

近红外二区荧光成像技术的临床研究进展

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摘要: 近红外荧光成像是外科手术中实现术中导航的关键技术之一。近些年随着近红外二区(NIR-II, 900~1700 nm)光学生物成像理论的日趋成熟, NIR-II 荧光成像技术成为临床手术导航领域的一大研究热点。本文基于 NIR-II 光学生物成像理论, 简要介绍了 NIR-II 荧光探针及成像系统的发展现状, 就 NIR-II 荧光成像技术在活体小动物手术与人体临床手术中的研究展开综述, 讨论了该技术在未临床手术中的发展潜力以及临床转化中需要面临的难点。

关键词: 荧光成像技术; 近红外二区; 成像导航手术

中图分类号: O43 文献标识码: A

Clinical research progress on the fluorescence imaging in the second near-infrared window

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Abstract: The near-infrared fluorescence imaging is a vital technology that enables the image-guided surgery. In recent years, the maturation of the optical bioimaging theory in the second near-infrared window (NIR-II, 900-1700 nm) has led to the emergence of NIR-II fluorescence imaging as a significant research area in the imaging-guided surgery. This paper provides a succinct overview on the current development state of NIR-II fluorescence probes and imaging systems based on the NIR-II optical bioimaging theory. Furthermore, it reviews the studies conducted on the NIR-II fluorescence imaging in the small animal and clinical surgery, and discusses the potential and challenges of this technology in the clinical surgery, including the difficulties that need to be addressed in the future clinical translation.

Key words: fluorescence imaging, the second near-infrared window, imaging-guided surgery

引言

近些年, 近红外荧光成像技术作为一种光学成像手段已经成为最受关注的术中导航技术之一, 被广泛地运用于前哨淋巴结显影、肿瘤切除、血管造影和术中解剖等多种外科手术之中^[1]。不同于术中冷冻切片等其他术中影像技术, 近红外荧光成像技术可以在手术过程中无缝使用, 完全不会干扰原本的手术流程、延长手术/麻醉的时间^[2], 能够在手术

过程中进行实时指导, 消除了术前诊断与术中操作之间存在的隔阂。由于组织中几乎没有近红外波段的自发荧光, 使用具有近红外荧光的造影剂可以极大地提高术中荧光信号的信号背景比^[3]。因此, 近红外荧光成像技术能够发现传统手术过程中无法察觉的隐匿病症, 弥补了传统外科手术中对手术医生经验的高度依赖^[4]。

尽管计算机 X 射线断层造影(Computed Tomog-

收稿日期: 2023-03-15, 修回日期: 2023-04-17

Received date: 2023-03-15, Revised date: 2023-04-17

基金项目: 国家重点研发计划(2022YFB3206000), 国家自然科学基金(61975172 和 62035011), 以及中国博士后科学基金资助项目(BX20220260)

Foundation items: Supported by the National Key R&D Program of China (2022YFB3206000), the National Natural Science Foundation of China (61975172 and 62035011), and the China Postdoctoral Science Foundation Funded Project (BX20220260)

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raphy, CT)、核磁共振成像(Magnetic Resonance Imaging, MRI)、正电子发射断层成像(Positron Emission Tomography, PET)等术前影像技术日趋完善,但这些影像技术无法兼顾时间分辨率、空间分辨率、安全性等多个指标,并且没有显著改善手术边缘的阳性率问题^[5]。而不同于CT、MRI、PET等影像技术,近红外荧光成像技术作为一种分子影像技术,并非通过解剖学上的异常定位病灶,具有较高的特异性。

目前,近红外荧光导航系统主要利用近红外一区(NIR-I, 760~900 nm)窗口进行成像,并被广泛用于癌症切除、血管吻合等显微外科手术中。相较于NIR-I窗口,近红外二区(NIR-II, 900~1 700 nm)窗口具备穿透深度更大、信号背景比更高、生物自发荧光更小等光学特性^[6],在手术导航领域具备更佳的应用前景,但受限于理论、光学结构、探测器、荧光探针的发展,市面上仍然缺少临床获批的NIR-II荧光成像系统。

本文基于NIR-II窗口光学生物成像理论、临床NIR-II荧光探针、NIR-II成像系统发展进程、临床NIR-II荧光导航手术案例,介绍当下NIR-II荧光成像技术在临床手术导航中具备的特点,以及发展过程中需要解决的难点。

1 近红外二区荧光成像技术

近红外荧光成像技术作为一种光学成像方法,它利用近红外相机捕捉靶向目标受激发后产生的近红外荧光信号^[7]。由于正常生物组织中基本不具备近红外荧光信号,该成像方法能够获得高对比度的荧光图像,这比临床手术中传统的可见光波段荧光成像方法更有优势。此外,得益于近红外光在生物组织中受到的散射作用较小,近红外光能够穿透到组织深处,近红外荧光成像技术可以捕获到表面组织以下一定深度的荧光信息。

目前,基于NIR-I窗口的荧光成像技术在肿瘤切除^[8-12]、血管吻合^[13, 14]等多种临床手术中得到广泛运用,提高了手术的精细程度。近些年来,随着研究人员利用皮肤、大脑等生物组织对近红外光的光学特性进行不断探索,具备更佳成像性能的NIR-II窗口被提出。长期以来,近红外波段在生物成像中的优势主要归功于其在生物组织中受到较低的吸收作用与散射作用,认为低散射作用以及低吸收的共同作用是获取高质量荧光图像的关键,因此大多数研究工作主要聚焦于近红外IIa(NIR-IIa, 1 300~

