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用于荧光内窥镜的陷波滤光片的研制

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摘　要：基于荧光内窥镜的实际应用确定陷波滤光片的技术指标，以光学薄膜理论为基础设计陷波滤光片结构，采用 Essential Macleod 软件辅助进行膜系设计，分析膜层敏感度，选择合适镀膜设备、工艺控制方法制备陷波滤光片。制备的滤光片通带透射率均值达到 97% 以上，截止背景达到 OD6 以上，透射波前畸变低于 $\lambda/4$ @632.8 nm，满足医疗健康微创精准手术的应用需求。

关键词：荧光内窥镜；滤光片；陷波膜系；近红外荧光；吲哚菁绿
中图分类号：O436.1　　**文献标识码：**A　　**doi：**10.3788/gzxb20245301.0131001

0　引言

随着我国对精准医疗需求的不断提升，极大减小创伤的微创治疗越来越得到医患人员的重视。荧光内窥镜是外科微创手术的重要医疗器械之一，它的分子影像技术用于直接观察指导微创治疗全过程，其工作原理为：将吲哚菁绿（Indocyanine Green，ICG）[1-2]通过局部组织或静脉注射的方式引入人体，用特定光谱近红外光照射后产生荧光，进而使荧光内窥镜同时实现可见光和近红外荧光成像。在评价对不同图像融合方案的感知中，检测和识别目标效果最好的是近红外光，而感知全局场景可见光效果最好[3]，因此，采用可见光获取组织背景、场景位置等信息，采用荧光图像捕获肿瘤大小、边界等信息，将两者图像特征信息精准叠加，可帮助医生更加精确地识别和定位肿瘤、检出微小病灶、标记肿瘤边界，进而顺利切除肿瘤[4-5]。同时实现可见光和近红外荧光分子成像的荧光内窥镜，将是“靶向外科”必备视觉监测系统，是内窥镜的新理论和前沿技术。其中荧光内窥镜用陷波滤光片关键技术研究将决定着荧光内窥镜成像清晰度和病灶部位荧光图像的准确识别，决定了在临床上是否可以有效地辅助诊疗和实现精准医疗[6-7]，具有重要的临床应用前景和科学意义。

在荧光内窥镜的应用过程中，需要在患者体内注射吲哚菁绿，由于吲哚菁绿的量子产率低、荧光信号弱、荧光图像信噪比低，因此，提高荧光内窥镜中的荧光弱信号的信噪比是急需解决的问题。而系统内的滤光器件对于信噪比有较大的影响，目前针对荧光内窥镜的滤光片鲜有报道，本文设计并制备了用于荧光内窥镜光学系统的陷波滤光片。

1　滤光片设计

1.1　技术参数

采用 ICG 作为荧光探针，通过局部组织或静脉注射方式[8]，与血液中的血浆蛋白结合，在 750～810 nm 近红外光的激发下，释放出 835 nm 左右的荧光信号。ICG 的光谱响应（Ex 为激发光谱，Em 为发射光谱）如图 1 所示。根据 ICG 荧光探针的特性，荧光内窥镜分别以白光光源和近红外光源作为照明光源和荧光信号

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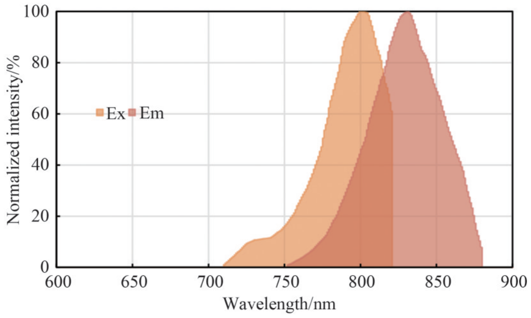


图1　吲哚菁绿归一化强度谱线
Fig. 1　Normalized intensity spectrum of Indocyanine green

激发光源，双光源通过内窥镜导光管对人体组织进行照射，摄像系统采集携带有用信息的图像信号，实现同时对白光的组织信号成像和近红外光激发的荧光组织信号成像，并可对图像精准叠加。

