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·基础研究·

无托槽隐形矫治器真性垂直压低下切牙的转矩有限元分析

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【摘要】 **目的** 探讨无托槽隐形矫治器压低下切牙过程中，施加不同转矩对下切牙矢状向位移的影响，为实现下切牙真性垂直压低(不伴唇舌向移动的压低)临床设计提供参考。**方法** 本研究通过单位伦理委员会审批。选取1名下中切牙-下颌平面角(incisor mandibular plane angle，IMPA)为94°的志愿者，基于其锥形束CT(cone-beam computed tomography，CBCT)及口内扫描数据，建立高精度三维有限元模型。在下切牙设置0.2 mm压低量并分别施加根唇向转矩0°，1°，2°，3°，共计4组工况，分析下切牙位移趋势和牙周膜应力分布。**结果** 根唇向转矩0°时，下切牙表现冠唇向、根舌向倾斜的压低，根唇向转矩1°~3°时，下切牙由冠唇向、根舌向逐渐转变为冠舌向、根唇向倾斜的压低；根据矢状向位移量折线图推断，中切牙与侧切牙分别在根唇向转矩1.8°和2.5°接近实现真性垂直压低；下尖牙始终表现为伴牙冠唇倾的伸长；下切牙及尖牙牙周膜应力主要集中于根尖部和牙颈部，施加根唇向转矩后，切牙颈部牙周膜应力集中区由唇侧转为舌侧；尖牙颈部牙周膜应力主要集中于唇侧。**结论** 无托槽隐形矫治器压低下切牙过程中施加适宜转矩控制有助于实现真性垂直压低，从而提高压低效率。

【关键词】 正畸学； 错㓉畸形； 有限元分析； 无托槽隐形矫治器； 切牙压低； 下颌骨；转矩控制； 应力分布

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True vertical intrusion of mandibular incisors with torque control using clear aligners: a finite element analysis

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【Abstract】 **Objective** This study investigated the effect of applying different torque values on the sagittal displacement tendency of mandibular incisors during intrusion using clear aligners, with the aim of providing a reference for achieving true vertical intrusion (intrusion without labiolingual movement) of mandibular incisors in clear aligner therapy. **Methods** This study was approved by the institutional ethics committee. A volunteer with an incisor mandibular plane angle of 94° was selected. Using cone-beam computed tomography and intraoral scan data, a high-precision three-dimensional finite element model was established. An intrusion amount of 0.2 mm was set for the mandibular incisors, and four simulation groups were defined by applying 0°, 1°, 2°, and 3° of root labial torque. The displacement tendency of the incisors and the stress distribution within the periodontal ligament were analyzed. **Results** When 0° of root labial torque was applied, the mandibular incisors exhibited intrusion accompanied by crown-labial, root-lingual inclination. When 1° – 3° of root labial torque was applied, the mandibular incisors exhibited intrusion ac-

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companied by the inclination gradually shifted from crown-labial, root-lingual towards crown-lingual, root-labial. Based on the line graph of sagittal displacement, the central incisors and lateral incisors approximated true vertical intrusion when 1.8° and 2.5° of root labial torque was applied, respectively. The mandibular canines consistently exhibited extrusion accompanied by labial crown inclination. Stress within the periodontal ligament of the incisors and canines was primarily concentrated at the root apex and cervical region. After applying root labial torque, the area of stress concentration in the incisors cervical periodontal ligament shifted from the labial side to the lingual side. The stress in the periodontal ligament at the cervical region of the canines is predominantly concentrated on the labial side. **Conclusion** Applying appropriate torque control during mandibular incisor intrusion with clear aligners facilitates true vertical intrusion, thereby enhancing the efficiency of the intrusion.

【Key words】 orthodontics; malocclusion; finite element analysis; clear aligner; incisor intrusion; mandible; torque control; stress distribution

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前牙深覆𬌗是常见错𬌗畸形，不仅影响美观，还对口腔健康及功能有不利影响[1]，其矫治策略主要为压低前牙和(或)升高后牙。对于高角成年患者，前牙压低是主要手段[2-3]，传统矫治技术采用平面导板、摇椅弓、压低辅弓或种植钉等[4-5]。

随着数字化技术应用，无托槽隐形矫治提供矫治深覆𬌗的新方法[6]。尤其对于中位和低位笑线患者，压低下切牙是隐形矫治前牙深覆𬌗最常用的方法。按照压低是否伴有矢状向倾斜移动，分为唇倾压低、舌倾压低与真性垂直压低[7]。真性垂直压低指牙齿压低过程中未发生唇舌向偏斜[8]。

根据以往研究，无托槽隐形矫治器压低下切牙无论整体压低还是分步压低，均表现为伴唇舌向倾斜的相对压低[9-10]。由于下切牙牙槽骨较窄，过度唇倾或舌倾会导致下切牙牙龈退缩及牙根吸收[11]，并增加骨开窗或开裂的风险。如何实现真性垂直压低，是正畸医师需关注的问题。

三维有限元分析是计算机模拟的力学分析技术，可将牙周膜纳入研究中，已被广泛用于解决复杂口腔生物力学问题[12]。有限元分析模拟多种临床设计，从而避免不必要的重复临床试验[13]。

目前采用有限元分析隐形矫治实现真性垂直压低下切牙的相关研究较少。本研究运用有限元分析模拟无托槽隐形矫治器压低下切牙，同时配合转矩控制，为实现下切牙真性垂直压低的矫治设计提供参考。

