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# 上颌扩弓动物模型及应用效果的研究进展

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【摘要】 上颌扩弓是临床上颌骨横向发育不足的主要治疗方法，为评估其机制、效果以及稳定性，在动物体内模拟上颌扩弓是主要研究方式，上颌扩弓动物模型在口腔正畸学研究中具有重要意义。上颌扩弓动物模型选择动物种属时，鼠和兔的饲养成本相对较低，但其口腔结构及咀嚼习惯与人类存在显著差异，且骨代谢速率远高于人类，因此在将研究成果转化为临床应用时需予以充分考虑；小型猪和犬的解剖结构及生理特征与人类较为相似，然而较高的饲养成本及伦理问题限制了其广泛应用。对于上颌扩弓动物模型造模方法，口内空间小的鼠类多采用弹性不锈钢丝弯制的扩弓装置，分为前腭缝扩弓和后腭缝扩弓两种方式；兔、小型猪及犬口腔操作空间充足，能够负载传统的牙支抗螺旋扩弓、微种植钉辅助扩弓及新兴磁力扩弓等多种扩弓装置。目前上颌扩弓动物模型的应用研究包括：探究机械力诱导骨重塑机制，为临床正畸治疗提供促进骨重建的潜在治疗靶点；对不同扩弓矫治器比较评估，以验证新型扩弓器的矫治效果，为其临床应用提供实验证据；筛选扩弓治疗的辅助措施，探究加速腭中缝成骨的药物和物理手段，以缩短临床扩弓的保持时间，为患者提供更高效、舒适的治疗方案。本文对上颌扩弓动物模型及应用效果进行综述，旨在为研究人员应用上颌扩弓动物模型提供参考。

【关键词】 口腔； 正畸； 错𬌗畸形； 上颌横向发育不足； 上颌扩弓； 动物模型； 正畸装置； 应用前景

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**Progress on animal models of maxillary expansion and its application effect**

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【Abstract】 Maxillary expansion serves as the principal treatment for maxillary transverse deficiency in clinical practice. Simulating maxillary expansion in animals is the main research approach to assess its mechanism, effect, and stability. Thus, the animal model of maxillary expansion holds great significance in orthodontic research. Rats and rabbits are typically selected for common animal models because the maintenance cost is relatively low; however, their oral anatomy and masticatory behaviors differ significantly from those of humans, and their bone metabolism rates are substantially higher. Consequently, these factors should be carefully considered when extrapolating research findings and applying them to human clinical applications. Miniature pigs and dogs exhibit maxillofacial structures and chewing patterns that closely resemble those of humans; however, their broader application in research is constrained by high maintenance costs and ethical concerns. Rats with small oral space typically require the use of an elastic stainless steel wire expansion appliance, which can be divided into anterior maxillary expansion and posterior maxillary expansion. Rabbits, miniature pigs, and dogs have sufficient oral space and can be fitted with a variety of expansion appliances, including traditional tooth-borne expansion, microimplant-assisted expansion, and new magnetic expansion appliance. Animal

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models of maxillary expansion are currently used to study the mechanism of mechanically induced bone remodeling in order to provide potential therapeutic targets to promote bone remodeling in clinical orthodontic treatment; different orthodontic devices have been compared and evaluated to verify the correction effect of a new type of orthodontic device and provide experimental evidence for its clinical application; and supplementary methods of maxillary expansion have been screened to explore drug and physical therapy to accelerate the osteogenesis of the palatal suture, so as to shorten the retention time of clinical maxillary expansion and provide patients with more efficient and comfortable treatment. This paper summerized advances in animal models of maxillary expansion and the application effects in order to provide a reference for using an animal model of maxillary expansion.

**【Key words】** stomatology; orthodontic; malocclusion; maxillary transverse deficiency; maxillary expansion; animal model; orthodontic appliances; application prospect

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上颌横向发育不足(maxillary transverse deficiency,MTD)是临床正畸常见的问题之一,表现为上牙弓狭窄和上下颌牙弓及基骨宽度不调,常伴有前牙拥挤、后牙反𬌗和腭穹隆高拱等[1]。相比垂直向和矢状向的发育,横向发育开始和结束的时间相对较早[2]。MTD很难通过生长发育的进程自发缓解,未经治疗可造成咬合紊乱甚至是阻塞性睡眠呼吸暂停综合征(obstructive sleep apnea hypopnea syndrome,OSAHS)等问题[3-4],因此早期诊断和矫正十分重要[5]。