1 400 nm)窗口以及近红外IIb(NIR-IIb, 1 500~1 700 nm)窗口,避开了具有较大水吸收的1 400~1 500 nm波段。2021年,浙江大学钱骏教授团队对近红外波段进行全区域的模拟仿真,并进行了各个波段的活体生物荧光成像,包含了过往不被看好的1 400~1 500 nm^[15]波段。研究发现,生物组织对光的适度吸收可以有效地吸收被散射的光子,从而有效地抑制图像背景噪声^[15-17],提高输出图像的信号背景比,如图1所示。基于上述工作,NIR-II窗口被扩展为900~1 880 nm,在传统近红外窗口的基础上补充了近红外IIx(NIR-IIx, 1 400~1 500 nm)窗口、近红外IIc(NIR-IIc, 1 700~1 800 nm)窗口以及近红外III区(NIR-III, 2 080~2 340 nm)窗口。如图1(b)的仿真结果所示,NIR-IIc窗口在1 mm的成像深度下依旧具备优异成像的效果,其成像效果完全不弱于NIR-IIa窗口与NIR-IIb窗口,兼顾了信号强度以及信号背景比,是临床荧光导航手术中值得开发的成像窗口之一;NIR-IIx窗口与NIR-III窗口利用组织吸收进一步抑制被散射的荧光,尽管有效的荧光信号也受到一定程度的削弱,但整体信号背景比得到显著提升。可以预见,在合适的探针支持下,NIR-IIx窗口与NIR-III窗口在临床荧光导航手术中将具有最佳的引导效果。

通过小鼠^[18-21]、兔子^[22, 23]、类灵长类动物^[24, 25]等多种临床前的验证实验,NIR-II多个窗口被证实在穿透深度、空间分辨率、组织自发荧光等关键指标上具备更大的优势,有望取代目前主流的NIR-I荧光成像技术,成为未来临床导航手术中更好的荧光窗口选择。

2 近红外二区荧光成像系统

近红外荧光成像技术作为一种光学成像方法,其系统与大多数外科手术具有良好的兼容性,所有的成像器件都可以集成到一个紧凑的开放性设备、腹腔镜等手术器械中(图2所示)^[26],从而进行无接触的实时观测,实现近红外荧光的可视化工作,便于手术医生能够同时兼顾正常白光视场以及带有荧光标记物信息的荧光视场^[27]。然而,不同于NIR-I窗口,NIR-II窗口与可见光波段的跨度更大,因此临床手术中一直缺乏一套紧凑的且同时支持可见光波段以及NIR-II波段的荧光成像系统。

目前,NIR-II荧光信号的捕获主要依赖具备高量子效率的窄带隙镓砷(InGaAs)半导体探测器,相较于探测NIR-I或可见光波段的硅基探测器,钢

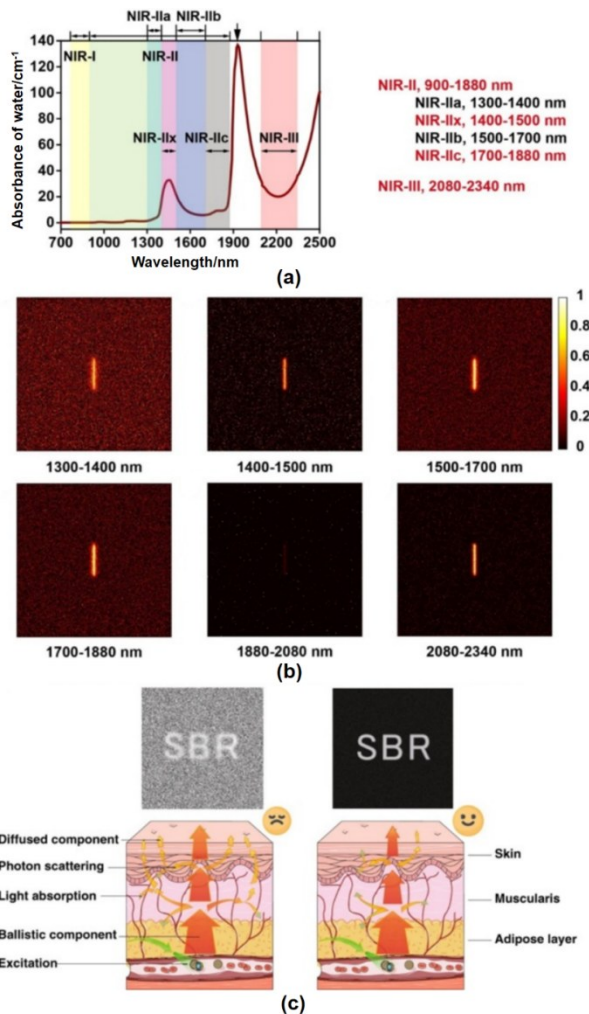


图1 NIR-II窗口光学生物成像理论^[15], (a)700~2 500 nm 内的水分子的吸收光谱, (b)1 300~2 340 nm 窗口内生物组织近红外成像的蒙特卡罗方法模拟结果, (c)弹道光子和散射光子在组织中的传播以及荧光成像的信号背景比示意图, 较小光吸收(左)和适当光吸收(右)的生物组织对比

Fig. 1 The mechanism of the NIR-II optical bioimaging^[15], (a) the light absorption spectrum of water within 700-2 500 nm, (b) the simulation results of the NIR bio-tissue imaging via Monte Carlo method in 1 300-2 340 nm, (c) the schematic diagram of light propagation in tissue, the propagation of excited ballistic and diffused emission photons in the bio-tissue with small (left) and moderate (right) light absorption and the resulting SBRs of the fluorescence imaging

