激光增材制造技术在眼科中的应用

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摘要　总结了增材制造技术在个性化眼科医疗、精准眼科医疗、移动眼科医疗、眼视光学和眼科仿生领域的近期应用与未来发展前景。激光增材制造技术凭借易于定制和高效率的优势，有望令病人获得更具人性化、更有针对性、更加普及化的眼科医疗服务。

关键词　激光技术；激光增材制造；三维打印；眼科；应用前景

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Application of Laser Additive Manufacturing Technology in Ophthalmology

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Abstract　The recent applications of the additive manufacturing technology in the fields of personalized ophthalmology，precision ophthalmology，mobile ophthalmology，optometry and ophthalmic bionic，and its future prospects are reviewed. With the advantages of high efficiency and convenient of customization，the laser additive manufacturing is expected to help patients to obtain more humanistic，more targeted and more widespread ophthalmic medical services.

Key words　laser technique；laser additive manufacturing；three-dimensional printing；ophthalmology；application prospects

OCIS codes　140.3390；170.4470；170.1610

1　引　　言

增材制造技术，又称三维(3D)打印技术，由光固化(SLA)技术[1]发展而来。SLA 技术利用紫外激光将高分子聚合物固化，一层成型之后再照射下一层，逐层成型直到最终完成整个物体形状的成型。现在绝大部分 3D 打印机均采用这种逐层打印的模式。常见的 3D 打印技术包括针对金属或陶瓷的激光烧结(LS)技术[2-18]，可打印精细结构的粉末喷墨技术[19-29]，价格低廉的熔融沉积(FDM)技术[30-43]等。3D 打印技术发展迅速，从日常用品[44-46]到航天设备[47]，从武器[48]到食物[49]，在各行各业均有应用。在医疗领域，3D 打印技术已经被广泛应用于骨科[50-52]、牙科[53-55]、整形[56-58]、疾病建模[59-61]、药物生产[4,20,62]等。

3D 打印技术进入眼科领域较晚，但发展迅猛，特别在最近两三年，相关论文及报道逐渐增多[63-66]。国内外多个课题组开展了 3D 打印在眼科中的应用研究，部分成果在临床已经取得成功，有的甚至已达到商业标准。3D 打印技术可根据病人情况灵活改变设计文件，进而打印出个性化的器件；制造流程简洁高效，病人、医生的反馈可立即体现在产品设计和

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加工上，产品的研发效率高；相对于过去将设计文本交于模具加工公司生产，3D 打印产品的价格和时间成本均大大降低。本文综合了近几年激光 3D 打印技术在眼科中的应用报道，讨论了 3D 打印制造技术为个性化眼科医疗、精准眼科医疗、移动眼科医疗、眼视光学和眼科仿生学等领域带来的变化与发展。

2　3D 打印与个性化眼科整形

在眼科或面部整形领域，个体的差异性是医生面对的最大问题。对于眼眶受损需要修补或者需要植入义眼的病人，医生和病人不仅希望能最大限度地恢复眼部功能，而且希望植入物或假体能够尽可能合身、美观，但统一生产的相同规格植入物很难满足每一个病人的需求。3D 打印技术可以灵活方便地修改设计文件，生产完全个性化的植入物，同时 3D 打印技术可以小批量生产且精度高，可满足每一个病人的需求。

2.1　眼眶骨重建与整形

眼眶骨结构复杂，弧度不定且个体差异大，传统植入物的选择和调整难免存在误差[67]。现在，医生可以通过 3D 打印技术为患者提供个性化的眼眶骨[68]。整个打印过程如图 1 所示。首先为了得到准确的眼眶骨参数，需要对病人眼眶周边进行计算机断层扫描(CT)和核磁共振(MRI)检查，再根据扫描数据，利用专业软件绘制出正常的眼眶骨三维图形，得到用于 3D 打印的格式文件，3D 打印机根据该文件即可制备出相应的植入物。

