Identification of material parameters based on Mohr-Coulomb failure criterion for bisphosphonate treated canine vertebral cancellous bone

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Abstract

Nanoindentation has been widely used to study bone tissue mechanical properties. The common method and equations for analyzing nanoindentation, developed by Oliver and Pharr, are based on the assumption that the material is linearly elastic. In the present study, we adjusted the constraint of linearly elastic behavior and use nonlinear finite element analysis to determine the change in cancellous bone material properties caused by bisphosphonate treatment, based on an isotropic form of the Mohr-Coulomb failure model. Thirty-three canine lumbar vertebrae were used in this study. The dogs were treated daily for 1 year with oral doses of alendronate, risendronate, or saline vehicle at doses consistent, on a mg/kg basis, to those used clinically for the treatment of post-menopausal osteoporosis. Two sets of elastic modulus and hardness values were calculated for each specimen using the Continuous Stiffness Measurement (CSM) method (E\textsubscript{CSM} and H\textsubscript{CSM}) from the loading segment and the Oliver-Pharr method (E\textsubscript{O-P} and H\textsubscript{O-P}) from the unloading segment, respectively. Young’s modulus (E\textsubscript{FE}), cohesion (c), and friction angle (\phi) were identified using a finite element model for each nanoindentation. The bone material properties were compared among groups and between methods for property identification. Bisphosphonate treatment had a significant effect on several of the material parameters. In particular, Oliver-Pharr hardness was larger for both the risendronate- and alendronate-treated groups compared to vehicle and the Mohr-Coulomb cohesion was larger for the risendronate-treated compared to vehicle. This result suggests that bisphosphonate treatment increases the hardness and shear strength of bone tissue. Shear strength was linearly predicted by modulus and hardness measured by the Oliver-Pharr method (r\textsuperscript{2}=0.99). These results

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show that bisphosphonate-induced changes in Mohr-Coulomb material properties, including tissue shear cohesive strength, can be accurately calculated from Oliver-Pharr measurements of Young’s modulus and hardness.

Keywords
Material parameter identification; Mohr-Coulomb failure criterion; Nanoindentation; Trabecular bone; Finite element method

Introduction
Nanoindentation has been widely used to study tissue mechanical properties (elastic modulus and hardness) of both cortical [1–3] and cancellous bone [4–8]. The method and equations used to calculate bone tissue modulus and hardness in these studies were based on the assumption that the bone was linearly elastic and, therefore, the material properties remained constant independent of the indentation depth [9]. In the present study, we altered the constraint of linearly elastic behavior and use nonlinear finite element analysis to determine the change in cancellous bone material properties caused by drug treatment.

Bone tissue ultrastructure and the accumulation of damage at the ultrastructural level are not completely understood [3]. In particular, the failure criterion for bone tissue at the nanoscopic level was not known until recently. Tai et al. [3] determined that a cohesive-frictional model, specifically a Mohr-Coulomb pressure dependent failure criterion (in short, Mohr-Coulomb criterion), could accurately reproduce experimental force-displacement data measured using an atomic force microscope.

In Tai et al.’s study [3], they performed a series of indentation tests on bovine cortical bone tissue using an atomic force microscope. To identify the failure properties of the tissue, they used a finite element model of the indentation process. In their models they assumed a Young’s modulus of GPa and a Poisson’s ratio of 0.3. They showed that the models matched the experimental data when the friction angle (ϕ) and the cohesion (c) were set to 15° and 100MPa (Fig. 1), respectively. This was an important study, because it demonstrates that the Mohr-Coulomb criterion appears to be a good material model for compressive loading of bone tissue. A limitation of the study is that their approach required assuming that the Young’s modulus was fixed. In the current study, we have developed a method to determine all of the material parameters (modulus, cohesion, friction angle) except the Poisson’s ratio, which we left as unchanged.

Bisphosphonates (BPs) increase average mineralization of trabecular bone tissue [10–12]. Studies in beagle dogs, using doses at and above those used for treatment of osteoporosis, have shown BP treatment also results in microdamage accumulation and a reduction in bone toughness in vertebrae [13–16]. With an increase in both bone mineralization and microdamage, it is not clear how BPs might affect bone tissue nano-level mechanical properties (elastic modulus and hardness), since mineralization and microdamage have opposite effects. The results of the current study are intended to partially clarify this mixed effect of increasing both bone tissue mineralization and microdamage because nanoindentation can directly measure the bone tissue mechanical properties.