镓砷探测器的整体制造工艺尚不成熟, 现在仍处于快速发展阶段(图3所示)^[28]。高性能的镓砷探测器普遍需要制冷模块, 整体尺寸、重量较大; 缺乏同时提供RGB与短波红外通道(900~1 700 nm)的镓砷相机; 探测芯片的像元数较少、像元比较大。想要兼顾可见光波段以及NIR-II波段, 目前必须同

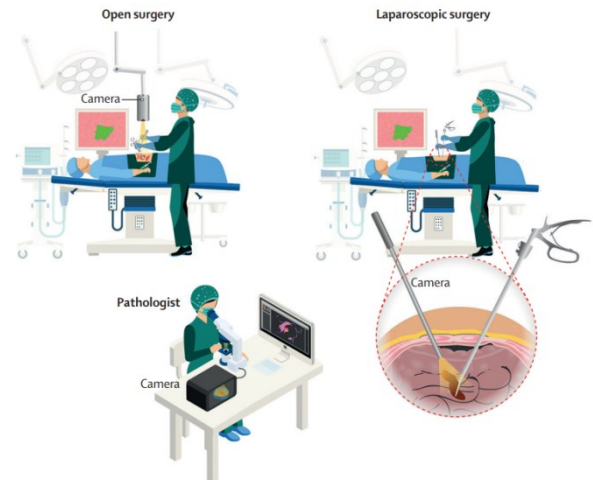


图2 所有的成像器件都可以集成到一个紧凑的开放性设备、腹腔镜等手术器械中, 进行无接触的实时成像^[26]

Fig. 2 All imaging equipments can be integrated into a compact open-field device or within laparoscopic and other surgical instruments for contact-free and real-time imaging^[26]

时使用多台相机。中国科学院自动化研究所田捷教授团队采取多个通道相机并行放置的方式构建了开放式NIR-II荧光手术导航系统, 并进行了首次临床实验^[29]。而在微创手术广泛应用于临床的今天, 搭载NIR-II荧光成像系统的双通道内镜系统是临床手术不可或缺的一部分, 也是未来需要重点攻关的难题之一。因此, 为了满足微创手术术中实时成像, 确保术中快速切换相机或多相机同时工作, 需要相关的光学元件必须在可见光波段以及NIR-II波段同时具备较高的透过率、较小的像差, 而这对光学系统的设计是一个巨大挑战。

3 近红外二区荧光探针

NIR-II临床导航手术推进较慢的另一重要因素就是缺乏合适的NIR-II荧光探针。尽管目前已有许多可代谢、高亮度的NIR-II探针被开发出来, 包括小分子荧光染料^[30, 31]、聚集诱导发光纳米颗粒^[32-35]、有机共轭聚合物纳米颗粒^[36, 37]、量子点^[38-41]、稀土掺杂纳米探针^[42-44]等多种类别, 但绝大多数的荧光探针都没有经过临床测试。

所幸, 在1959年通过FDA认证、被广泛运用于多种荧光导航手术的花菁类小分子荧光探针吲哚菁绿(ICG)^[45, 46]被证实在NIR-II波段依旧有可观的荧光分量^[47]。ICG不仅具备高摩尔消光系数、较高的荧光量子产率, 还具有较好的生物安全性, 被广泛运用于术中血管造影、淋巴管造影、肿瘤切除

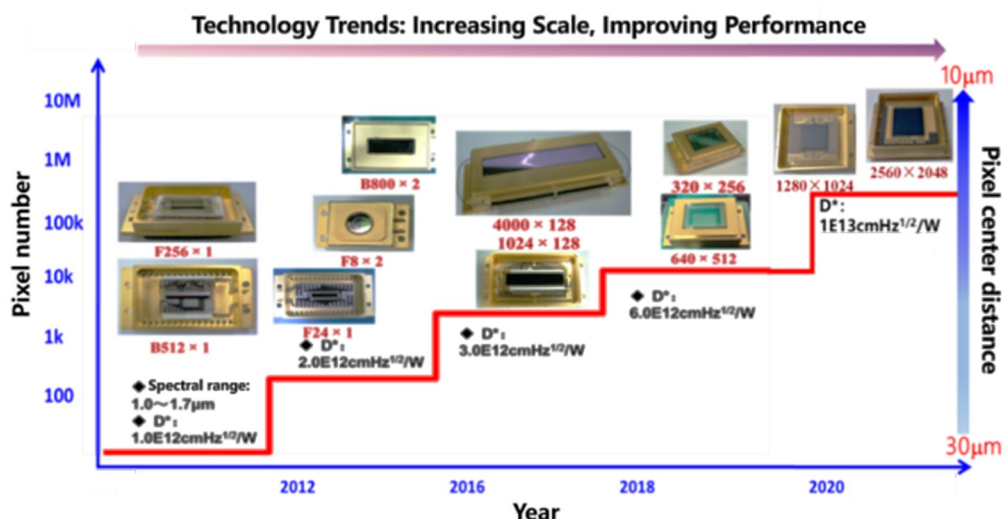


图3 上海技物所1~1.7 μm InGaAs焦平面探测器发展进程^[28]

Fig. 3 The development roadmap of 1-1.7 μm InGaAs FPA in SITP^[28]