1　对象和方法

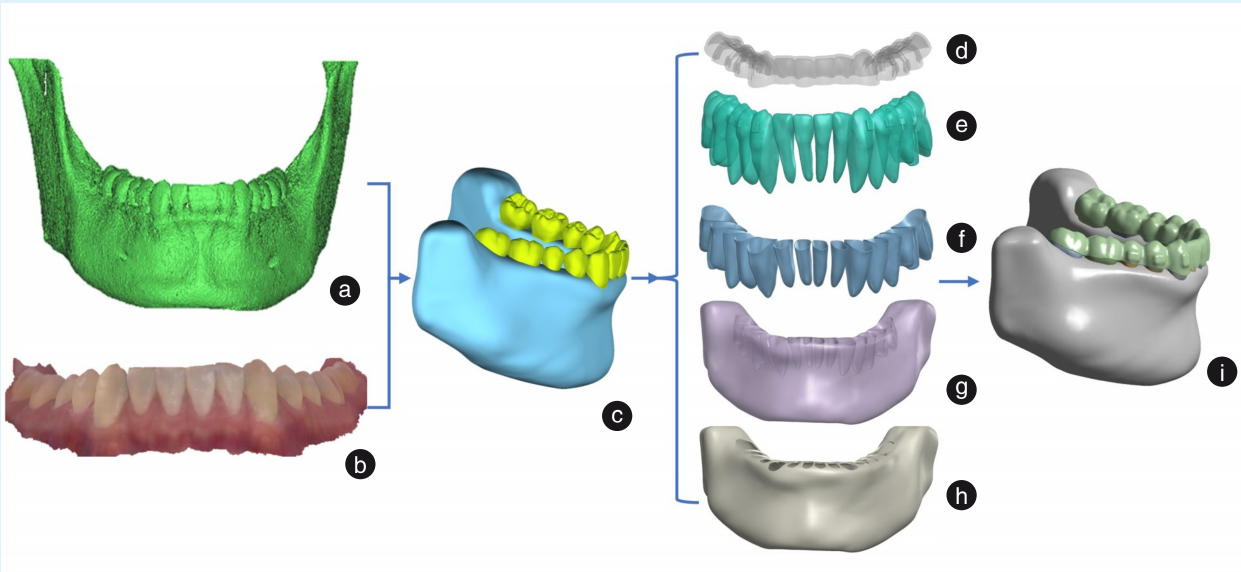
1.1　研究对象

选取1名下中切牙-下颌平面角(incisor mandibular plane angle, IMPA)为94°的志愿者，纳入标准：下颌牙列完整，牙弓两侧基本对称，牙齿解剖形态正常，牙体及牙周组织健康，覆𬌗覆盖关系正常，无颞下颌关节疾病，无全身性疾病。本研究通过单位伦理委员会审批(审批号：2023125)，志愿者签署知情同意书。采用锥形束CT(cone-beam computed tomography, CBCT)、Itero Element口腔数字扫描仪取得下颌骨与牙列数据，分别转变成医学数字通讯图像标准(digital imaging and communications in medicine, DICOM)、立体光刻(stereo lithography, STL)格式数据输出。

1.2　方法

1.2.1　构建高精度有限元模型　将DICOM文件导入Mimics 21.0软件，提取下颌骨和牙齿三维模型，输出为STL格式(图1a)。将口扫数据导入3-Shape 2021软件(图1b)，通过GEOMAGIC软件将口扫数据与CBCT中下颌牙齿数据匹配并整合(图1c)。参照既往研究设置牙周膜厚度为0.25 mm[14]，将冠、根表面分别向外偏移0.25 mm和0.75 mm，作为制作牙周膜和矫治器的模板[15]，以产品模型数据交换标准(standard for the exchange of product model data, STP)格式导出。参考Guo等[16]创建附件方法，构建长3 mm、宽2 mm、厚1 mm的矩形附件，于

尖牙放置垂直矩形附件，于第一、二前磨牙放置水平矩形附件[17]；将中切牙、侧切牙分别沿牙长轴伸长0.2 mm，并施加0°、1°、2°和3°根唇向转矩，获得下颌牙列模型；将移动前的下颌牙冠沿法线向外均匀扩展0.75 mm，获得矫治器模型[18-19]，在SOLIDWORKS 2022软件将上述模型组装（图1d~1h），形成高精度有限元模型（图1i），以STP格式保存。将模型导入ANSYS workbench 2021R1软件计算分析。



a: 3D model of the mandible and dentition reconstructed from cone-beam computed tomography (CBCT) data; b: intraoral scan (IOS) data of the mandibular dentition; c: high-precision integrated model achieved by merging IOS data with data from CBCT; d: clear aligner model; e: mandibular dentition model with attachment geometries; f: periodontal ligament model of the mandibular dentition; g: mandibular cancellous bone model; h: mandibular cortical bone model; i: high-precision 3D finite element model

Figure 1　Establishment of the high-precision three-dimensional finite element model

图1　高精度三维有限元模型建立

1.2.2　材料参数设置　设置材料为连续、均质、各向同性的线弹性。材料的弹性模量和泊松比[20]见表1。

表1　无托槽隐形矫治模型中的材料参数

Table 1　Material parameters in clear aligner models

Material	Elastic modulus/MPa	Poisson′s ratio
Teeth	19 600	0.30
Periodontal membrane	0.67	0.45
Cortical bone	13 700	0.26
Cancellous bone	1 370	0.30
Clear aligner	528	0.36
Clear aligner attachments	12 500	0.36