上颌扩弓是MTD的经典治疗手段之一,利用矫形力扩张尚未完全骨化的腭中缝协调上下颌宽度,并提供间隙[6]。此外上颌扩弓还可以改善舌位和鼻咽体积缓解上呼吸道阻塞[7],与腺样体扁桃体切除术联合治疗能够有效改善儿童OSAHS[8-9],但目前扩弓存在较高的复发率[10]。

多种动物模型被应用于上颌扩弓实验当中,通过建立上颌扩弓动物模型,可研究机械力诱导骨重塑的机制、比较不同扩弓矫治器的效果和筛选扩弓治疗的辅助措施[11]等。笔者将对上颌扩弓动物模型的建立方法及应用进行综述。

## 1 动物种属的选择

### 1.1 鼠

鼠类因成本低、繁殖快、易于饲养和管理、造模耐受性强,能提供大量样本,广泛用于科学研究中。

大鼠与小鼠均广泛用于上颌扩弓模型的建立,大鼠的操作难度更低,应用更广。常用品系包括SD大鼠、Wistar大鼠、C57BL/6小鼠。近年来,使用基因敲除小鼠研究相应基因在成骨方面作用的研究也逐渐增加[12-13]。实验动物多选择5~8周龄,其中6周龄鼠因处于生长发育期[14],常用于模拟人类青春期扩弓。

扩弓装置多用弹性不锈钢丝弯制,分为前腭缝扩弓和后腭缝扩弓,以前者居多。大鼠的扩弓力值多在50~150 g,在扩弓7 d后,100 g组在扩张腭中缝的同时扩弓力造成的牙效应更小,表明100 g是大鼠前腭缝扩弓的最优力值[15];Jin等[16]建立的大鼠微种植钉辅助快速扩弓(microimplant-assisted rapid palatal expansion,MARPE)模型证明100 g为后腭缝扩弓的最优力值;小鼠扩弓多在30~100 g,以50 g左右居多[17-18]。口内造模后,初戴的不适及加力的疼痛使动物短期内进食困难,体重降低,通常可在1~3 d适应并缓解。

操作方面,鼠类的颌骨尺寸较小,这要求扩弓装置的制作和安装更精细。口腔生理功能方面,鼠类口腔结构及咀嚼习惯与人类差异较大[19],其前牙不断生长且啃食食物,加载于前牙的装置易脱落。在代谢方面,鼠的代谢速度远高于人类[20],在扩弓后的骨改建过程中表现为不同于人类的骨愈合过程和骨密度变化趋势。综上所述,将鼠类扩弓动物模型的研究结果向人类临床应用转化时需要谨慎考虑各方面差异带来的影响。

### 1.2 兔

兔类动物成本较低、生长周期短,且性情温顺,对于饲养环境适应性较强。研究多采用雄性新西兰白兔,不同文献采用的兔龄在8周龄[21]、

3 ~ 4月龄[22]、20 ~ 24周龄[23]、24 ~ 30周龄[24]不等。

相较鼠类,兔的口腔空间更大,视野良好,可操作性更强。这使得兔可以装载Hyrax螺旋扩弓器[22],定期加力,能够更好地模拟临床正畸扩弓过程。兔的牙齿较大,便于在磨牙上预备固位形,增强扩弓装置的固位力。相较于鼠类,兔的观察周期更长,可进行更长时间的保持期研究。此外尚有部分研究将Hyrax螺旋扩弓器置于兔颅骨正中矢状缝上,利用微种植钉固定,以模拟腭中缝扩张[23-24]。

同鼠类似,兔的咀嚼习惯和力量与人类不同,骨重建速度较人类更快,可能会影响扩弓实验结果的外推,需要在实验设计及结果分析时加以考虑。

### 1.3　小型猪

小型猪的颌面部结构在许多方面与人类相似,已经广泛应用于口腔颌面部生物研究中[25]。

在可操作性方面,小型猪体型适中,便于在口内安装上颌扩弓装置,可在上颌磨牙带环固位[26],对于扩弓后的调整和检查操作较为便利。

口腔生理功能方面,小型猪的口咽结构及咀嚼功能与人类相似[27],是扩弓对咀嚼功能影响的理想动物模型;肥胖小型猪作为OSAHS动物模型[28-29],可评估上颌扩弓对OSAHS治疗的潜在价值。小型猪的硬腭形态及其生长发育模式与人类相似,其骨骼成分、密度和质量方面也与人类相近[30],常被应用于微种植体相关的实验中[31],因此在研究种植支抗式扩弓方面更具优势。