等^[1]。此外,已有大量研究工作通过动物实验证实了ICG的NIR-II荧光成像较NIR-I荧光成像具备更加优异的表现,为NIR-II成像的临床转化铺平了道路。但作为一种非靶向的荧光探针,ICG难以区分良性肿瘤与恶性肿瘤,ICG在其他组织中的积累可能会造成肿瘤假阳性诊断结果^[48]。因此,临床可用的靶向近红外探针依旧是一个亟需解决的问题,需要近红外荧光团和靶向分子的稳定结合,以实现靶向肿瘤细胞的荧光检测,提升NIR-II成像技术对外科手术的引导效果。

4 近红外二区成像技术辅助下的活体小动物导航手术

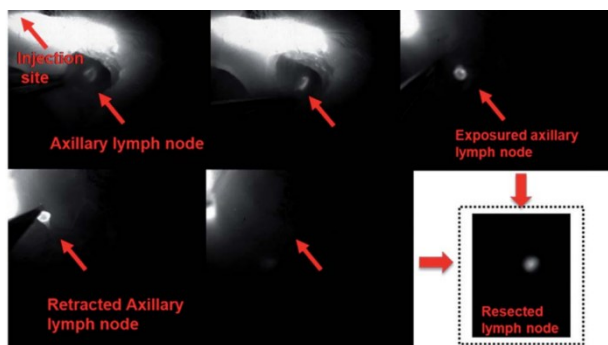


图4 NIR-II荧光图像引导下前哨淋巴结切除术^[49]

Fig. 4 The NIR-II fluorescence imaging guided sentinel lymph node resection^[49]

随着近十几年的发展,NIR-II窗口成像理论、成像系统日趋完善,出现了一批基于NIR-II成像技术的活体导航手术案例,为NIR-II成像技术的临床

转化打下坚实的基础。武汉大学洪学传教授团队于2017年利用NIR-II探针在荷瘤小鼠模型中清晰地描绘了肿瘤轮廓,并在NIR-II成像技术辅助下实现了前哨淋巴结的切除手术(图4所示)^[49],证实了NIR-II荧光成像技术能够在手术中对病灶边界进行准确描绘。之后,大量新型的NIR-II探针被运用于多种病灶的标记,实现了NIR-II荧光成像引导下的手术切除工作:中国科学院苏州纳米技术与纳米仿生研究所王强斌教授团队构建了NIR-II水性量子点探针,实现脑胶质瘤^[50]、乳腺癌转移瘤^[51]的导航手术;复旦大学张凡教授课题组利用稀土掺杂下的转换纳米颗粒实现了卵巢癌腹腔转移瘤以及淋巴结转移瘤的切除手术^[52]。并且,随着高亮度、长波长、高生物兼容性、高特异性NIR-II探针的开发,NIR-II荧光成像技术被运用于多种生物场景中,为未来的临床转化提供了基础。上海交通大学冯少清团队与复旦大学陈俊团队合作开发出高热稳定性、高生物兼容性的NIR-II水性量子点探针,能够在皮瓣移植的动物模型上实现皮瓣灌注情况的持续可视化^[53];上海交通大学沃雁团队与复旦大学陈俊团队合作开发出能够标记脂肪干细胞的NIR-II水性量子点探针,在大鼠坐骨神经损伤模型中记录了脂肪干细胞在神经再生过程中的迁移和分布^[54]。

此外,研究人员根据NIR-II的光学特性,开发出新的导航模式。为减少手术过程中的损伤,浙江大学林辉教授团队、钱骏教授团队以及苏州大学李盛亮教授联合开发了术中NIR-II多通道成像的模

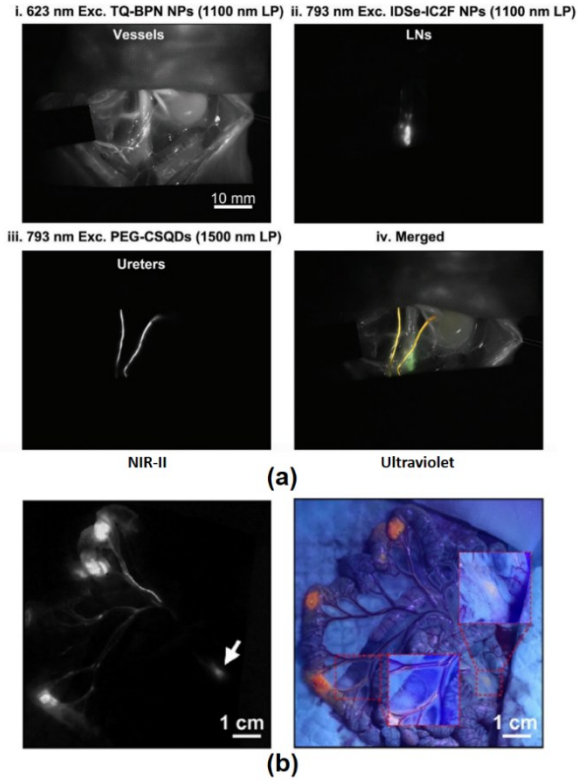


图5 (a)小鼠淋巴结、血管和输尿管的三通NIR-II荧光成像^[21], (b)肠系膜淋巴结及其淋巴管的NIR-II和可见荧光混合成像^[55]

Fig. 5 (a) The triple-channel NIR-II fluorescence imaging of LNs, blood vessels, and ureters on rats^[21], (b) the hybrid NIR-II and visible fluorescence imaging of mesenteric lymph nodes and corresponding lymphatic vessels^[55]