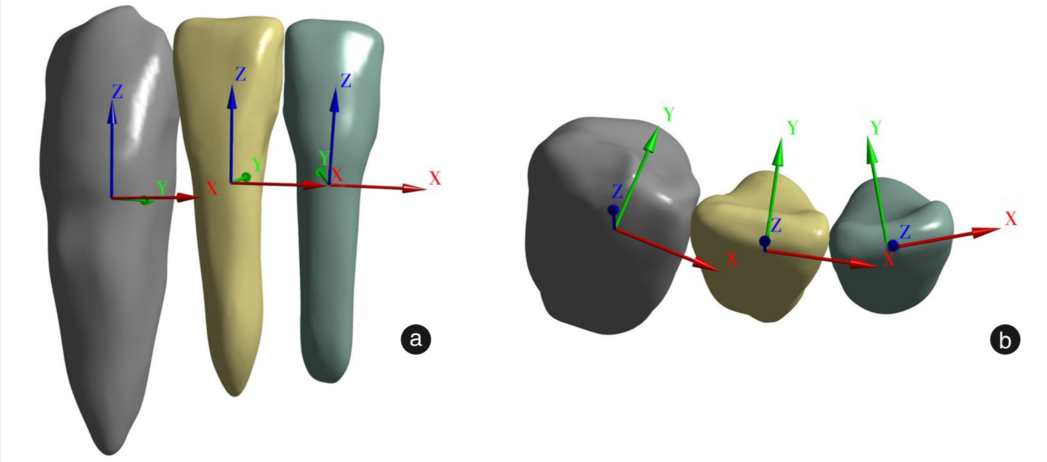
1.2.3　坐标系建立及观测点选取　下切牙及尖牙三维方向位置不一致，因此分别为右侧下切牙及尖牙建立局部坐标系（图2），X轴代表近远中向，正值为近中向；Y轴代表唇舌向，正值为舌向；Z轴代表垂直向，正值为切𬌗向。本研究选取切牙切缘中点、尖牙牙尖为牙冠观测点；切牙、尖牙根尖点为牙根观测点。

1.2.4　边界条件设定　下颌骨下缘施加固定约束，限制各向自由度。在牙冠与附件、牙根与牙周膜、牙周膜与松质骨之间设定面-面绑定接触关系，在牙冠、附件与矫治器之间设定摩擦接触关系，摩擦因数为0.2[21]。将模型划分为四面体结构，模型网格密度为0.2 mm。

1.2.5　研究分组　依据施加根唇向转矩度数（0°、1°、2°、3°）分为4组工况。工况1：根唇向转矩0°；工况2：根唇向转矩1°；工况3：根唇向转矩2°；工况4：根唇向转矩3°[22]，每组均设置0.2 mm压低量。

1.3　主要观察指标

由于下颌牙列左右对称，为简化实验数据，只分析下颌右侧切牙及尖牙在观测点的三维位移



Coordinate system is established based on the three-dimensional position of the mandibular right anterior tooth. The red arrow represents the X-axis, with positive values indicating the mesial direction; the green arrow represents the Y-axis, with positive values indicating the lingual direction; and the blue arrow represents the Z-axis, with positive values indicating the incisal/occlusal direction. a: labial view of the mandibular anterior teeth coordinate system; b: occlusal view of the mandibular anterior teeth coordinate system

Figure 2　Coordinate system of the mandibular right incisors and canines in the clear aligner model

图2　无托槽隐形矫治模型下颌右侧切牙及尖牙坐标系

量、牙周膜最大等效应力。

2　结　果

2.1　模型验证结果

选用未施加转矩控制的模型(工况1)验证结果有效性。切牙及尖牙位移趋势为:中切牙、侧切牙伴牙冠唇倾、牙根舌倾压低;尖牙伴牙冠唇倾伸长。牙周膜von Mises应力集中于牙颈、根尖部。

2.2　施加转矩控制后下切牙及尖牙位移方向及位移量变化

如图3、图4所示,矢状向上,尖牙发生冠唇向、根舌向倾斜移动;中切牙和侧切牙均由冠唇向、根舌向移动逐渐直立,再转变成冠舌向、根唇向移动,切牙矢状向位移量先减少后增加。

如图4所示,根唇向转矩2°(工况3)时,中切牙冠根唇舌向位移量最少,根唇向转矩3°(工况4)时,侧切牙冠根唇舌向位移量最少。根据下切牙矢状向位移量折线图,根唇向转矩1.8°时,中切牙冠根同步移动,矢状向位移量极接近于0 mm;根唇向转矩2.5°时,侧切牙冠根同步移动,矢状向位移量极接近于0 mm。