小型猪饲养成本高,需要专门的饲养设施和管理条件,限制了其广泛应用。一部分研究采用了猪离体上颌骨进行研究[32-34],但在离体组织无法进行长时间的扩弓观察。

### 1.4　犬

近年来犬类广泛应用于口腔领域,尤其是种植方面的研究,在正畸领域应用尚少。

比格犬性格温顺,适合饲养和管理,适合进行长期的实验研究。研究用犬多采用6月龄[35],此时期的比格犬处于生长发育阶段。Liu等[36]使用比格犬模型探究扩弓力对于植骨区的影响,为临床唇腭裂治疗提供参考。

目前犬类已被用于MARPE[37]和新型磁力扩弓矫治器[35]等研究中。但比格犬的购买和饲养成本较高,且涉及相关伦理问题,目前仍未被广泛应用于上颌扩弓实验中。

## 2　扩弓造模方法

### 2.1　前腭缝扩弓

**2.1.1　单眼圈簧法**　目前应用于上颌扩弓实验研究最多的建模方法是较为成熟的上颌扩弓动物模型。以大鼠为例,造模利用0.014英寸不锈钢丝弯制直径1.5 ~ 2 mm的小圈曲,双侧连接5 ~ 8 mm长延伸臂,延伸臂末端弯制成弧形提供固位[15, 38]。末端伸入上切牙之间,使用光固化树脂粘接固定(图1a)。若需对扩弓保持及复发进行研究,则需在扩弓期结束之后使用光固化树脂粘固小圈曲,消除扩弓簧的张力,以起保持器的作用;保持期结束后拆除扩弓器,以研究复发。

此方法通过调整扩弓簧延伸臂的打开角度能够实现不同的扩张力值,且易于改造成保持器,是鼠类扩弓建模最常用的方法。然而此方法仍存在一些缺陷,如常规鼠的上颌切牙间邻接紧密,难以将上颌扩弓器置于上切牙间,强行塞入也难以粘接固位。随着前腭缝的扩展,扩弓力的方向无法保持垂直于腭中缝。将扩弓器转为保持器时,仅用树脂粘固无法完全固定扩弓簧,仍会对中切牙施加部分张力。

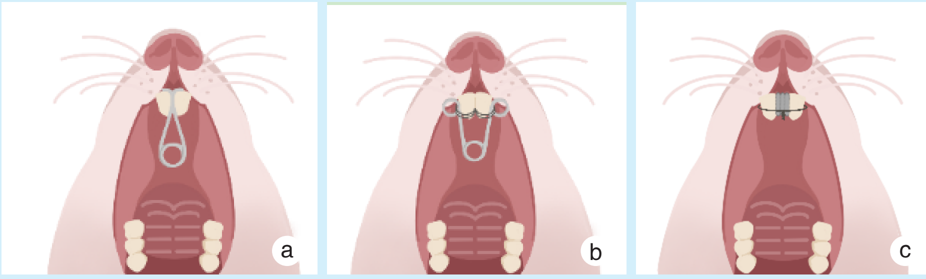
为进一步解决以上建模方式存在的技术问题,多项研究对此扩弓簧进行了改造。部分研究将扩弓簧延伸臂末端弯制为圈型,放置于上颌中切牙远中,使用金属结扎丝固位[39-41](图1b)。另有部分研究结束后拆除扩弓器,使用不锈钢方丝粘固于上颌中切牙之间作为保持器[38, 42],或直接用树脂粘固中切牙进行保持[43]。Zhao等[15]在原装置基础上进行了改良,在上颌切牙之间进行邻面去釉,扩大牙缝便于延伸臂置入;在延伸臂近小圈曲2 mm处增加一处弯折,将小圈曲及延伸臂弯折上缘一同粘固保持,以进一步消除扩弓力。