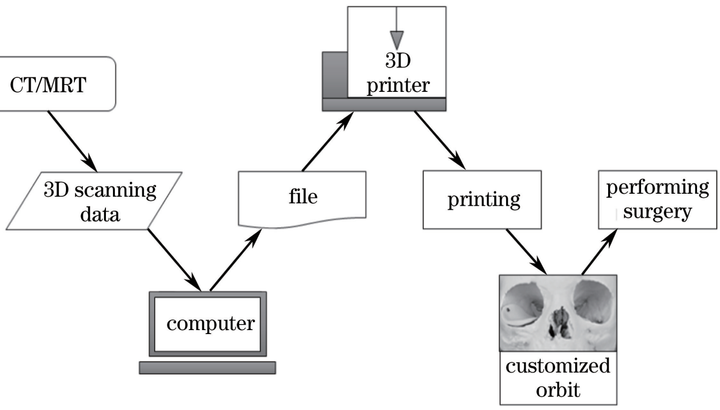

图 1　3D 打印眼眶骨的流程示意图

Fig. 1　Flow chart of 3D printing of orbital bone

2016 年，Mourits 等[69]使用 3D 打印技术为一位 6 岁中国小男孩进行了眼眶骨重构手术，并获得成功。患者天生单眼小眼症并伴有巨大的眼眶囊肿，眼眶骨已经严重变形。医生通过 3D 成像(CT 和 MRT)技术，获得囊肿和眼眶周边的数据，生产出眼眶骨及周边骨骼的模型，如图 2(a)所示。根据所得的模型，设计并打印出要植入的眼眶骨，如图 2(b)所示。在手术之前，医生根据打印出的个性化眼眶骨模型和植入物，充分考虑肿瘤切除后产生的空间和重建物植入之后可能占用的空间，进行了调整。患者术后恢复良好，两眼基本对称，如图2(d)所示。该手术的难点在于：患者年龄小，部分需重建的骨头厚度小于 1 mm，依靠传统方法准确定位手术位置十分困难，而 3D 打印技术很好地保证了该手术的成功实施。

这一类 3D 打印方式通常采用选择激光烧结(SLS)或者粉末喷墨技术，打印材料采用钛合金或者高分子聚合物(如聚甲基丙烯酸甲酯)。从上述例子中可以看到，3D 成像技术可让医生获得非常准确的病情数据，3D 打印技术可制备准确有效的植入物，两者的结合可令患者获得非常个性化的医疗服务。

2.2　彩色义眼制作

眼球缺失的病人需要佩戴义眼，义眼没有视觉功能，主要作用是美观，通常材料是特殊的玻璃或者亚克力。批量成产的义眼模样一致，很难满足每一个人的要求，高端义眼是手工制作的，眼球细节需要人工在玻璃上手绘，制作时间长、价格昂贵。英国 Fripp Design 公司自 2013 年开始，采用基于粉末喷墨原理的 3D 全彩打印机 Spectrum Z-Corp 510[70-71]，为客户定制义眼。3D 打印的每一个义眼都可以精确地描绘出虹膜、静脉网络等细节，以匹配佩戴者的另一只眼睛，并且 3D 打印技术具有速度快、成本低的优势。