如图5所示,同工况下,中切牙压低量低于侧切牙,切牙压低量随转矩度数增加先增大再减小;中切牙在根唇向转矩1°(工况2)时压低量最大;侧切牙在工况3时压低量最大。

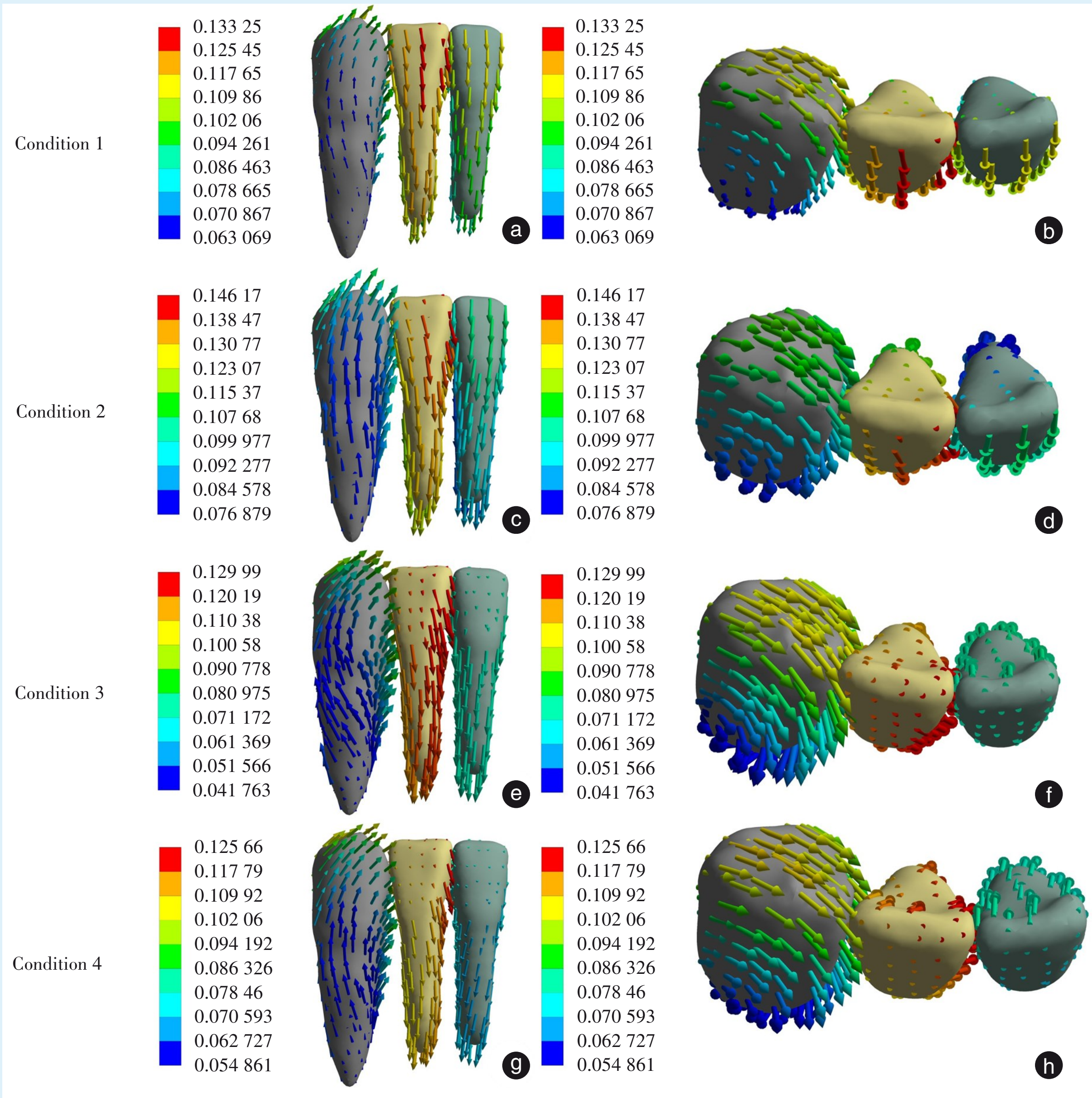
2.3　下切牙及尖牙牙周膜最大等效应力水平与分布

施加转矩控制前后,下切牙及尖牙牙周膜最大等效应力水平无明显变化,同牙位各工况应力水平相近,如图6所示,侧切牙牙周膜最大等效应力水平最高,其次是中切牙,尖牙最小。

下切牙及尖牙牙周膜应力分布如图7所示,牙周膜应力主要分布于牙颈部和根尖区;工况1切牙及尖牙牙周膜应力集中分布于唇侧颈部;工况2与工况3中切牙牙周膜应力逐渐集中于舌侧颈部,工况3、工况4中切牙牙周膜应力集中于舌侧颈部;工况1至工况3侧切牙牙周膜应力集中于唇侧颈部,工况3、工况4,侧切牙牙周膜应力逐渐集中于舌侧颈部;工况1至工况4尖牙牙周膜应力主要分布于唇侧颈部。

3　讨　论

有限元分析是模拟正畸牙齿移动的有效工具[23]。无托槽隐形矫治器通过弹性形变施力使牙齿移动到设计位置[24],本研究采用有限元分析无托槽隐形矫治器压低下切牙的生物力学效应,由于矫治器直接与牙冠接触,因此牙冠形态精细程度直接影响分析的准确性[18]。目前国内外大多使用CBCT重建牙列及颌骨模型,几何仿真性欠精准。研究表明,口内数字印模技术误差仅为



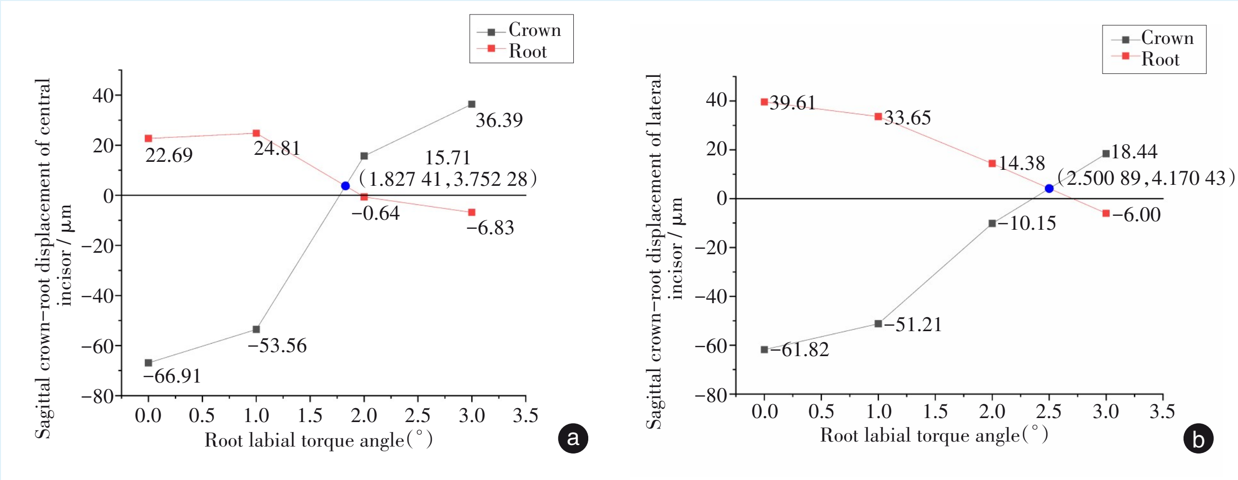
Condition 1 served as the control group with no labial root torque applied, while Condition 2, Condition 3, and Condition 4 received labial root torque at 1°, 2°, and 3°, respectively. The central incisors exhibited intrusion accompanied by crown labial inclination and root lingual inclination in Condition 1 and Condition 2, while demonstrating intrusion accompanied by crown lingual inclination and root labial inclination in Condition 3 and Condition 4. The lateral incisors displayed intrusion accompanied by crown labial inclination and root lingual inclination in Condition 1 to Condition 3, but exhibited intrusion accompanied by crown lingual inclination and root labial inclination in Condition 4. The canines consistently showed extrusion accompanied by crown labial inclination across all conditions. a & b: displacement trend under Condition 1 and occlusal views of the displacement trend under Condition 1; c & d: displacement trend under Condition 2 and occlusal views of the displacement trend under Condition 2; e & f: displacement trend under Condition 3 and occlusal views of the displacement trend under Condition 3; g & h: the displacement trend under Condition 4 and occlusal views of the displacement trend under Condition 4