**2.1.2　不锈钢扩张环法**　使用0.5 mm不锈钢丝弯制3圈,形成厚度为1.5 mm的不锈钢扩张环,缓慢推入中切牙之间[44-45](图1c)。为稳定扩张环,在中切牙的远中龈缘磨出凹槽,并使用结扎丝固定。

由于此方法将上颌中切牙间行1.5 mm宽的即刻扩张,无法模拟临床缓慢加力的扩弓方式。Reis等[46]将该模型应用于上颌快速扩弓后c-Fos基因表达水平的研究,以评估上颌骨快速扩弓后的疼痛。

### 2.2　后腭缝扩弓

**2.2.1　双眼圈簧法**　双眼圈簧法首先需要制取鼠上颌模型,根据模型使用0.014、0.016英寸的澳丝




a: expansion appliance bonded to the mesial of the maxillary incisors. b: expansion appliance bonded to the distal of the maxillary incisors. c:stainless steel expansion ring fixed between maxillary incisors

Figure 1　Animal models of anterior maxillary expansion appliances

图1　前腭缝扩弓装置动物模型

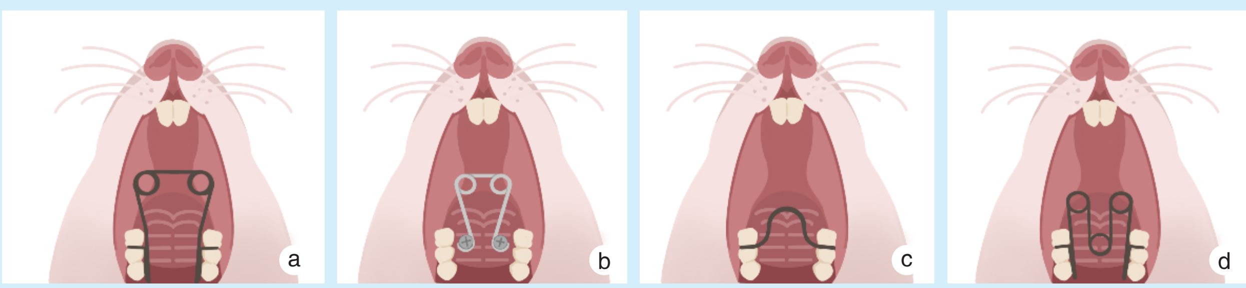
或不锈钢丝弯制双眼圈簧,双侧连接延伸臂。牙支持式扩弓器主要分为两种安装方式,一种将延伸臂直接粘结到两侧上颌第一、二磨牙的咬合面上[47-49];另一种延伸臂向外弯折,从腭侧插入上颌第一、二磨牙邻接点之下,再将其与大鼠磨牙腭侧粘接固定[50-52],第二种方法同时包含机械固位与粘接固位,增强了装置的固位力(图2a)。同单眼圈簧法一样,在扩弓期结束后可粘固小圈曲消除扩弓加力,以进行保持期的研究。冯光耀等[53]将双眼圈簧延伸臂沿唇颊侧弯制,从颊侧将末端插入上颌第一、二磨牙之间,制成扩弓后的缩弓器,进行上颌牙弓反复扩缩的实验研究。

另有研究使用双眼圈簧建立种植支抗辅助上颌扩弓模型(图2b)。Jin等[16]将定制不锈钢螺钉植入双侧上颌第一、二磨牙之间的腭侧牙槽骨,将0.016英寸不锈钢丝弯制的双眼圈簧延伸臂末端弯折环绕螺钉,并粘接固定,成功建立了大鼠的MARPE模型。

目前此方法多用于鼠类动物,相较于单眼圈簧法能够更好模拟临床扩弓的模式,然而磨牙区操作有一定难度,在日常检查方面也无法清晰可视。

2.2.2　“Ω”型扩弓簧法　Koehne等[54]将0.016英寸澳丝弯制成“Ω”型,将末端插入上颌第一、二磨牙之间并粘固,建立小鼠后牙扩弓模型(图2c)。Sun等[12]分别将0.008和0.010英寸镍钛丝弯制成“Ω”型,插入小鼠上颌第一、二磨牙之间,以分别产生10 g和20 g的力。

2.2.3　“W”型扩弓簧法　“W”型扩弓簧使用0.014英寸澳丝弯制,末端回折插入上颌第一、二磨牙之间或于磨牙腭侧粘接固定(图2d);Xu等[55]在此基础上进行了改良,在上颌磨牙的腭侧粘接腭管,将扩弓簧末端插入腭管中,此方法可以将装置从口内取出重新激活加力而免于重新粘接。




a: expansion appliance with two coils; b: microimplant-assisted expansion appliance with two coils; c: Ω-shaped expansion appliance; d: W-shaped expansion appliance with three coils