为保障荧光内窥镜视野同时实现可见光成像与近红外荧光成像，光谱透射区设计为：$T>97\%$@435 nm～680 nm & @820 nm～880 nm；为避免激发光源信号对荧光信号干扰，截止带背景设计为：OD≥6@750 nm～800 nm。

1.2　产品结构设计

基底选择：因使用的光谱波段为435～880 nm，所以选择K9光学玻璃（光谱如图2）即可。

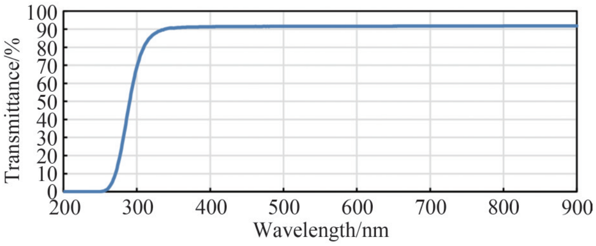


图2　K9玻璃光谱
Fig. 2　Spectrum of K9

为了提高光学系统的信噪比：1)滤光片的设计尽量提高透射区光谱的透射率；2)增加激发光背景截止深度。本文采用双面镀膜的结构（如图3），分别为陷波膜系（Notch）和增透膜系（AR）。

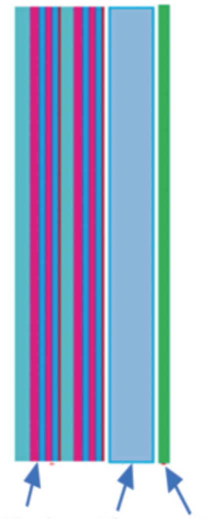


图3　陷波滤光片结构设计
Fig.3　Structure of notch filer

1.3　膜系设计

1.3.1　陷波膜系设计

在应用光谱波段范围内,滤光片透射大部分波长的光,有效截止特定波长阻带内的光,即从某一波段透射光谱中去除某一波带的滤光片,称之为陷波滤光片,其功能与带通滤光片相反。陷波滤光片制造的关键技术是提高通带的透射率和截止带的深度。目前陷波滤光片的膜系设计方法[9-11]主要有:皱褶(Rugate)滤光片法[12-13],折射率阶梯变化的Rugate滤光片法,高低折射率系数匹配法。Rugate滤光片法指折射率沿基底表面随膜厚有规律周期性变化,如按正弦波或余弦波变化,这种结构的滤光片主要特点是消除了材料间折射率的突变,具有仅反射一定波段且透射所有其它波段光谱的特性,因此理想的Rugate滤光片不会出现高级次反射带[14]。Rugate滤光片的膜系设计已趋于成熟,然而Rugate滤光片的制备仍然较困难,目前找不到一种材料可以按设计要求实现形状连续变化的折射率的膜层。折射率阶梯变化的Rugate滤光片法是用折射率成阶梯形变化的不连续的薄膜结构代替Rugate滤光片,虽然不是真正意义上的Rugate滤光片,但可实现类似的性质,抑制高级次反射带。其实现原理为:由多层不连续薄膜组成一个周期的Rugate滤光片的折射率轮廓。一个周期内分的层数越多,越接近Rugate滤光片,抑制高级次反射带效果越好,反之一个周期内分的层数越少,抑制高级次反射带效果变差,可通过多种阶梯变化折射率材料或两种材料共镀技术实现,然而阶梯变化折射率材料难于寻找,共镀技术对镀膜机的膜厚工艺控制要求极高,不易实现。高低折射率系数匹配法是陷波滤光片的主要设计方法,针对本次陷波滤光片的光谱指标要求,采用该方法更适合。

