8.40 mg/MC) (Mell et al., 2018).

Table 3
Comparison of linear regression results for the clinically relevant 10 mm square sample space and the expanded sample space used for verification of the analysis. Both polynomials have very similar coefficients, demonstrating the robustness of the results and the technique. AP CoR defines the AP location of the femoral center of rotation and SI CoR defines the SI location of the femoral center of rotation.

	Model coefficients	Standard error	t-Statistic	p-Value
Clinically relevant 10 mm × 10 mm square solution space				
Intercept	4.6375	0.0163	284.91	1.70E-60
AP CoR	0.0297	0.0019	15.65	2.27E-17
SI CoR	0.0856	0.0018	46.98	3.27E-33
SI CoR:AP CoR	0.0015	0.0003	4.31	1.26E-04
SI CoR^2	0.0037	0.0003	10.75	1.24E-12
Expanded solution space for model verification				
Intercept	4.6598	0.0256	181.73	1.15E-53
AP CoR	0.0286	0.0025	11.59	1.57E-13
SI CoR	0.0900	0.0037	24.49	1.30E-23
SI CoR:AP CoR	0.0012	0.0002	5.19	9.06E-06
SI CoR^2	0.0033	0.0003	11.91	7.22E-14

Table 4
ANOVA of model and linear and non-linear terms. The model is highly significant compared to a constant model.

	Sum of squares	Degrees of freedom	Mean squares	F-statistic	p-Value
Total	12.89	39	0.331		
Model	12.73	4	3.182	679.0	1.24E-32
Linear	12.05	2	6.026	1285.9	1.74E-33
Nonlinear	0.68	2	0.338	72.2	3.80E-13
Residual	0.16	35	0.005		

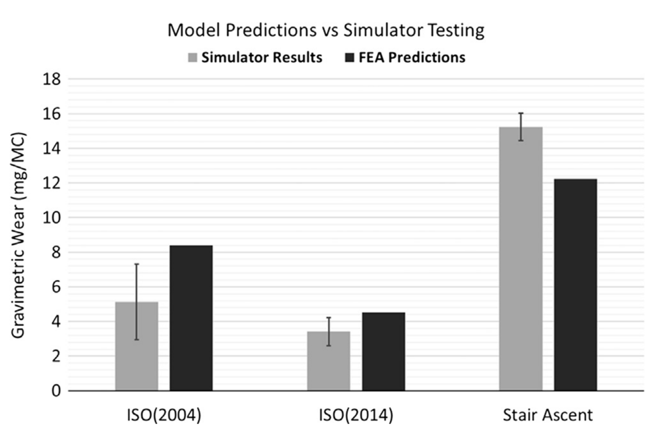


Fig. 8. Model validation. Comparison of 3 simulator experiments to FEA wear predictions. The computational wear predictions follow the relative trends for the experiments. The wear model had a high coefficient of determination ($R^2 = 0.84$) when compared to simulator tests. Results are reported in mg/million cycles (MC) for ISO 14243-3:2004 (ISO(2004)), ISO 14243-3:2014 (ISO(2014)), and a wear test using the average of 20 TKR patients stair ascent data as input (Stair Ascent). Error bars are ±standard deviation. ISO(2004) results are from (Mell et al., 2018).

4. Discussion

We developed a novel computational framework for efficiently performing large parametric studies of TKR wear. Using this method, we demonstrated that choice of femoral CoR can lower volumetric wear by 8.5% or increase volumetric wear by up to 35% within the investigated sample space and for this particular implant design. Examinations of the FEA predicted wear scars also show that wear scar location is sensitive to changes in the femoral CoR (Fig. 7). Further, the results show that volumetric wear and wear scar parameters are more sensitive to variations in the femoral CoR in the SI direction than changes in the AP direction (Fig. 6).

The linear regression fit the sample space well ($R^2 = 0.987$, $p < 0.001$) and the resulting polynomial approximation is useful to visualize and characterize the sample space as running additional FEA simulations is computationally expensive (Fig. 6). While the differences in wear for CoRs in the vicinity of the reference CoR were not great enough to account for all of the variability seen in wear results during simulator testing (McEwen et al., 2005; Pal et al., 2008), it was shown to be a significant source of variation that could manifest as experimental error. The results from this study suggest that femoral CoR positioning errors on the order of millimeters could be a significant source of variation in volumetric wear. In addition, for simulator tests of high flexion activities such as chair rising and sitting, no standardized location of the CoR is provided. In general, during high flexion activities, the CoR should be located farther posterior and inferior due to the smaller radii of the femoral posterior condyles (relative to the distal radii). Our results suggest that this would lead to lower wear than if an alternative CoR was used.