Figure 3　Changes of mandibular incisors and canines displacement directions in clear aligner models before and after applying torque control

图 3　施加转矩控制前后无托槽隐形矫治模型下切牙及尖牙位移方向变化

(0.015±0.004) mm[25]。本研究将 CBCT 数据与光学扫描数据整合，模型几何仿真性增强，从而提高有限元分析准确性。

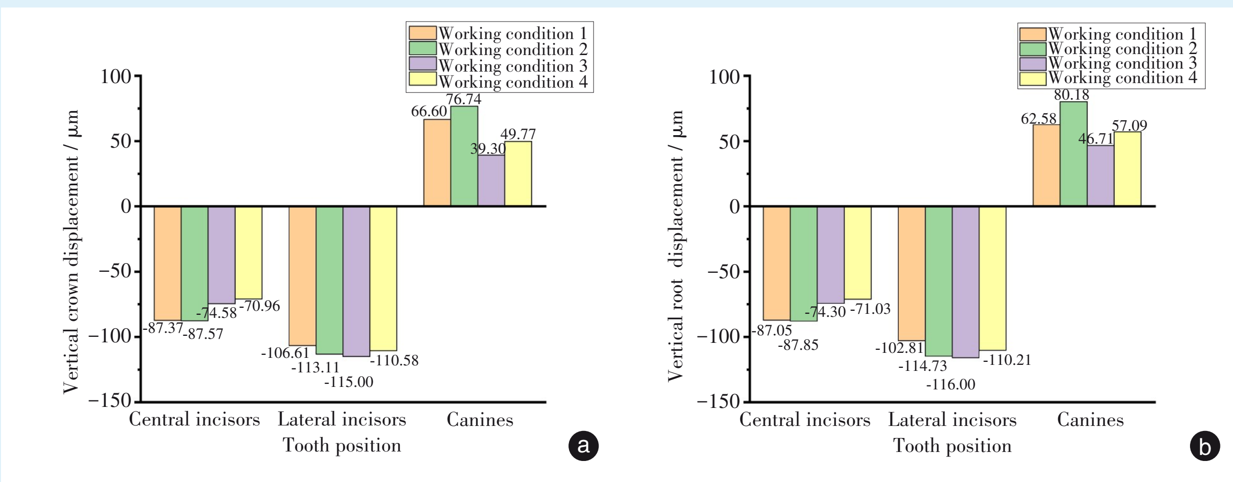
相对于固定矫治器，无托槽隐形矫治器压低下切牙时合力方向更接近牙体长轴，理论上更易实现真性垂直压低[26-27]。但研究表明，无托槽隐形



a: the central incisors exhibited labial crown movement and lingual root movement in Condition 1 and Condition 2, while demonstrating lingual crown movement and labial root movement in Condition 3 and Condition 4. When 1.8° of root labial torque was applied, the crown and root of the central incisor moved synchronously, and the sagittal displacement was nearly 0 mm. b: the lateral incisors exhibited labial crown movement and lingual root movement in Condition 1 to 3, while demonstrating lingual crown movement and labial root movement in Condition 4. When 2.5° of root labial torque was applied, the crown and root of the lateral incisor moved synchronously, and the sagittal displacement was nearly 0 mm. Condition 1 served as the control group with no labial root torque applied, while Condition 2, Condition 3, and Condition 4 received labial root torque at 1°, 2°, and 3°, respectively

Figure 4　Sagittal displacement of the crown and root of central incisors and lateral incisors in clear aligner models before and after applying torque control

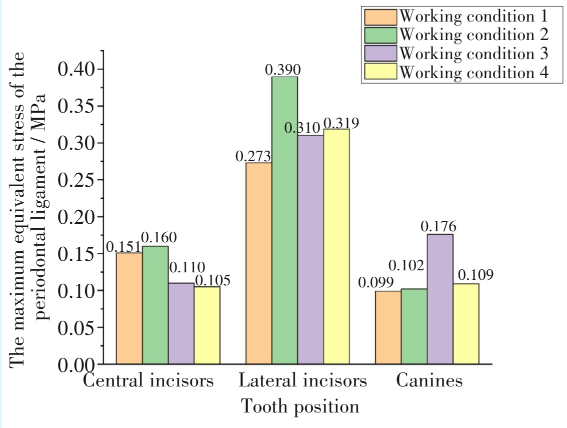
图 4　施加转矩控制前后无托槽隐形矫治模型中切牙与侧切牙冠根矢状向位移量



a: the intrusion amounts of the central incisor crown in descending order were: Condition 2, Condition 1, Condition 3, and Condition 4; while the intrusion amounts of the lateral incisor crown in descending order were: Condition 3, Condition 2, Condition 4, and Condition 1. b: the root intrusion amounts of the central incisor in descending order were: Condition 2, Condition 1, Condition 3, and Condition 4; while the root intrusion amounts of the lateral incisor in descending order were: Condition 3, Condition 2, Condition 4, and Condition 1. Condition 1 served as the control group with no labial root torque applied, while Condition 2, Condition 3, and Condition 4 received labial root torque at 1°, 2°, and 3°, respectively