陷波膜系采用的初始结构为

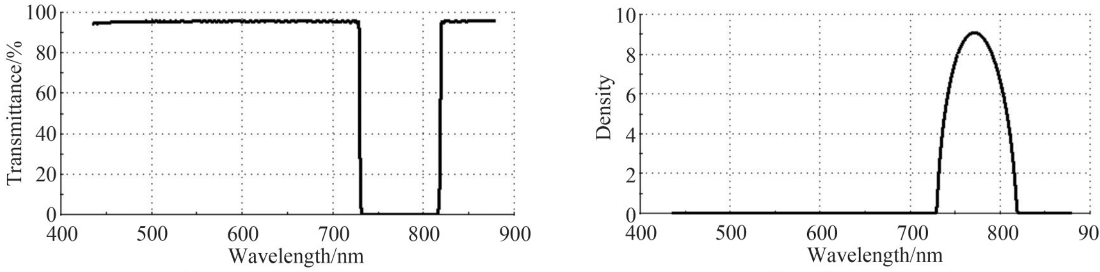
$$\text{Sub}\left|\left(\alpha H\beta L\right)^{n}\right|\text{Air} \tag{1}$$

式中,Sub、Air分别为入射、出射介质;H、L分别为高、低折射率材料;α、β分别为高、低折射率材料系数;n为循环次数。由多层介质高反射膜理论可得截止带宽度Δg[15]为

$$\Delta g=\frac{2}{\pi}\arcsin\left(\frac{n_{\mathrm{H}}-n_{\mathrm{L}}}{n_{\mathrm{H}}+n_{\mathrm{L}}}\right) \tag{2}$$

式中,n_{H}和n_{L}分别表示高低折射率,$n_{\mathrm{H}}/n_{\mathrm{L}}$和$\alpha$、$\beta$系数决定了$\Delta g$,$n_{\mathrm{H}}/n_{\mathrm{L}}$与$\Delta g$正向关,即两种材料折射率差值越大,$\Delta g$越宽,反之越窄,$\left|\alpha-\beta\right|$与$\Delta g$负向关,即系数$\left|\alpha-\beta\right|$越大,$\Delta g$越窄,反之越宽;循环次数$n$越大,反射截止带截止越深。该膜系光谱截止带附近两侧的通带波纹较大,可在膜系两侧增加匹配层减小波纹,也可以通过软件优化的方法去除。

本文采用Essential Macleod软件做为膜系设计辅助,结合光谱指标,通过软件的Reference Wavelength调整波长位置,Link All Materials调整α、β系数,最终确定初始膜系为$\text{Sub}\left|\left(2.7\text{H}1.4\text{L}\right)^{45}\right|\text{Air}$,其中Sub为K9基底,$H$为$\text{Nb}_2\text{O}_5$,$L$为$\text{SiO}_2$。利用辅助软件的Optimac和Needle Synthesis细化合成后的陷波膜系总厚度为14 μm,膜系设计光谱曲线如图4所示,膜系光谱在435 nm～680 nm & 820 nm～880 nm波段高透射,在750 nm～800 nm深截止。



(a) Transmission spectrum　　(b) Background spectrum

图4　陷波膜系设计光谱

Fig. 4　Design spectrum of single notch film

1.3.2 增透膜系设计

为了提升收光效率，滤光片采用另外一面增加增透膜的设计，减少透射区的光谱反射，即对435 nm～680 nm & 820 nm～880 nm波段增透膜设计。采用Essential Macleod软件做为膜系设计辅助，最终优化后的膜系结构为$\mathrm{Sub}|0.37L0.76H0.74L3.34H0.2L1.6H2.3L|\mathrm{Air}$，其中Sub为K9基底，$H$为$\mathrm{Nb_2O_5}$，$L$为$SiO_2$，经过优化后的增透膜光谱曲线如图5所示，在435 nm～680 nm & 820 nm～880 nm波段的平均透射率为95.5%。