As discussed in the introduction, Brockett et al. previously compared two locations of femoral CoR under displacement control, the ISO standard and the Leeds group method (distal CoR), and concluded that the location of the CoR was a large factor influencing wear in TKR simulator testing (Brockett et al., 2016). When using predictions from our linear regression model, we find the difference between the distal CoR and the ISO Standard to be a comparatively large 1.5 mm^3/MC. Pal et al. used the location of femoral CoR as a parameter in a larger probabilistic study under force control, however did not directly report its influence on wear (Pal et al., 2008). They found that wear was only weakly sensitive to changes in the femoral CoR as compared to the other parameters studied, however as in our study, it was found that wear was more sensitive to changes in femoral CoR in the SI direction as compared to the AP direction.

Our coupled wear-FEA model had a high coefficient of determination when compared to experimental data ($R^2 = 0.84$), and we previously demonstrated the ability of the model to replicate the distribution of wear scars (Mell et al., 2018). Although the model compares favorably both qualitatively and quantitatively to experiments performed so far, there are several opportunities for further development of the framework. First, additional model validation in the form of experimental testing is underway. In a future study, we will use model predicted wear of component malalignment to determine an experimental test to run, in order to evaluate the predictive strength of the model. Second, for the investigation of sensitivity of TKA wear to femoral CoR, additional sources of variability are likely significant. For example, in our study the initial position of the femoral component relative to the tibial component was kept constant across all simulations. This is consistent with the ISO Standard definition of the component reference position (ISO 14243-3, 2014). In real world testing, particularly for a low to moderately conforming component such as the one used in this study, an effort would be made to manually center the contact on the polyethylene component—another source of experimental variability in volumetric wear. While the model does not perfectly replicate experimental testing results, the standard deviation for wear rates during mechanical testing can be large and helps explain the discrepancy between the model and the experiments. Large variability in wear rates have been reported, as high as ±5.9 mm^3/MC (McEwen et al., 2005). The standard deviations during our experimental testing were large as well, ranging from ±0.79 mg/MC, to as high as ±2.18 mg/MC. There are many sources of variability present in mechanical testing (Pal et al., 2008; Zietz et al., 2015), that were not tightly controlled in the current study. For example, the component starting position could be an additional source of inconsistency during TKR simulator studies. Due to the relative flatness of the NexGen tibial components used in this study, it is difficult to consistently find the dwell point on the tibial plateau to rest the femoral component. Further, medio-lateral and varus/valgus movements on the simulator were not controlled, but could freely adjust, hence causing variation in motion patterns. Future FEA studies could investigate the wear contribution of these factors.

There are several limitations to this study in addition to those already discussed. First, the results of this study are limited to the displacement controlled ISO Standard. While displacement control may be more desirable for implant designs which are less constrained and where movement is less restrictive, such as the NexGen CR (Zimmer-Biomet, Warsaw, IN) implants used in this study, displacement control may be also be more affected by changes in boundary conditions such as the location of femoral CoR. As this study was focused on displacement controlled mechanical testing, a future study comparing force control to displacement control should be performed. Another limitation is that this study was done using a single implant model. It is unclear how these results would translate to another implant, and a future study using multiple implant types such as a single radius design or a more highly conforming implant should be conducted. Finally, this study was performed using a numerical model of TKR wear. While numerical models offer a significant advantage in time and resources as compared to mechanical testing, they only offer a prediction and should be used to supplement to mechanical testing and not as a replacement.

In conclusion, variations in the location of the femoral CoR can represent a source of variability in the preclinical testing and evaluation of the wear performance of TKRs. Care should be taken when selecting a femoral CoR for a mechanical wear test and its position marked carefully. This variability should be kept in mind when comparing wear results between groups, simulators, or studies that may have used different femoral CoRs. This study represents the first attempt at quantifying the effect on wear of different femoral center of rotations across a large sample space.

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Conflict of interest statement

The authors have no conflicts to disclose.

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