Figure 5　Vertical displacement of dental crown and root in mandibular incisors and canines in clear aligner models before and after applying torque control

图 5　施加转矩控制前后无托槽隐形矫治模型下切牙及尖牙牙冠与牙根垂直向位移量



Under the same working conditions, the lateral incisor generally exhibited the highest maximum equivalent stress level in the periodontal ligament, followed by the central incisor, while the canine showed the lowest stress level. Condition 1 served as the control group with no labial root torque applied, while Condition 2, Condition 3, and Condition 4 received labial root torque at 1°, 2°, and 3°, respectively

Figure 6　The maximum equivalent stress of the periodontal ligament of mandibular incisors and canines in clear aligner models before and after applying torque control

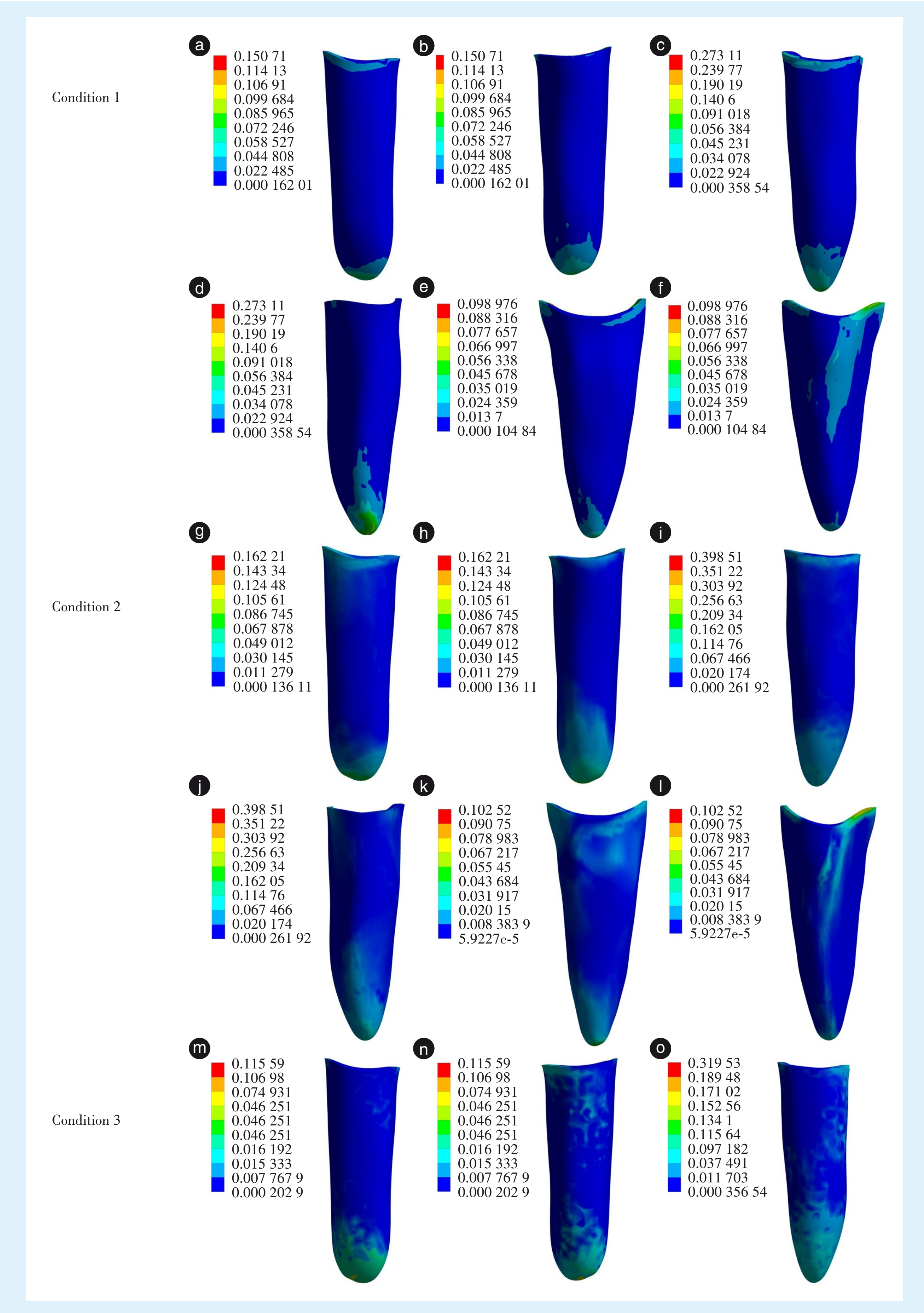