式,利用NIR-II窗口高分辨率、高信噪比的特点,实现了靶向目标以及周边组织、管道、器官的可视化,在淋巴切除手术中避免了不必要的损伤(图5(a))^[21]。虽然NIR-II荧光成像在手术导航中具有分辨率高、穿透深度大的优点,但NIR-II图像无法被肉眼观测到,这对外科医生的手眼协调有较高的要求,增加了手术难度。林辉教授团队与钱骏教授团队对手术导航方式进行优化,基于混合有NIR-II荧光探针(ICG)与可见荧光探针(黄连素)的“鸡尾酒”,实现了NIR-II和可见荧光混合成像引导的新型导航手术模式(图5(b))^[55],NIR-II荧光图像能够提供皮下微小病灶的位置信息,而可见荧光图像则能提高手术操作性,加快手术速度。

5 近红外二区成像技术辅助下的临床手术

5.1 应用于肿瘤外科中的近红外二区成像技术

据近些年世界卫生组织(World Health Organiza-

tion, WHO)与国际癌症研究机构(International Agency for Research on Cancer, IARC)对全球癌症流行病学的数据统计以及评估,癌症已然成为全球范围内导致死亡的主要原因之一,且全球范围内癌症的病发率以及死亡率依旧处于迅速增长阶段^[56]。迄今为止,外科手术依旧是肿瘤治疗的重要手段之一^[57],依托于NIR-I荧光成像技术的术中导航系统在肿瘤切除手术中已经得到广泛运用,实现微小病灶、病灶边界、关键神经或管道的显示工作。但其

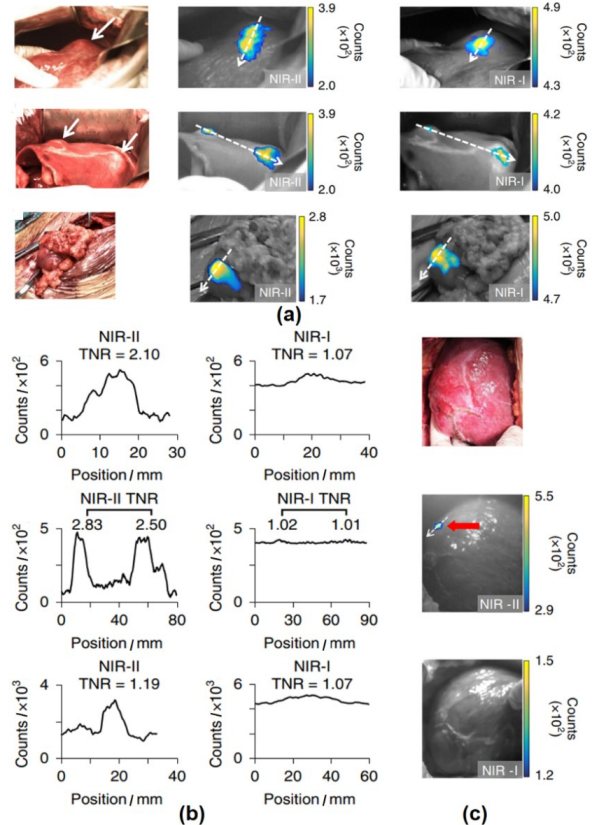


图6 不同类型肝癌患者的术中NIR-II/I区肿瘤图像^[29], (a)从上至下依次为肝癌结节、肝内转移灶、肝外转移灶的术中NIR-II/I区图像, (b)图(a)中白色箭头区域NIR-I和NIR-II图像的强度分布, (c)仅在NIR-II通道中检测到肝脏上的微小病灶

Fig. 6 The intraoperative NIR-II/I imaging of patients with different types of liver cancer^[29], (a) the intraoperative NIR II/I images for a nodule of liver cancer, intrahepatic metastases, and extrahepatic metastases, respectively, (b) the cross-sectional intensity distribution of NIR-II and NIR-I images in the white arrow region in (a), (c) a small intrahepatic metastasis in the right liver was successfully detected by the NIR-II imaging, as shown by the red arrow. However, the NIR-I imaging failed to detect the lesion

背景噪声较大、对深层组织的成像能力较差,若将荧光成像波段拓展至NIR-II窗口,将进一步提高荧光导航手术的精准性、减少术中的损伤。

中国科学院自动化研究所田捷教授团队首次将开放式的NIR-II荧光导航系统运用于临床肿瘤切除手术中,将可见光、NIR-II/I探测模块并排整合,利用ICG对肿瘤进行实时成像,对23名肝癌患者进行了NIR-II荧光导航的肿瘤切除手术^[29]。对原发性肝细胞癌、肝内转移灶或肝外转移灶癌症患者的术中NIR-II/I肿瘤图像进行比对分析,NIR-II肿瘤荧光图像均比NIR-I荧光图像具有更高的信号背景比与肿瘤信号对比度(图6(b)),并且在NIR-II通道中能够定位到部分NIR-I通道无法探测到的微小病灶信号(图6(c)),如图6所示。该工作突破以往离体层面、动物层面的研究工作,首次在临床层

面上证实了NIR-II荧光成像技术相较于NIR-I窗口具备更佳的临床导航效果,证实了NIR-II荧光成像技术在临床导航手术中具有巨大的潜力,推动了NIR-II成像技术未来的临床转化。