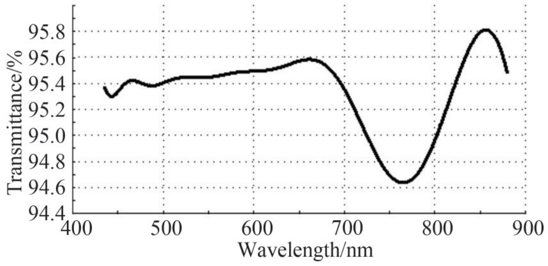
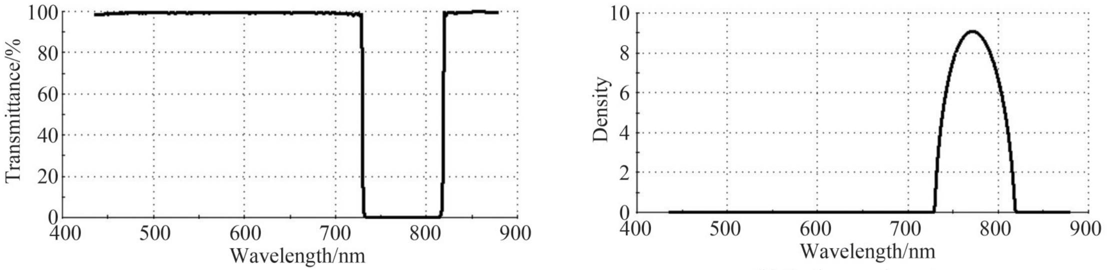


图5 增透膜系设计光谱

Fig. 5 Design spectrum of single anti-reflective film

陷波膜系与增透膜系组合的堆栈结构的理论设计光谱如图6所示，所有光谱指标优于指标要求。



(a) Transmission spectrum

(b) Background spectrum

图6 陷波滤光片堆栈设计光谱

Fig. 6 Design spectrum of notch filter

2 滤光片制备

因陷波膜系的非规整性，涉及膜层厚度陡变（厚层和超薄层衔接）控制；另一方面，深截止的光谱指标要求，必然会造成总膜层较多且较厚。所设计的膜系共108层，膜层总厚度14 μm，各膜层的膜厚分布不规整，如图7，有极薄层和超厚层，这对镀制工艺实现要求较高。

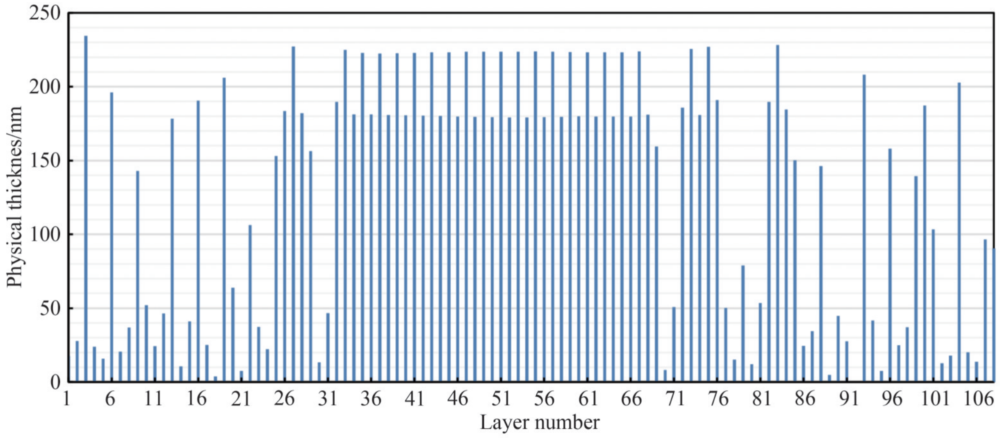


图7 陷波膜系各膜层的膜厚分布

Fig. 7 Every physical thickness of notch film

为获得理想光谱效果的滤光片，采用Essential Macleod软件对膜系进行误差模拟，图8是标准偏差0.5%的模拟结果，图9是标准偏差0.3%的模拟结果，从模拟结果发现膜厚误差控制0.5%，光谱在820～840 nm的透射会出现较大波纹，透射率最低降到80%风险几率较大，会严重影响发射光谱的收光率，使用效果变差；而膜厚误差控制在0.3%以内，可以保障整体光谱性能不会出现较大变化。因此采用工艺控制精度高的德国等离子体辅助反应磁控溅射镀膜设备HELIOS 400进行工艺实现。该镀膜设备采用一种中频孪生靶反应磁控溅射与RF等离子源辅助沉积相结合的溅射镀膜技术[16-17]，并配有直接光控系统，具有成膜速率稳定，膜厚控制精准，膜层致密等优点。