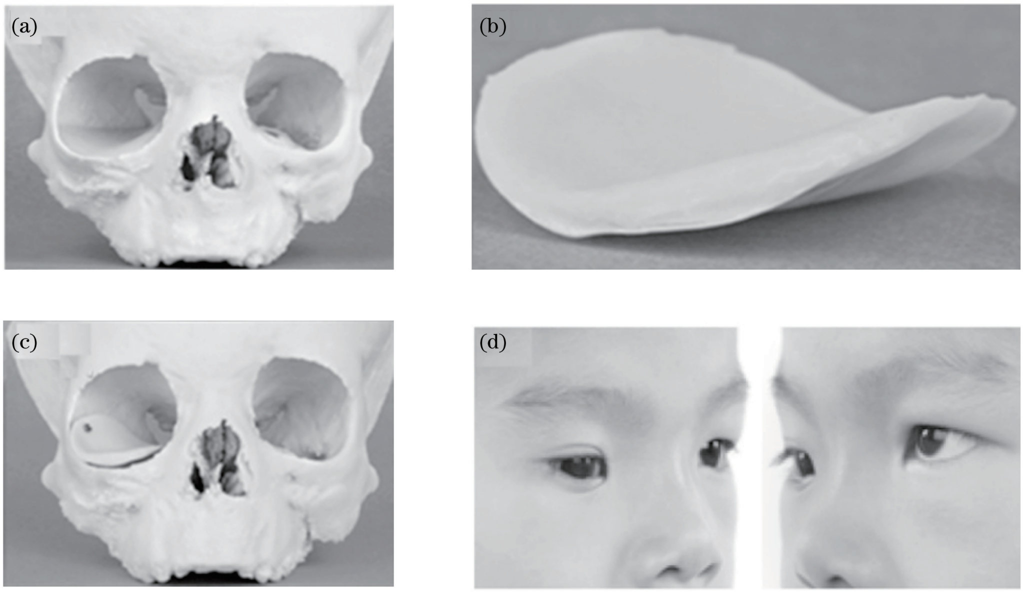

图 2 (a)术前眼眶骨畸变的头骨模型；(b)植入物；(c)将植入物放置于模型内；(d)术后照片

Fig. 2 (a) Preoperative skull model with deformed orbital bone; (b) implant; (c) model with implant; (d) pictures after surgery

3 3D 打印与精准眼科手术

3.1 立体定向眼科肿瘤手术

治疗肿瘤的常规方法是放射治疗，包括质子束治疗、带电粒子治疗、伽马刀立体定向治疗等。立体定向治疗需要获得十分准确的病灶位置和肿瘤体积，从而确定射线走向和放射剂量。成人眼内肿瘤最常见的是葡萄膜黑色素瘤[72]，体积通常较小且在人眼后极部，不易精确对准，如图 3 所示。

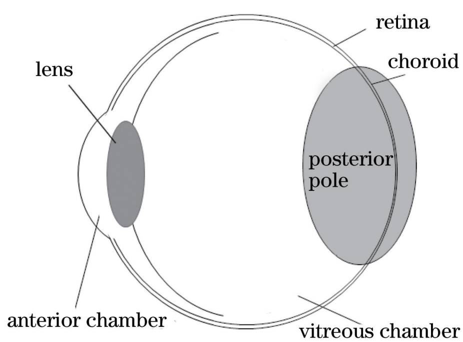

图 3 人眼结构示意图

Fig. 3 Structural diagram of human eyes

为了解决这一问题，2017 年，Furdova 等[73]尝试使用 3D 打印技术寻求手术的合理方案。首先依靠 CT、MRI 等技术重构眼底的立体图像，使用 FDM 打印机和聚乳酸打印人眼和肿瘤的 3D 模型，然后观察并测量肿瘤模型的位置和体积，寻求最佳的治疗方案。目前，该方法仍处于探索阶段，未来有望对医生的治疗方案产生重要的积极影响。

3.2 精准给药

3D 打印制药是通过层层打印的方式，打印出具有特殊外形或复杂内部结构的药品，从而控制药物到达病灶的位置或药物释放的进程，让人体对药物的利用更为合理[4,74-77]。例如，当医生对患有眼内肿瘤的病人采用放射治疗手段时，需要确定放射射线的方向和剂量，由于患者面部高低起伏不一，实际到达病灶处的放射量可能不均匀甚至放射射线没有准确到达病灶。为了解决这一问题，通常会在患者体表放置一层石蜡，以减小可能存在的位置差异。石蜡层的制作通常有两种方式：一是医生根据病人脸部形状进行手工制作，该方法可以根据每个病人的情况进行给药，但是准确度较差，且费时费力；另一种方法是通过计算机控制的铣床进行研磨制造[78]，与手工制造相比，该方法准确度较高，但该技术掌握在美国 Decimal 公司手中。采用 3D 打印技术有望改变这一现状，Łukowiak 等[79]对此进行了尝试，使用 3D 打印机为 11 位病人量身定做不同的石蜡层。由于打印时间过长，这种 3D 打印石蜡层技术尚处于试验阶段，未应用于临床。但试验结果表明，相比于传统手工制作，3D 打印的石蜡层精度更高，更适合表面不规则的皮肤，均匀性更好。