In this study, we (1) develop a new method for identifying the material parameters of the Mohr-Coulomb criterion for bone tissue using nanoindentation; (2) determine whether the material properties identified by either of the methods (Oliver-Pharr (O-P), Continuous Stiffness Measurement (CSM), and the Mohr-Coulomb FE model) differ with bisphosphonate treatment;
(3) compare the material property results among the O-P, CSM and FE method, and (4) demonstrate that the material properties from the finite element results can be predicted using the Oliver-Pharr experimental results.

Materials and Methods

Bone samples

Thirty-three canine second lumbar vertebrae were used in this study. The specimens were collected during a previously completed BP treatment study [14]. Briefly, the beagle dogs were treated daily for 1 year with oral doses of alendronate sodium (ALN, 0.20 mg/kg/day, n=12), risedronate sodium (RIS, 0.10 mg/kg/day, n=10), or saline vehicle (VEH, n=11). These bisphosphonate doses approximate, on a mg/kg basis, those used for the treatment of post-menopausal osteoporosis.

The vertebrae were collected after one year of treatment and histologically processed, embedded in PMMA, and analyzed for standard bone histomorphometry [14]. The cut surface of each embedded specimen block was polished with successively finer grades of carborundum paper and polishing powders before nanoindentation.

Nanoindentation

A Nano Indenter XP system (MTS Nano Instruments, Oak Ridge, TN) was employed to measure force and displacement during indentation of the polished bone specimen. Two sites were selected randomly in two different trabeculae of each specimen using an optical microscope at 50× magnification. Using a Berkovich shape diamond indenter tip (E_i=1141 GPa, v_i=0.07), one hundred nanoindentation tests were performed at each site using a 10x10 array pattern, with 15 µm spacing in both horizontal and vertical directions. The 15 µm spacing was selected to avoid interference between different separate indentation tests, each of which left a 3 µm triangular residual cavity. The indentation procedure was under displacement control. After the surface was identified, the indenter was advanced to 500 nm at a speed of 10 nm/s to avoid the effect of bone surface roughness. A typical indentation load-displacement curve included a loading segment, a 10 second holding period at maximum load, an unloading segment, and a 50 second holding period for thermal drift measurement at 10% of maximum load (Fig. 2). Thermal drift of the nanoindentation system was calculated from the thermal drift holding segment, and used to correct modulus and hardness calculation. Due to some technical issues, such as surface approaching failure, between 60–200 nanoindentation tests finished successfully for each specimen.

A technique named Continuous Stiffness Measurement (CSM) was used to measure stiffness (S_{CSM}) during the primary loading procedure using a 2 nm magnitude oscillation with a frequency of 45 Hz. With the known frequency and the measured displacement, phase angles and force, S_{CSM} and thereafter elastic modulus and hardness can be calculated as continual functions of surface penetration depth. The unloading segment of the load-displacement curve was analyzed using a mathematical solution derived by Oliver and Pharr [8]. Two sets of elastic modulus and hardness were calculated for each specimen using the CSM method (E_{CSM} and H_{CSM}) from the loading segment [8,17] and the Oliver-Pharr method (E_{O-P} and H_{O-P}) from the unloading segment [1,6,8,17], respectively. E_{CSM} and H_{CSM} were averaged from 200 to 500 nm in the modulus-displacement curve and the hardness-displacement curve, respectively, because the initial calculations of modulus and hardness were unstable.

Finite element model

One sixth of the nanoindentation geometry was modeled as a three-dimensional 22 finite element model in ABAQUS (ABAQUS Inc., Providence, RI) (Fig. 3). The Berkovich tip was
modeled as a rigid surface. A convergence study was performed to determine the required mesh size for the model. The height of modeled bone tissue was 10 µm and the radius was 16 µm. There were 300 elements in the rigid tip surface, and 5040 elements in the bone tissue block. The contact surface was assumed to be frictionless.