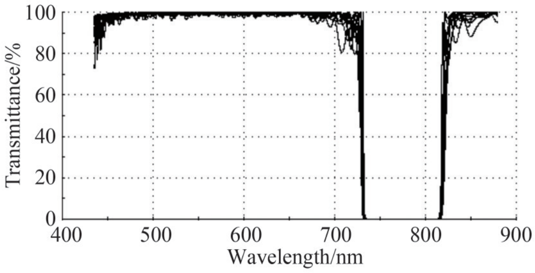


图8　膜厚0.5%标准偏差模拟

Fig. 8　Thickness standard deviation of 0.5%

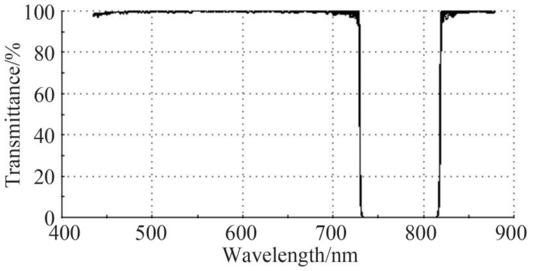


图9　膜厚0.3%标准偏差模拟

Fig. 9　Thickness standard deviation of 0.3%

增透膜系与陷波膜系采用相同的材料设计，因此用相同的溅射设备镀制。在$h=1$ mm、$\Phi=25$ mm的K9玻璃基底上镀制，基底先经超声波清洗并烘干处理，保证洁净；镀膜真空室加热200 ℃，保持30 min除气恒温；离子对基底轰击120 s进行表面活化；Nb_2O_5、SiO_2的沉积速率均设定约为0.5 nm/s，进行镀膜沉积；沉积过程通过氧分压传感器λ-sensor监控氧含量，保证溅射膜层充分氧化；设备的OMS（Optical Monitoring System）膜厚控制系统通过Backward、Offset、Forward多种算法结合的方式计算并矫正膜厚判停，实现复杂膜系膜厚控制，获得符合设计要求的膜层。

3　滤光片结果测试

采用Varian分光光度计Cary 5000进行光谱测试，单面第一次镀制陷波滤光膜光谱测试结果如图10所示，陷波左侧上升沿出现塌肩现象，右侧上升沿出现塌坑现象，而右侧沿对于荧光信号的捕获至关重要，会减少原本较弱的发射光的能量获取，降低荧光成像的信噪比，进而造成荧光图像不清晰，影响病灶部位边界的精准识别。

采用Essential Macleod软件对陷波膜系各层敏感度进行分析，结果如图11所示，发现膜系中敏感度较高的膜层有47、49、53、55，重点对这4层进行返演模拟，发现这四层设计膜厚基本相同，均为223.6 nm，若每层膜厚减少1 nm便会出现图10镀制光谱效果。针对该问题采取措施：对这四层膜采用多监控片的膜厚控制方式，合理分配监控片，尽可能将敏感层设置在监控片控制最精准层位置，减少敏感层误差对整体光谱的影响。