由于ICG本身并不具备靶向性,在使用ICG进行荧光导航手术时,病变的肝细胞癌以及良性的肝硬化结节会同时发出荧光信号,导致临床上会出现假阳性的案例^[59]。田捷教授团队利用ICG-IRDye800CW探针进行NIR-II荧光导航手术,能够精准地显示肝细胞癌与肝实质之间的边界(边界的信号背景比达到10.43),从而在术中对肝硬化患者进行精准的肝细胞癌检测,保留肝实质,降低术后并发症的风险^[58]。手术中的成像效果显示出了NIR-II荧光导航足以在手术中对病变区域进行快速、精准的划分,如图7所示。

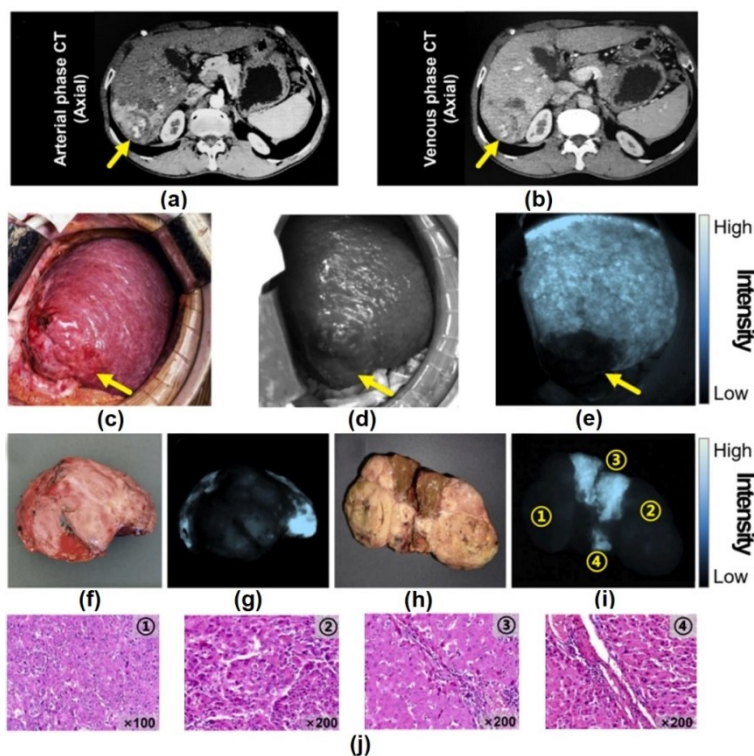


图7 肝癌切除手术中荧光成像和病理结果^[58], (a-b)术前增强CT显示右肝叶存在病变, (c-e)病变切除前的体内图像, (c)可见光图像, (d)白光照明下NIR-II图像, (e)能够在肝脏实质中检测到NIR-II荧光图像, 病变边缘对比度高达10.43, (f, g)切除的病灶上的荧光边缘有助于实现完全切除, (h-i)NIR-II荧光在体外病灶上的分布, 取四个典型标本(①~④)进行病理分析, (j)病理结果显示, ①为中度分化的HCC, ②为中低度分化的HCC, 有荧光信号的③和④为肝硬化

Fig. 7 The intraoperative fluorescence imaging and the pathological results in hepatectomy^[58], (a - b) the enhanced CT results showed a lesion in the right liver lobe, (c - e) show the in vivo images before lesion resection, (c) was acquired in the visible light spectrum while (d) was the white-light observation using the NIR-II imager, (e) the NIR-II fluorescence was detected in the liver parenchyma and the lesion was visualized with a high contrast of 10.43, (f, g) the fluorescent margin on the resected lesion aided to achieve a complete resection, (h - i) exhibit the distribution of the NIR-II fluorescence on the lesion ex vivo, four typical specimens (①~④) were taken for pathological analyses, (j) the pathological results showed that ① was the moderately differentiated HCC, ② was the moderately-poorly differentiated HCC, the fluorescent ③ and ④ were the cirrhosis

NIR-II 成像技术同样也被运用于脑胶质瘤的切除手术中,相较于 NIR-I 窗口, NIR-II 成像技术能够显示更多深层血管、微小血管(图 8),有助于减少术中对血管的损伤,能在不损害神经功能的情况下,提高肿瘤完全切除率和病人术后生存率^[60, 61]。NIR-II 成像技术对脑胶质瘤的检出率以及完全切除率均达到 100%,远高于以往的 NIR-I 窗口以及白光波段成像。近期,田捷教授团队将 NIR-II 成像技术同深度卷积神经网络相结合,实现了在手术期间实时提供原位脑胶质瘤的病理诊断,协助神经外科医生确认最佳切除区域^[62]。

术中保留盆腔自主神经对于避免宫颈癌患者术后膀胱功能障碍是至关重要的^[63]。然而,多数细小的盆腔自主神经很难通过肉眼看到,这使得在手术中存在一定的损伤风险。在根治性子宫颈切除术

中,通过 NIR-II 成像技术实时显示盆腔中的微小神经,帮助外科医生在手术中避免对盆腔自主神经造成损伤,保障宫颈癌患者术后膀胱功能健全^[64]。

由于肾癌在生长过程中主要以液体为主,因此在保留肾单位手术中切除囊性肾肿块的同时容易造成肿瘤的破裂^[66]。随着恶性肿瘤的破裂,癌细胞会在腹腔内进行转移,患者将面临癌症复发的风险^[67]。传统基于 ICG 的 NIR-I 荧光导航系统由于无法精准地确定肿瘤边缘,手术边缘的残留肿瘤信号会被边缘肾实质的强烈荧光所淹没,术后边缘的阳性率高达近 10%,给患者带来巨大的隐患。近期, NIR-II 成像技术被用于囊性肾肿块的切除手术中(图 9)^[65]。由于正常组织会表现出比肿瘤组织更强的荧光信号,肿块的边缘更加清晰,并且通过鉴定术后边缘以及切除的病灶基底是否同时具备强烈