The isotropic form of the Mohr-Coulomb material model (Fig. 1), is controlled 6 with four parameters: (1) Young’s modulus (E), (2) Poisson’s ratio, (3) cohesion (c), and (4) friction angle (ϕ). The two yield parameters (c and ϕ) determine the stresses at which the material fails. Bone tissue elastic modulus (E_{FE}), and Mohr-Coulomb criterion parameters (cohesion c and friction angle ϕ) were chosen in a systematic fashion so that the results of the FE calculation (peak load and unloading stiffness) spanned the observed experimental results. No viscoelastic material property was incorporated into the finite element model, so the holding segment at the maximum load could not be simulated. In total, 1552 finite element simulations were performed (Table 1).

**Material parameter identification using the Finite Element Results**

By systematically varying the bone tissue elastic modulus (E_{FE}), cohesion (c) and friction angle (ϕ) of the Mohr-Coulomb material model, we were able to generate model data from the finite element results that could be matched with the experimental results. Pairs of finite element peak load and unloading stiffness were matched with experimental values from a particular nanoindentation experiment using the following selection radius (R):

\[
R > \sqrt{\left(\frac{W_S(F_{FE} - F_{Exp})}{2} + \frac{W_S(S_{FE} - S_{Exp})}{2}\right)}
\]

where \(F_{FE}\) and \(F_{Exp}\) were the maximum loads from FE simulation and experiment, respectively, and \(S_{FE}\) and \(S_{Exp}\) were the initial unloading slopes from FE simulation and experiment, respectively. From the 1552 finite element results, we were able to segregate those similar to the actual test using Eqn. 1. The parameters \(w_F\) and \(w_S\) were used to set the relative importance of unloading slope and force in grouping the finite element results with each experimental result. In this study, \(w_F\) was selected as 1, and \(w_S\) as 100 in order that the initial unloading slope and the maximum load were represented by numbers of the same order of magnitude.

For each set of experimental nanoindentation results, a region was defined using the selection radius. If a pair of maximum load and initial unloading slope from FE simulation fell into the region, the FE simulation was considered as a matched FE simulation to the nanoindentation. The identified elastic modulus, cohesion and friction angle for each experimental nanoindentation were calculated by averaging of the material properties of the matched FE simulations (Fig. 4).

**Validation of the parameter identification method**

Whether the averaging method produced valid results was tested using four randomly selected nanoindentation tests from each group, totally tests. New FE models were built using the identified E_{FE}, c and ϕ for the nanoindentation with a selection radius of 0.25. The maximum loads of the selected nanoindentation ranged 20 from 2.36 to 6.91 mN and the initial unloading slopes were from 0.260 to 0.841 mN/nm. The maximum loads and initial unloading slopes were compared to the counterparts from experiment.

The differences in the maximum loads from FE with experiment were from −0.50% to 2.15%, and that in the initial unloading slopes were from −4.20% to 9.87%. The linear regression for the maximum loads and the initial unloading slopes from FE and experiment were:

\[
F_{FE} = 1.0042F_{Exp}(r^2=0.9987) \quad \text{and}
\]

\[
W_S(F_{FE} - F_{Exp})^2 + W_S(S_{FE} - S_{Exp})^2
\]

\(1\)
\[ S_{FE} = 0.9859 S_{Exp} (r^2 = 0.9924), \]  

where \( F_{FE} \) and \( F_{Exp} \) were the maximum loads from FE simulation and experiment of the selected specimens, respectively, \( S_{FE} \) and \( S_{Exp} \) were the initial unloading slopes from FE simulation and experiment of the selected specimens, respectively. Both the slopes of both linear regressions and \( r^2 \) values were closed to 1, which indicated the parameters identified using the averaging method were valid.