Figure 2　Animal models of posterior maxillary expansion appliances

图2　后腭缝扩张装置动物模型

2.2.4　螺旋扩弓法　相较于鼠类,口腔空间充足的兔、小型猪以及比格犬等动物可采用螺旋扩弓器。通过在尖牙及磨牙上制作个别带环[26, 37],或使用自凝塑料制作分离基托[22],再将矫治器粘接于上颌牙弓上,实现传统的牙支抗螺旋扩弓。通过在螺旋扩弓器上焊接或打孔等方式,可以个性化制

作MARPE[37]。使用螺旋扩弓器更接近临床上的正畸扩弓方式，能够定量加力，且更容易粘固保持，为人类上颌扩弓治疗提供更直接的参考。

2.2.5　磁力扩弓矫治器　磁力扩弓通过磁体间的斥力作用于支抗牙，由于扩弓过程具有个体差异，磁力扩弓矫治器对不同个体的组织适应性改建提供了个体化调节时间。目前磁力扩弓矫治器在正畸领域有一定的应用前景，但其与传统扩弓方法的效果和稳定性差异仍需要进一步研究。研究常使用比格犬，在尖牙和第一磨牙上制作个别带环，将带环与磁力扩弓矫治器相焊接，建立比格犬磁力扩弓模型[56]。Tong等[35]使用比格犬，基于钕-铁-硼磁铁的排斥力结合再激活系统设计了一种磁力扩弓器，与牙支抗扩弓和种植支抗扩弓进行对比研究。

### 2.3　扩弓模型的建立效果

腭中缝和牙槽骨宽度的增加标志着上颌扩弓模型的成功建立。前腭缝扩张模型在扩弓7 d后，前腭缝呈“V”形显著加宽[15]；而后腭缝扩张模型的腭中缝呈平行扩增。MARPE模型的前后腭缝均有明显扩张，且扩张效率更高[16]。这些动物模型的扩张特征提供了多个扩张位点[57]，有助于全面了解上颌扩弓的生物反应。

除腭中缝的扩张，牙支持式扩弓模型还通过牙的颊倾扩大牙弓宽度[49]。明确扩弓的牙效应和骨效应在扩张和复发时的比例有助于理解其潜在机制并促进扩弓疗效的稳定性，对临床上选择合适的扩弓策略具有重要意义[58]。

## 3　研究应用

### 3.1　探究机械力诱导骨重塑机制

利用上颌扩弓动物模型可以对上颌骨骨缝在力学作用下发生的生物学变化进行观察，并探究其中介导骨重建的机制（表1）。Guerrero等[18]利用小鼠扩弓模型，探究上颌快速扩弓中涉及的细胞变化和潜在分子通路，证明了该模型作为机械诱导骨重塑模型的可行性。

**表1**　上颌扩弓动物模型探究机械力诱导骨重塑机制

Table 1　Exploration of the mechanism of bone remodeling by mechanical force using animal models of maxillary expansion

| Animal | Research target | References |
|---|---|---|
| Gli1-LacZ Transgenic mice | Glioma-associated oncogenehomolog 1 positive（$Gli1^+$）cell | [59] |
| miR-21 deficient (miR-21$^{-/-}$ ) mice | miR-21 | [60] |
| Proline-rich tyrosine kinase 2 genetic knockout (Pyk2-KO) mice | Pyk2 | [12] |
| Phosphatidylinositol-3-kinase γ deficient (PI3K$\gamma^{-/-}$ ) mice | PI3Kγ/Akt axis | [13] |
| Wistar rats | Vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF-2) | [44] |
| Wistar rats | M2 macrophages | [61] |
| SD rats | Piezo type mechanosensitive ion channel component1（Piezo1） | [62] |
| SD rats | Nuclear transfer factor kB (NF-kB) | [63] |
| C57BL/6 mice | alpha-7 nicotinic acetylcholine receptor (α7nAChR) | [64] |
| C57BL/6 mice | T cells | [17] |
| C57BL/6 mice | Neutrophils | [65] |