调整敏感层工艺控制后，镀制单面陷波滤光膜光谱测试结果如图12所示，陷波两侧上升沿未现塌肩、塌

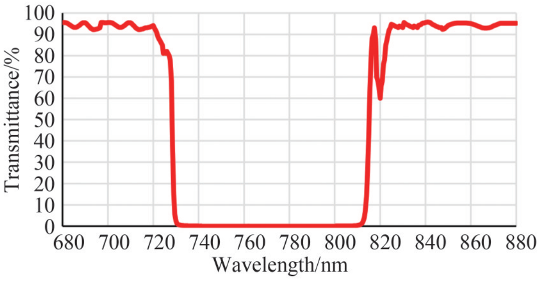


图 10 陷波滤光膜光谱测试结果

Fig. 10 Test spectrum of single notch film

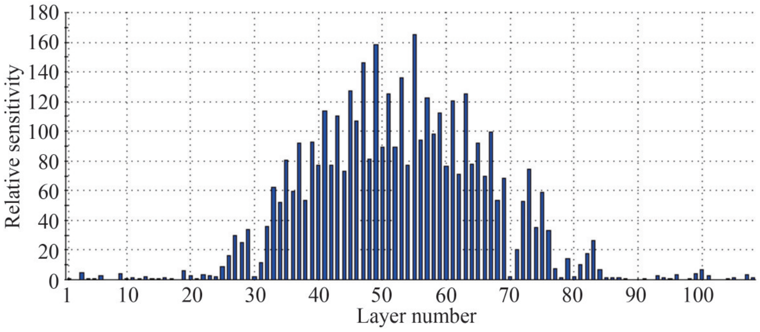
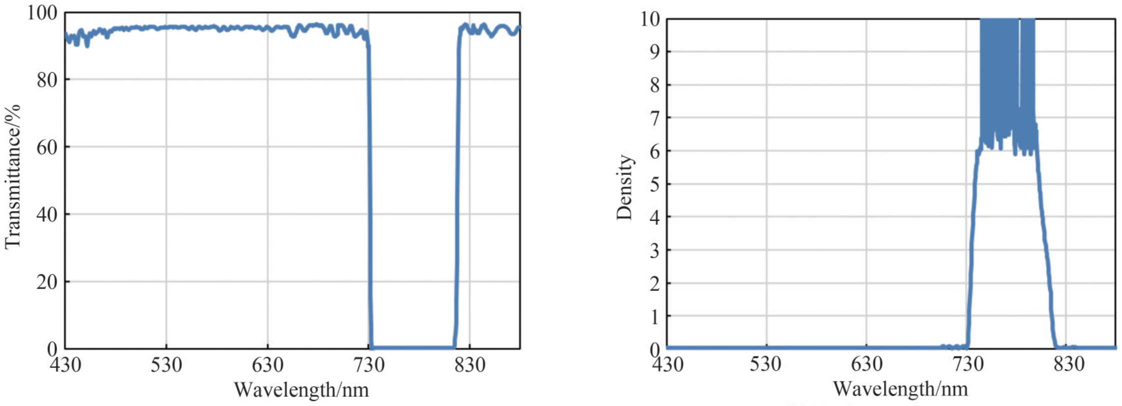


图 11 陷波膜系膜层敏感度分析

Fig. 11 Layer sensitivity of notch film



(a) Transmission spectrum

(b) Background spectrum

图 12 陷波滤光膜光谱测试结果

Fig. 12 Test spectrum of single notch film

坑现象，光谱 Tavg>95%@435 nm～680 nm & @820 nm～880 nm，OD≥6@750 nm～800 nm；单面增透膜光谱测试结果如图 13 所示，Tavg>95.4%@435 nm～680 nm & 820 nm～880 nm；双面镀膜后陷波滤光片的产品光谱测试和设计光谱如图 14 所示，Tavg>97%@435 nm～680 nm & @820 nm～880 nm，OD≥6@750 nm～800 nm，实测结果与设计光谱相符，满足荧光内窥镜用陷波滤光片所有光谱指标。

因该滤光片用于透射式成像系统，为减少因该滤光片引入的像差，提高成像质量，滤光片的透射波前畸变控制要求≤λ/4 CA PV @632.8 nm。为此采用透射波前畸变精度高于≤λ/4 CA PV @632.8 nm 指标要求的基底，结合镀膜工艺进行控制。图 15 是采用 zygo 干涉仪测试的透射波前畸变，在通光孔径内的测试结果为 0.076λ PV @632.8 nm，满足应用要求。