**Determination of the selection radius**

The selection radius was tested at 0.25 and 0.5 to determine whether it had an effect on the results. Two sets of identified \( E_{FE} \), \( c \) and \( \phi \) were identified and compared between the two different selection radiuses using linear regression:

\[ E_{FE}|_{R=0.50} = 0.9988 \cdot E_{FE}|_{R=0.25} (r^2 = 0.9996), \]  

\[ c|_{R=0.50} = 1.0091 \cdot c|_{R=0.25} (r^2 = 0.9975) \text{and} \]  

\[ \phi|_{R=0.50} = 0.9985 \cdot \phi|_{R=0.25} (r^2 = 0.5739). \]  

The \( E_{FE} \) and \( c \) were not sensitive to the selection radius, and the errors between the differences between the identified parameters were less than 1% and \( r^2 \) values were close to 1. Identified friction angles using two different selection radiuses did not as match well (\( r^2 = 0.57 \)), but considering the narrow range of \( \phi \) (12.845–12.989° for \( R=0.50 \), 12.825–13.026° for \( R=0.25 \)), the error was still acceptable. The following analyses were based on the identified material parameters using a selection radius of 0.25.

**Statistics**

The moduli and hardness measured using nanoindentation (\( E_{CSM} \), \( H_{CSM} \), \( E_{O-P} \), and \( H_{O-P} \)), the identified modulus (\( E_{FE} \)), cohesion (\( c \)) and friction angle (\( \phi \)) were first averaged over each dog specimen. The mean material parameters were compared among groups, using ANOVA and Tukey HSD as post-hoc (JMP 6, NC).

Linear regression was used to study the relationships between the measured moduli and hardness within each group. ANCOVA was used to compare differences in the relationships between the measured moduli and hardness across groups. Significant level was 0.05. Stepwise regression was used to probe the relationship between the identified material parameters (\( E_{FE} \), \( c \) and \( \phi \)) and the measured moduli and hardness. Linear regression was used to study significant relationships identified by stepwise regression.

**Results**

\( E_{CSM} \) was higher in the RIS group, but not in the ALN group, compared to the VEH group (\( p=0.025 \)). No difference was observed in \( E_{O-P} \) among the three groups (\( p=0.11 \), Fig. 5a).

\( H_{CSM} \) and \( H_{O-P} \) were significantly higher in both the ALN- and RIS- treated groups compared to VEH (\( p=0.002 \) & 0.0028, Fig. 5b), but there was no significant difference between the two BP groups.

\( E_{CSM} \) was linearly correlated with \( H_{CSM} \) in the ALN, RIS and VEH groups (\( r^2 = 0.47, 0.74 \& 0.84, p<0.018 \)), respectively. The slopes and intercepts of the linear correlations were not different among the three groups (\( p=0.43 \) & 0.76, ANCOVA). Correlation was found between \( E_{O-P} \) and \( H_{O-P} \) in the RIS and VEH groups (\( r^2 = 0.59 \& 0.75, p<0.01 \), but not in the ALN.
The identified bone tissue moduli were 13.36±0.72 GPa in the ALN group, 13.30±1.06 GPa in the RIS group, and 12.54±0.98 GPa in the VEH group, respectively. There was no difference in $E_{FE}$ between the three groups ($p=0.085$, ANOVA, Fig. 5a). The modulus estimated using finite element modeling (VEH: 12.54±0.98 GPa, ALN: 13.36±0.73 GPa, RIS: 13.30±1.06 GPa) was significantly smaller than the modulus calculated using the Oliver-Pharr (VEH: 16.78±1.36 GPa, ALN: 17.88±1.04 GPa, RIS:17.76±1.5 GPa) or the CSM (VEH: 19.51±1.31 GPa, ALN: 20.66±1.31 GPa, RIS:20.8±1.25 GPa) methods within each group ($p<0.0001$). The cohesion was significantly higher in the RIS group (131.50±1.96 MPa) than in the VEH group, and there was no difference between the ALN (126.79±1.79 MPa) and VEH (120.57±1.87 MPa) groups ($p=0.001$, Fig. 5c). The friction angles were around 12.91° and not different between the three groups ($p=0.79$, Fig. 5d).

Forward stepwise regression results showed $E_{FE}$ was predicted by $H_{CSM}$ and $E_{OP}$ ($r^2=0.994$, Table 2), cohesion ($c$) was predicted by $E_{CSM}$, $E_{OP}$ and $H_{OP}$ ($r^2=0.988$), and friction angle was only predicted by $E_{OP}$ ($r^2=0.313$). The practical ability to predict the results of the finite element method calculations using only the Oliver-Pharr results were listed in Table 3.