### 3.2　不同扩弓器效果的比较评估

目前临床上有多种类型的上颌扩弓矫治器，如四眼圈簧扩弓器、传统螺旋扩弓器、MARPE以及新型的磁力扩弓器等。将不同矫治器应用于动物实验，通过对比扩弓量、扩弓速度、对牙以及牙周组织的影响等指标，可以评估不同矫治器的优缺点。Fox等[32]和Oliveira等[26]使用离体猪上颌骨建立MARPE模型，探究快速腭中缝扩张时牙槽骨和上颌周围骨缝的机械应变，证明MARPE在骨缝扩张过程中张力更恒定。Tong等[35]使用比格犬建立磁力扩弓器模型，将其与传统螺旋扩弓器比较，研究证实磁力扩弓器对支抗牙的力更加温和，为后续磁力扩弓的临床研究提供动物实验基础。根据动物模型中上颌扩弓矫治器的应用结果，可以对矫治器进行优化，以提高矫治器的临床应用效果。

### 3.3　筛选扩弓治疗的辅助措施

尽管上颌扩弓可以在短时间内显著扩张腭中缝，但其具有较高的复发率[66]。充分的成骨是降低复发率的关键，目前临床防止复发主要通过延长机械保持的时间来实现。然而保持期过长也会

大幅阻碍正畸序列治疗的进程[67]。因此亟需可靠且可推广的辅助加快扩弓的方法。

通过建立上颌扩弓动物模型，可以评估与扩弓联合使用的辅助措施对腭中缝处新骨形成的有效性（表2）。近年来已有激素类、化学制剂类、药物类、生物制剂类、蛋白质类和非手术物理措施等多种辅助方法纳入研究[11]。在动物实验中研究扩弓合并辅助措施的效果，可以为临床治疗提供更准确的预测模型。

**表2　通过上颌扩弓动物模型研究上颌扩弓治疗联合辅助措施的效果**

Table 2　Exploration of the effects of supplementary methods combined with maxillary expansion therapy using animal models of maxillary expansion

| Type of supplementary methods | Supplementary methods | Administration route | References |
|---|---|---|---|
| Hormones | Parathyroid hormone | Subcutaneous injection | [51, 55] |
| | Relaxin2 | Local injection | [43] |
| | Injectable estrogen - nanodiamond hydrogel | Local injection | [68] |
| Chemicals | Injectable mesoporous bioactive glass/fibrin gluecomposite hydrogels | Local injection | [15] |
| | Puerarin | Local Injection | [50] |
| | Matrine | Intraperitonealinjection | [52] |
| | Salvianolic acid B | Intraperitoneal injection | [69] |
| | Hydroxyapatite Nanoparticles(nHAP) | Surgically implanted with collagen sponge | [70] |
| Drugs | Isotretinoin | Via oral gavage | [42] |
| | Teriparatide | Local injection | [40] |
| | Bisphosphonates | Subcutaneous injection | [54] |
| | Simvastatin | Via oral gavage | [71] |
| Biologicals | Mesenchymal stem cells | Local injection | [41] |
| | Platelet rich plasma | Local injection | [21] |
| | Extracellular vesicles derived from M1 macrophages | Local injection | [72] |
| | MicroRNA-21-loaded upconversion nanoparticles | Local injection | [73] |
| Proteins | Lactoferrin | Local injection & Via oral gavage | [74-75] |
| | Obesity-associated protein | Local injection | [47] |
| Physicals | Laser | Irradiation | [71, 76-77] |
| | Photobiomodulation | Irradiation | [45] |

## 4　小结与展望

在口腔正畸学研究发展中，上颌扩弓动物模型仍有着诸多研究场景亟待发掘。如在基因研究方面，通过特定基因编辑动物建立上颌扩弓动物模型，可以探究某些基因在机械力诱导骨重塑中的作用；在生物材料研究领域，可以利用上颌扩弓动物模型测试新型生物材料在正畸领域的应用潜力。在口腔生理方面，可以更深入了解腭中缝成熟和骨化过程，以确定上颌扩弓的最佳时间和力值[78]。然而将上颌扩弓动物模型的相关研究转化为临床应用需要考虑多种因素，如种属间生理结构差异、经济成本和伦理问题等，研究者需要进行严谨的分析确保动物实验结果能够可靠地外推到临床实践中，未来还有望对其在正畸学乃至其他领域的应用有更多的探索。

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