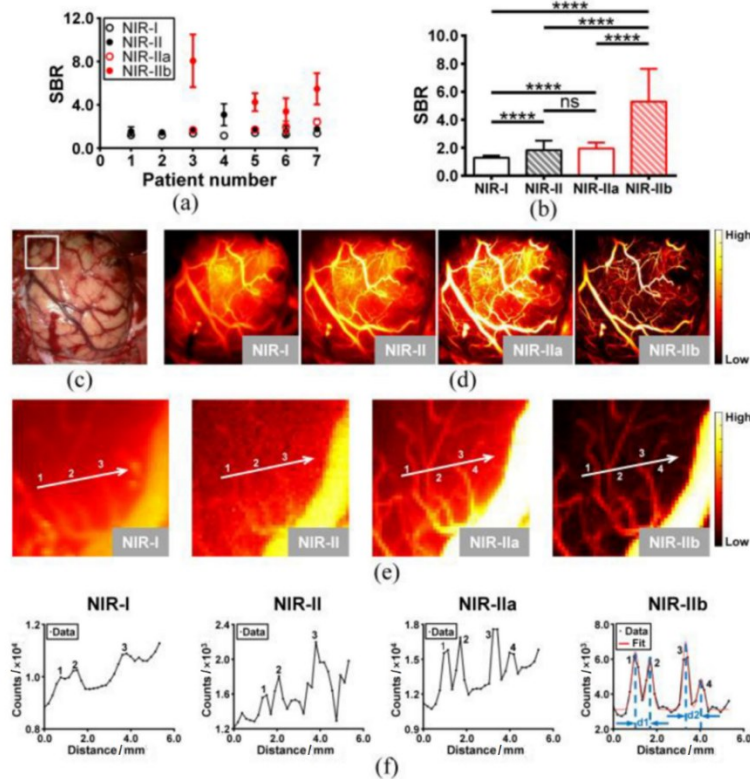


图 8 不同近红外窗口的脑部荧光图像比对^[61], (a)不同成像窗口下的脑血管信背比, (b)七名患者的平均信背比, (c-d)白光以及不同近红外窗口下的脑血管图像, (e) (c)中白色区域在各个近红外窗口的血管荧光图像,在 NIR-I 和 NIR-II 成像中可区分出 3 条静脉,在 NIR-IIa 和 NIR-IIb 成像中可区分出 4 条静脉, (f)白色箭头区域的强度分布曲线,其中血管 1、2 之间的距离 d_1 为 0.67 mm,血管 3、4 之间的距离 d_2 为 0.71 mm

Fig. 8 Comparison of multispectral fluorescence images^[61], (a) the vascular SBR in different spectra of each patient, (b) the mean vascular SBR of the seven patients, (c-d) the visible light and multispectral fluorescence images of cerebral vessels, (e) the fluorescence images of the enlarged view of the white rectangle in (c), three veins are distinguished in the NIR-I and NIR-II imaging while four are distinguished in the NIR-IIa and NIR-IIb imaging, (f) the cross-sectional intensity profiles, which correspond to the location and direction of white arrows in (e), respectively, d_1 indicated the center distance between vessel 1 and vessel 2, which was 0.67 mm, similarly, d_2 indicated the center distance between vessel 3 and vessel 4, which was 0.71 mm

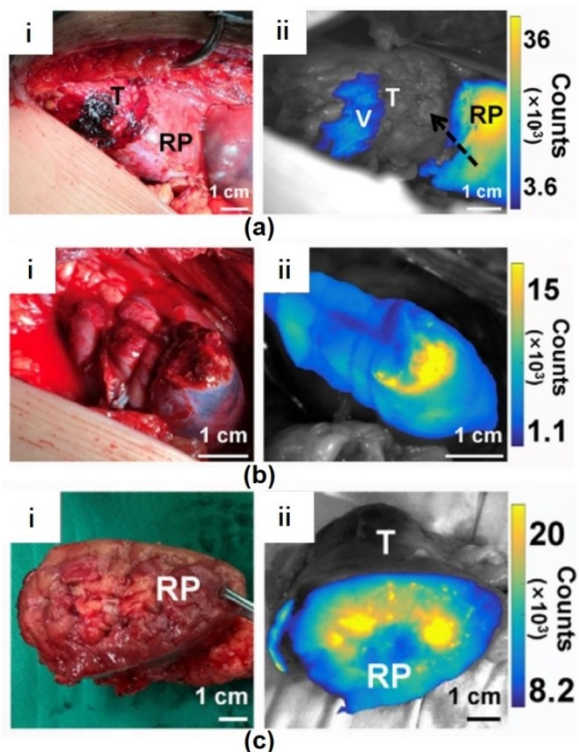


图9 术中NIR-II图像辅助的肾脏肿块切除手术^[65], (a) 肿瘤和肾实质的可见(i)和NIR-II(ii)图像, (b) 手术边缘的可见光(i)和NIR-II(ii)图像, (c) 肿瘤底部的可见(i)和NIR-II(ii)图像

Fig. 9 The intraoperative NIR-II image-assisted kidney mass resection^[65], (a) the visible and NIR-II images of the tumor and renal parenchyma, (b) the visible and NIR-II images of the surgical margins, (d) the visible and NIR-II images of the tumor base