**Discussion**

At doses consistent with those used to treat post menopausal osteoporosis, both alendronate and risedronate significantly increased tissue hardness of dog vertebral cancellous bone at the nano-level. Hardness is a useful tool for estimating bone strength [18], but it is not a mechanical property in the same sense as Young’s modulus, cohesion or friction angle. As a result, the goal of this study was to develop a finite element method to analyze bone tissue nanoindentation load-displacement data and determine the actual failure properties of bone tissue; cohesion and friction angle. Our method showed that the cohesion of the bone tissue was increased by bisphosphonate treatment, and this change in material properties was strongly predicted by modulus and hardness values measured using the Oliver-Pharr method. This result suggests that the increases in hardness and modulus of bone tissue calculated using the traditional Oliver-Pharr method reflect an increase in the cohesion of bone tissue after bisphosphonate treatment. The percentage increase in tissue cohesion compared to vehicle-treatment was 9% for risedronate and 5% for alendronate. These increases were not, however, statistically different from each other.

Both risedronate and alendronate resulted in higher bone tissue elastic moduli compared to control (VEH group) for the $E_{CSM}$ measure, although no statistical difference existed between the ALN and VEH groups. For all $E_{OP}$, however, an average increase with bisphosphonate treatment was observed with all being nearly significant. For $E_{FE}$, increases in modulus were 6.5% for alendronate and 6.1% increase for risedronate. There was no difference between the drugs in their effect of increasing modulus, by all means of estimating mechanical properties.

The modulus estimated using finite element modeling was significantly smaller than the modulus calculated using the Oliver-Pharr or the CSM method within each group. The meaning of this is unknown. However, that $E_{FE}$ was closely predicted by $E_{OP}$ alone ($r^2=0.989$) demonstrates that both estimates are similar in their ability to discriminate changes in modulus.

The friction angle ($\phi$) decreased with $E_{OP}$ ($r^2=0.31$), but no statistically significant change with bisphosphonate treatment was demonstrated. A decreased friction angle along with an increased cohesion after bisphosphonate treatment is consistent with the findings of increased overall bone strength with bisphosphonate treatment in this animal model [13,14].
The finite element modeling in the current study is an approach to estimate bone tissue failure properties at the nanometer level. The finite element method has been used to probe material behaviors during nanoindentation of various materials, including thin film materials [19], polymers [20] and bone [3]. In the current study, we demonstrate that the Mohr-Coulomb failure parameters of canine vertebral bone are (1) changed by treatment with bisphosphonates and (2) that the failure parameters ($c$ and $\phi$) can be predicted using the modulus and hardness estimated using the Oliver-Pharr equation. The first result is the main significance of our study, however, the broader practical importance of the study are the regressions of Table 3. With those results, the Oliver-Pharr modulus and hardness measured by nanoindentation can be associated with a modulus and a set of Mohr-Coulomb material parameters that can be used in finite element analysis.

Limitations of our study include: First, the isotropic Mohr-Coulomb failure criterion is not able to model all bone failure mechanisms. Bone tissue failure is a complex anisotropic process that cannot be fully described by such a simple criterion. Second, we ignored strain rate and time dependence of the elastic material properties. Consequently, the holding segment of the nanoindentation loading at maximum load was not simulated. Finally, we assumed a constant Poisson’s ratio of 0.3 for the bone tissue. This is a commonly assumed value, but it remains an untested assumption. Bone is also known as a viscoelastic material [21,22]. The lack of viscoelastic material properties in our model limits its application. The current loading and unloading speed were 10 nm/s, which is a relatively low nanoindentation test speed. For a high-speed nanoindentation, modeling bone viscoelasticity would be more important. Hence, time dependent behavior of bone tissue would play an important role in bone mechanical properties, which would be the next step for our study.

Overall, the current study introduces a new finite element method to identify the failure parameters of bone tissue based on the assumption of a Mohr-Coulomb failure surface. The finite element analysis of the experimental data demonstrates that bisphosphonate treatment increases bone hardness by increasing tissue modulus and cohesion.