图 6　施加转矩控制前后无托槽隐形矫治模型下切牙及尖牙牙周膜最大等效应力

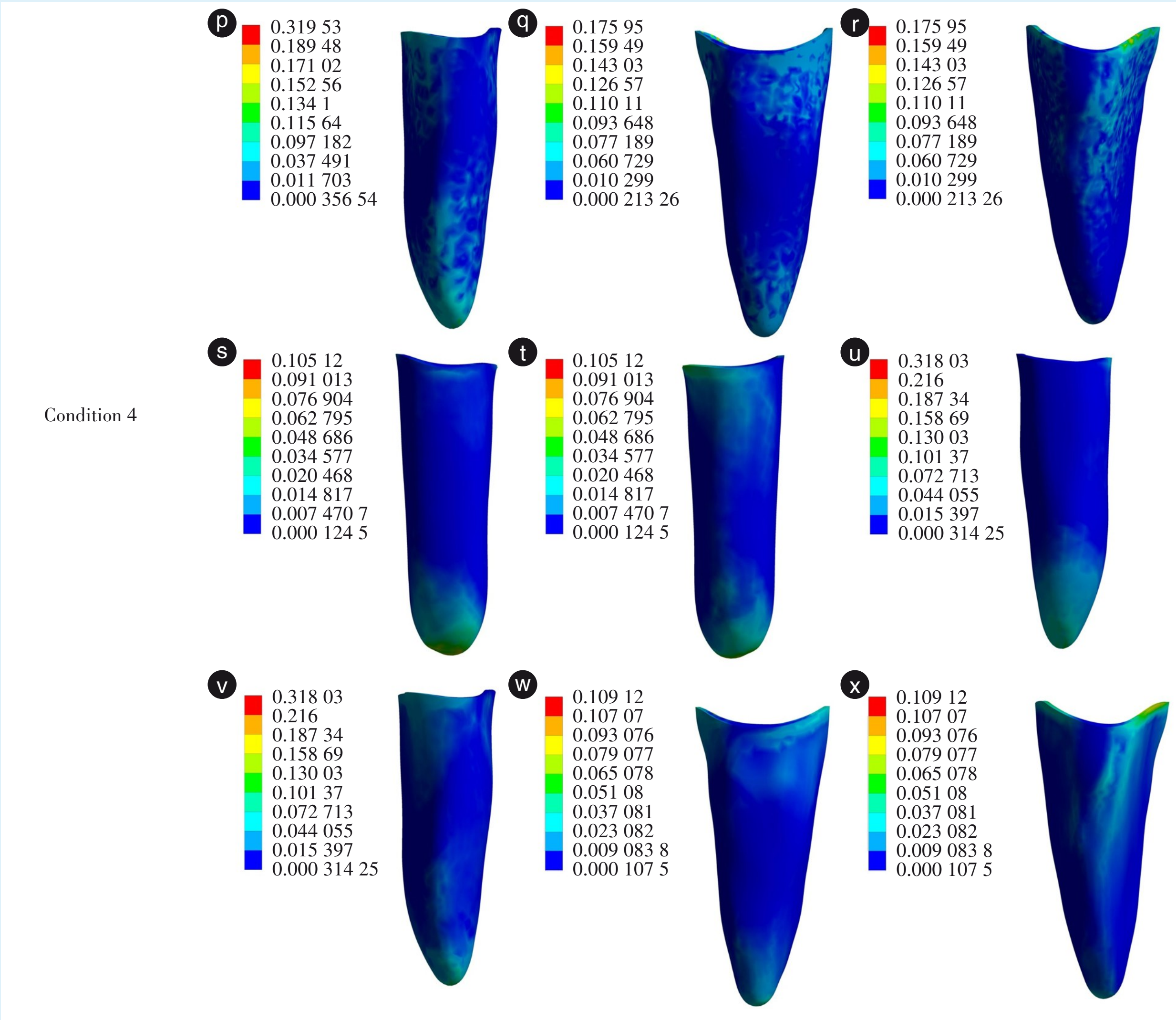
矫治器压低下切牙效率仅为 35%[28]，这可能与切牙发生唇舌向倾斜有关[29]。本研究结果显示，中切牙与侧切牙分别在根唇向转矩为 1°和 2°达到压低量最大值，说明适宜的转矩控制可增加压低量。Li 等[30]研究指出，下切牙压低时中切牙压低量低于侧切牙，该结果与本研究结果相似，这可能与切牙体积有关，下颌中切牙体积小于侧切牙，矫治器包裹程度较差；此外，中切牙更靠近牙列中线，矫治器加力受到影响也可能是原因之一[31]。尖牙始终表现为伸长移动，这体现尖牙作为支抗牙，受到矫治器压低切牙反作用力出现与切牙相反的位移趋势。

IMPA 是评估下中切牙相对于下颌平面位置的重要参考指标，代表下切牙唇舌向倾斜程度。按 Tweed 分析法的测量结果，中国人 IMPA 正常值为 93.9°±6.2°[1]。本研究志愿者 IMPA 为 94°，属标准正常范围。不施加转矩控制时，下切牙发生伴冠唇向根舌向倾斜压低，与陈玺茼等[32]、肖圣钊等[33]研究结果一致，可能因为矫治器施力方向在牙齿阻力中心唇侧。临床实际中为实现真性垂直压低，需设计相应反向转矩，以抵消下切牙压低过程中发生非设计的矢状向位移。因此，本研究结合预实验结果，参考临床上转矩控制角度，将施加的转矩度数分为 0°、1°、2°、3°。4 种工况中，中切牙和侧切牙分别在转矩 2°和 3°发生唇舌向移动的翻转，说明无托槽隐形矫治器配合适宜转矩控制可实现下切牙真性垂直压低。通过矢状向位移量折线图发现，中切牙与侧切牙分别在根唇向转矩 1.8°和 2.5°时接近实现真性垂直压低。然而，牙根长度、形态及矫治器材料等因素都可能对结果产生影响，但本研究结果仍可为临床矫治设计提供参考。在临床实际中，转矩控制可以参考本研究结果结合具体情况进行相应的调整，以实现下切牙真性垂直压低，提高压低实现率。