3.3 精细眼科手术器材

人眼体积小、结构复杂，眼科医疗器材必须十分精密。例如，应用在经结膜玻璃体切除手术中的套

管针，直径通常在 0.5 mm 左右。2017 年，Navajas 等[3]尝试使用 3D 打印机打印此类套管针，所采用的 3D 打印机为一台商业化 LS 打印机，打印选用的材料是一种树脂材料(丙烯腈-丁二烯-苯乙烯聚合物，ABS)，最终获得了直径为 0.7～0.8 mm 的套管针，并在猪眼上进行了试验。与商业化套管针相比，虽然 3D 打印出的套管针并不完美，但是若使用精度更高的 3D 打印机以及强度更大、韧性更好的打印材料，应该可以获得更好的试验结果。

4　3D 打印与移动眼科医疗

眼部疾病通常给患者带来非常大的痛苦，而且许多眼科疾病不单单是眼部一个器官的问题，更是全身系统性疾病的反映。如糖尿病、高血压等慢性病均会造成眼部的病变[80-81]。此类病人会被建议去眼科做检查以便医生更准确地了解病情[82-83]。然而，眼科医疗具有高度的专业性，眼科检查设备昂贵，导致在基层诊所或者社区医院进行较为全面的眼科检查非常困难。

3D 打印技术凭借其独特的高效率、低成本、易于定制化的特点，开始在面向大众的眼科基层医疗中发挥作用。2015 年，Chiong[84] 使用 3D 打印机，制备出可在智能手机上使用的眼底照相机和裂隙灯显微镜，成功获得了青光眼视盘和白内障患者的图像。该眼底相机由 7 个不同的打印部件组成，如图 4 所示，主要包括一个可调节的支臂、手机相机夹持部件(需要成对使用)、镜头夹持部件、相应的螺丝和螺母等附件。若采用面向家庭或个人的 FDM 打印机，打印材料可使用常见的商业材料，如尼龙等，整套材料费用在 40 美元以内，而成像效果却可以与专业的眼科检查器械相媲美。这些设备和手机相连，所采集的图像可以方便地分享给专业眼科医生。除此之外，相关的手机应用也已经推出，利用这些应用可以智能分析疾病隐患。该课题组为了在全球范围内推广这一应用，整套 3D 打印的设计代码是开源代码，任何基层临床医生或者普通人均可以下载并使用。2017 年，Jansen 等[85]在一位 22 岁的年轻人眼中发现了金属异物，所使用的检查工具即为在普通智能手机上可以使用的 3D 打印眼底照相机。

3D 打印技术的出现，让越来越多的医疗诊断成为可能，3D 打印技术的廉价与便利会给广大患者带来福音，普通人有望在接受检查和治疗的最初阶段(在社区医院、基层诊所甚至在家里)就能得到专业、高效的诊断和指导。

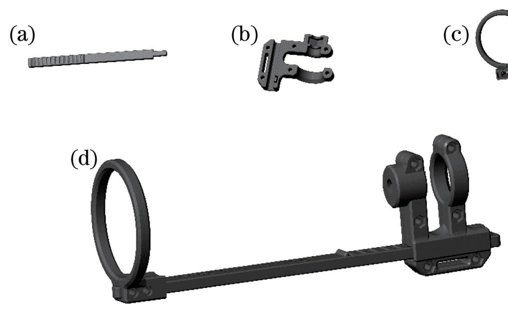

图 4　(a)可调节支臂；(b)手机夹持部件；(c)镜头夹持部件；(d)整套组装图

Fig. 4　(a) Adjustable arm; (b) cell phone clip; (c) lens ring; (d) assembly drawing