Acknowledgements

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References


In the Mohr-Coulomb material model, material failure is caused by shear stress, and the shear stress at failure is dependent upon the normal stress. The relationship between the shear stress at failure ($\tau$) and normal stress ($\sigma$) that defines the failure surface is $\tau = c - \sigma \tan(\phi)$, where $c$ is the cohesion and $\phi$ is the friction angle. (The failure surface is a cone that is symmetric about the mean stress, therefore, this figure shows only the positive shear branch of the failure surface.)
Figure 2.
A typical nanoindentation load-displacement curve, including loading, holding, unloading and thermal drift segments.
Figure 3.
One sixth of the nanoindentation was modeled as a three-dimensional finite element model in ABAQUS. The Berkovich tip was modeled as a rigid surface with 300 elements. There were 5040 elements in the bone tissue block, which had a height of 10 µm and a radius of 16 µm.
Figure 4.
(a) The maximum load vs. initial unloading slope was plotted for all FE simulations. The red arrow indicated the increasing directions of $E_{FE}$ and $c$, respectively. (b) If a pair of maximum load and initial unloading slope from FE simulation fell into the defined region, the FE simulation was considered as a matched FE simulation to the nanoindentation. The identified modulus, friction angle and cohesion for each nanoindentation were calculated by averaging the input parameters of all the matched FE simulations. The black circle represented the selection region with a certain selection radius.
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(a)

(b)

Bone. Author manuscript; available in PMC 2009 October 1.
Figure 5.
(a) $E_{CSM}$ was higher in the RIS group, but no difference in $E_{O-P}$ or $E_{FE}$ was found between the groups. (b) $H_{CSM}$ and $H_{O-P}$ in the BP treated groups were higher. (c) Cohesion (c) was higher in the RIS group than in the VEH group. (d) No difference was observed in friction angle between groups. ANOVA and Tukey- post-hoc analysis were used to compare means between the groups. Significant level is 0.05. *, **, # and ## indicate difference between groups.
Table 1
Lists of all FE simulation and the ranges of material parameters

<table>
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<th>Number of FE models</th>
<th>$E$ (GPa)</th>
<th>$\phi^\dagger$ (°)</th>
<th>$c^\ddagger$ (MPa)</th>
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<td>170–300</td>
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| Total               | 1552      | -                   | -                   |

$^\dagger$ The interval for $\phi$ is 1°

$^\ddagger$ The interval for $c$ is 10 MPa

* Only one friction angle was tested

* Bone. Author manuscript; available in PMC 2009 October 1.
Table 2

Linear regression results between the FE identified and experimental measured material parameters.

<table>
<thead>
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<th>Dependent variable</th>
<th>Multiple Linear Regression Parameters</th>
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<td>H_O–P (GPa)</td>
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<tr>
<td>Constant (GPa)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elastic modulus (E_FE, GPa)</td>
<td>1.879</td>
<td>0.6540</td>
<td>-</td>
</tr>
<tr>
<td>Cohesion (c, MPa)</td>
<td>-4.509</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Friction angle (ϕ, °)</td>
<td>-</td>
<td>-</td>
<td>-0.01922</td>
</tr>
</tbody>
</table>

† Linear regression parameter and p-value were reported for each single independent variable
‡ - indicates independent parameter not used to predict dependent
* parameters have a unit of GPa⁻¹
<table>
<thead>
<tr>
<th>Dependent variables</th>
<th>Multiple Linear Regression Parameters</th>
<th>overall p-value</th>
<th>$r^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$E_{O-P}$(GPa)</td>
<td>$H_{O-P}$(GPa)</td>
<td>Constant (GPa)</td>
</tr>
<tr>
<td>Elastic modulus $(E_{FE}, \text{GPa})$</td>
<td>0.7118</td>
<td>-</td>
<td>0.6301</td>
</tr>
<tr>
<td>Cohesion $(c, \text{MPa})$</td>
<td>-2.732</td>
<td>215.6</td>
<td>0.4566</td>
</tr>
<tr>
<td>Friction angle $^*$ $(\phi, ^\circ)$</td>
<td>-0.01922</td>
<td>-</td>
<td>13.25</td>
</tr>
</tbody>
</table>

$^*$ Linear regression parameter and p-value were reported for each single independent variable

$^\dagger$ indicates independent parameter not used to predict dependent

$^* \text{ parameters have a unit of } ^\circ/\text{GPa}$