下切牙牙槽骨较薄，无托槽隐形矫治器压低下切牙过程中压低方向偏差可能导致根尖抵唇舌侧骨皮质，增加骨开窗骨开裂风险[34-35]，这也是导致切牙牙根吸收的原因之一[36]。Li 等[37]的研究结果显示，牙周膜的应力应变分布与破骨细胞的分布一致。牙周膜生物力学分析是评估骨开窗、骨开裂及正畸牙根吸收风险性的重要参考[38]，本研究以牙周膜等效应力作为评价标准。结果表明牙周膜等效应力分布与牙齿移动情况密切相关，总体上牙周膜应力主要分布于牙颈部和根尖区，这与 Ma 等[39]研究结果一致。未施加转矩控制时，切牙及尖牙牙周膜应力集中分布于唇侧颈部；设置根唇向转矩后中切牙与侧切牙分别在 2°和 3°发生唇倾向舌倾的转变，因此唇舌侧牙周膜所受应力也发生转变。工况 1 至工况 4 尖牙牙周膜应力主要分布于唇侧颈部与根尖区，这与尖牙始终发生伴唇向倾斜伸长有关。同工况根尖部侧切牙等效应力高于中切牙。可能与侧切牙压低量高于中切牙有关，也可能是下颌侧切牙相较于中切牙牙冠体积大，矫治器包裹程度较好，受到矫治器作用力较大。

本研究不足之处：①本研究仅讨论了标准 IMPA，即相对直立的下切牙实现真性垂直压低的转矩考量，不同 IMPA 是否及如何影响下切牙压低有待进一步研究；②本研究仅涉及静态有限元分析，而临床实际是下切牙在矫治力作用下发生持续压低，属动态有限元范畴，因此分析结果与临床实际存在偏差。后续研究需对以上内容进一步探讨。


Condition 1
a
0.150 71
0.114 13
0.106 91
0.099 684
0.085 965
0.072 246
0.058 527
0.044 808
0.022 485
0.000 162 01
b
0.150 71
0.114 13
0.106 91
0.099 684
0.085 965
0.072 246
0.058 527
0.044 808
0.022 485
0.000 162 01
c
0.273 11
0.239 77
0.190 19
0.140 6
0.091 018
0.056 384
0.045 231
0.034 078
0.022 924
0.000 358 54
d
0.273 11
0.239 77
0.190 19
0.140 6
0.091 018
0.056 384
0.045 231
0.034 078
0.022 924
0.000 358 54
e
0.098 976
0.088 316
0.077 657
0.066 997
0.056 338
0.045 678
0.035 019
0.024 359
0.013 7
0.000 104 84
f
0.098 976
0.088 316
0.077 657
0.066 997
0.056 338
0.045 678
0.035 019
0.024 359
0.013 7
0.000 104 84
Condition 2
g
0.162 21
0.143 34
0.124 48
0.105 61
0.086 745
0.067 878
0.049 012
0.030 145
0.011 279
0.000 136 11
h
0.162 21
0.143 34
0.124 48
0.105 61
0.086 745
0.067 878
0.049 012
0.030 145
0.011 279
0.000 136 11
i
0.398 51
0.351 22
0.303 92
0.256 63
0.209 34
0.162 05
0.114 76
0.067 466
0.020 174
0.000 261 92
j
0.398 51
0.351 22
0.303 92
0.256 63
0.209 34
0.162 05
0.114 76
0.067 466
0.020 174
0.000 261 92
k
0.102 52
0.090 75
0.078 983
0.067 217
0.055 45
0.043 684
0.031 917
0.020 15
0.008 383 9
5.9227e-5
l
0.102 52
0.090 75
0.078 983
0.067 217
0.055 45
0.043 684
0.031 917
0.020 15
0.008 383 9
5.9227e-5
Condition 3
m
0.115 59
0.106 98
0.074 931
0.046 251
0.046 251
0.046 251
0.016 192
0.015 333
0.007 767 9
0.000 202 9
n
0.115 59
0.106 98
0.074 931
0.046 251
0.046 251
0.046 251
0.016 192
0.015 333
0.007 767 9
0.000 202 9
o
0.319 53
0.189 48
0.171 02
0.152 56
0.134 1
0.115 64
0.097 182
0.037 491
0.011 703
0.000 356 54



In Condition 1 where no torque control was applied, the periodontal ligament stress of the incisors and canines was distributed in the labial cervical region. After applying labial root torque, the periodontal ligament stress of the central incisors in Condition 3 and Condition 4 concentrated in the lingual cervical region. The periodontal ligament stress of the lateral incisors concentrated in the labial cervical region in Condition 2 and Condition 3, but shifted to the lingual cervical region in Condition 4. In all Condition from 1 to 4, the periodontal ligament stress of the canines was primarily distributed in the labial cervical region. a- f: labial and lingual views of equivalent stress distribution in the periodontal ligament of the right mandibular central incisor, lateral incisor, and canine under Condition 1; g-l; labial and lingual views of equivalent stress distribution in the periodontal ligament of the right mandibular central incisor, lateral incisor, and canine under Condition 2; m-r: labial and lingual views of equivalent stress distribution in the periodontal ligament of the right mandibular central incisor, lateral incisor, and canine under Condition 3; s-x: labial and lingual views of equivalent stress distribution in the periodontal ligament of the right mandibular central incisor, lateral incisor, and canine under Condition 4. Condition 1 served as the control group with no labial root torque applied, while Condition II, Condition 3, and Condition 4 received labial root torque at 1°, 2°, and 3°, respectively

Figure 7　Equivalent stress distributions of periodontium of mandibular incisors and canines in clear aligner models before and after applying torque control

图 7　施加转矩控制前后无托槽隐形矫治模型下切牙及尖牙牙周膜等效应力分布

【Author contributions】 Xu CX performed the experiments, analyzed the data and wrote the article. Ye PP, Bi YL participated in the study design and reviewed the article. Wang HN conceptualized and reviewed the article. All authors read and approved the final manuscript as submitted.

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