5　3D 打印与复杂视光学镜片

视光学是普通人接触眼科最多的领域，包括验光和配镜。使用 3D 打印机打印镜框比较简单，而制造透明的镜片则比较困难，这主要是因为若透明材料选择不当或是打印不均匀，则可能出现杂光和鬼像。

Khmyrov 等[86-87]尝试使用透明的石英颗粒，采用 SLM 制造透镜，即使用直径小于 20 μm 的石英玻璃粉末，用波长为 10.6 μm 的红外激光照射，打印的单层厚度为 100～200 μm。为了保证打印镜片的均匀性，必须精确控制紫外激光的参数，保持熔化温度恒定，这对于工业 SLM 打印机可能难以实现，因此尚未得到优良的激光 3D 打印透镜零件。

2017 年，荷兰 3D 打印光学公司 Luxexcel 取得突破性进展，首先采用构筑板确定镜片的形状，使用喷墨系统将硅聚合物喷洒到构筑板上，然后照射紫外激光或者红外激光进行固化。这样生产出来的镜片不用打磨抛光等后续处理便可直接使用，且部分眼镜镜片已经达到了相关行业标准[88-89]。

6　飞秒激光写入(FDLW)与眼科仿生

FDLW 是一种新型的 3D 打印技术，可用于微细精密加工领域，目前已成功应用在微米或纳米光学中[90-91]。该技术利用超短脉冲激光，在微时间尺度加工光敏材料，该材料可直接打印在多种基板上，打印出的模型无需后续处理便可直接使用。激光 3D 打印技术可轻松打印多种形状且不会增加更大的加工压力，在设计光学镜头时可以设计任意曲率的表面，而不用担心非常规曲率带来的加工难度和高昂的成本。

Thiele 等[92]利用该技术将微小透镜直接喷绘在一块金属氧化物半导体元件(COMS)成像面板

上，打印出了高度小型化的相机，用来模仿动物的眼睛，其中微小透镜用于模拟眼睛晶状体，CMOS 成像面板则用于模拟接收图像信号的视网膜。首先利用专业光学软件 Zemax 计算出想要的光学系统(即要模拟的动物眼睛)的各种参数，比如镜面曲率、成像距离等。然后根据这些数据设计 3D 打印文件，并由 FDLW 打印机制备透镜。由于打印基板就是 CMOS 成像面板，因此当打印结束时，透镜直接和 CMOS 成为一体，不需要采取其他措施便可以接收图像信息。Thiele 等一次性打印了 4 个直径为 300 μm的不同焦距的小透镜，每个透镜的制备需要 1～2 h。与一个真正的动物眼睛相比，该仿生眼的感光细胞数量过少，所成图像的分辨率不高。若采用更高密度的 COMS 成像面板，仿生眼可以拥有更多的成像像元，从而提高成像空间分辨率。随着激光 3D 打印技术的进步，小透镜的尺寸可以做得更小，这样可令仿生眼用在更微小的成像领域，例如内窥镜检查等。

7 结束语

综述了激光增材制造在眼科中的应用，总结了激光 3D 打印在眼科各个领域的最新应用和最新发展。激光 3D 打印技术具有易于定制化、高效率、低成本的优点，提高了医疗服务水平和眼科医疗器械的研发效率。目前，激光 3D 打印技术在眼科许多领域，如微小医疗器械、透明镜片等领域还处在探索阶段。但是，随着激光 3D 打印技术以及材料等方面的发展，很多问题将迎刃而解。国内眼科也在关注激光 3D 打印技术，2016 年国内首家激光 3D 打印眼科应用研发中心落户青岛市立医院。可以预见，激光 3D 打印技术在不久的将来会为眼科医疗带来新的革命。

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