的荧光信号,即可判断肿块是否切除完全,保证了切缘无阳性,避免了术中肿瘤破裂的风险,并最大限度地保留了正常组织。

NIR-II成像技术克服了以往NIR-I窗口分辨率低、成像深度、信号背景比不足的问题,解决了部分NIR-I荧光导航系统难以处理的临床问题,在多种癌症手术中都具备良好的表现,在肿瘤外科中具备巨大的临床转化潜力。

5.2 应用于血管造影术的近红外二区成像技术

鉴于ICG被注射进生物体后在被代谢前主要分布在血管网络中,并在血液中优先与蛋白结合发出强烈的荧光信号,能够显示血管的解剖结构,提供血管流量、血管尺寸等血流信息。血管吻合是外科各亚专科常用的手术方法,也是显微重建外科、血管外科和移植外科的重要组成部分^[68]。传统血管吻合的评价通常采用血管通畅检查或超声检查,这

两种方法在接触时都有损伤血管内皮的风险。而基于ICG的血管造影术作为无接触式的、标准化的成像技术,改变了以往血管吻合手术中主要依赖外科手术医生经验的情况,并避免造成血管额外损伤的风险。

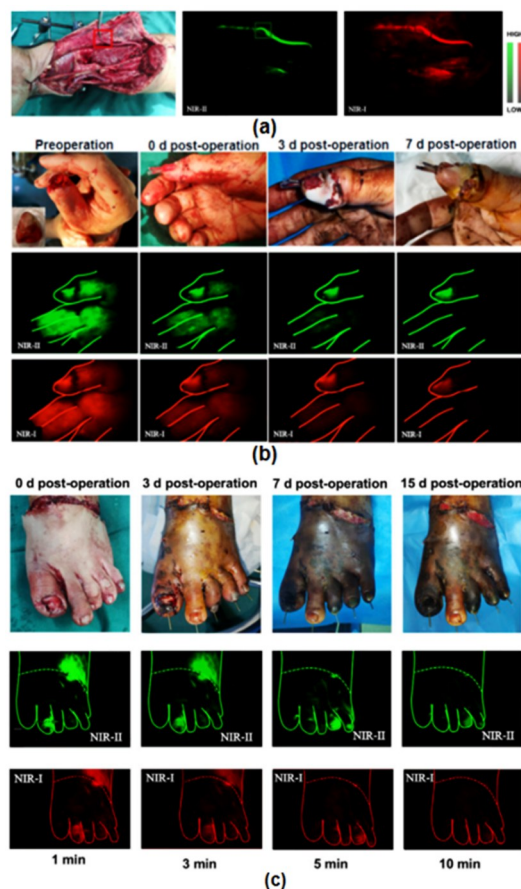


图10 基于ICG的NIR-II成像技术在显微手术中的运用^[69], (a)近红外成像用于评估吻合过程中的血管通畅, (b)拇指再植的近红外成像, (c)近红外成像技术用于撕脱伤重建

Fig. 10 Applications of the NIR-II imaging with ICG in microsurgery^[69], (a) the NIR Imaging for the assessment of vascular patency during anastomosis, (b) the NIR Imaging for a thumb replantation, (c) the NIR Imaging for the avulsion injury reconstruction

中国科学院上海药物研究所程震教授团队使用便携式的NIR-II成像系统对39例接受了血管吻合手术、拇指再植手术等显微外科手术的患者进行了ICG的术中成像,并同NIR-I图像进行对比^[69]。得益于NIR-II窗口更低的背景噪声、更高的信号背景比,基于NIR-II窗口的血管造影术能够检测到微小血管的血流情况,并且能够通过荧光强度的变化

实时观察动脉灌注和静脉回流等情况,如图 10 所示。

6 结语

在过去的几十年,得益于人们对荧光技术进行的大量研究,各种荧光成像技术已经进入手术室改变了传统的手术方式,让我们离精准医疗的目标更进一步,但在部分手术中也暴露出信号背景比不足、穿透深度有限等问题。而具备更佳光学性能的李R-II成像技术有望克服上述难题,推动荧光导航手术在临床领域进一步发展。然而,近红外成像技术仍然需要克服可用的荧光探针少和光学系统性能差这两个主要问题,以实现真正的临床转化。一方面,目前临床可用的NIR-II荧光探针只有ICG,作为一种非靶向的荧光探针,ICG在一些病症的诊断上有较高的假阳性率。并且ICG的NIR-II荧光占比小,NIR-II波段的荧光较弱,在临床使用中难以支持NIR-IIx、NIR-IIc等窗口的荧光成像。尽管许多长波长、高亮度的NIR-II荧光探针已进行了临床前的测试,但用于人体的数据却很少。另一方面,用于NIR-II荧光信号探测的铟镓砷探测器发展不够成熟、体型比较大,尤其不利于高集成度系统的开发,并且较大的波段跨度也是目前光学系统制作中的难点。目前逐渐出现的临床可用的NIR-II荧光成像系统,仅适用于开放式手术,缺少同内镜系统兼容的NIR-II成像模块。近两年涌现出的大量临床研究工作显示,NIR-II荧光成像技术相比传统的近红外荧光成像技术具有更好的成像效果,在临床手术中能够更精准地描绘病灶边缘、发现更微小的病灶、显示更细小的血管以及神经,提高手术质量,改善患者的预后。可以预见,随着NIR-II荧光成像技术的日趋完善,NIR-II荧光导航手术将为精准外科的实现奠定坚实的基础。

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