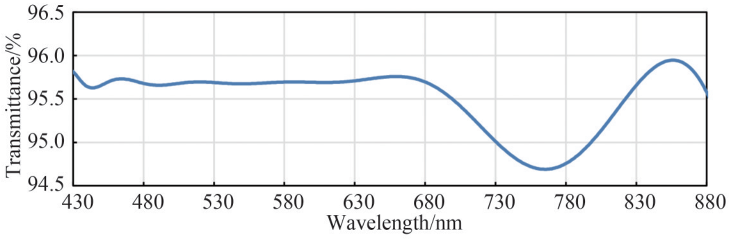
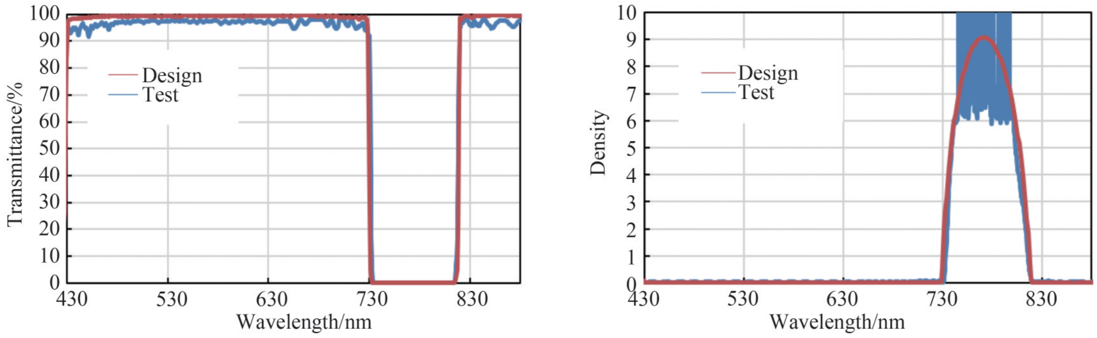


图 13　增透膜光谱测试结果

Fig. 13　Test spectrum of single anti-reflective film



(a) Transmission spectrum　(b) Background spectrum

图 14　陷波滤光片产品光谱测试和设计光谱

Fig. 14　Test spectrum and design spectrum of notch filter

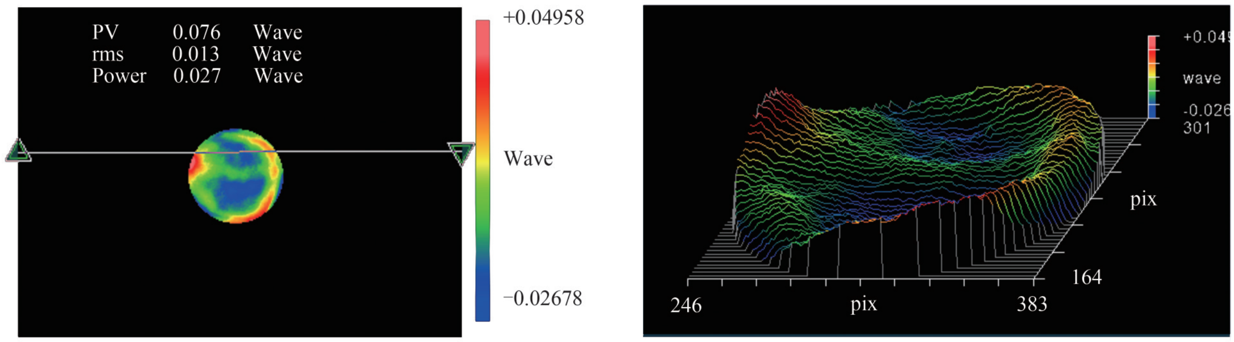


图 15　陷波滤光片产品透射波前畸变测试

Fig. 15　Test transmission wavefront distortion of notch filter

4　结论

以光学薄膜设计理论为基础，设计并制备了高性能荧光内窥镜用陷波滤光片。该滤光片达到预期设计指标要求：在可见光和荧光发射光谱波段高透射 $T>97\%$@435 nm～680 nm & @820 nm～880 nm，荧光激发光谱陷波波段深截止 OD≥6@750 nm～800 nm，透射波前畸变控制在 0.076λ CA PV @632.8 nm，为高端荧光内窥镜高清成像准确识别病灶部位起到关键作用。

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Investigation of Notch Filters for Fluorescent Endoscopes

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Abstract: Fluorescence endoscope, which enables simultaneous visible light imaging and near-infrared fluorescence molecular imaging, is a result of advanced endoscopic theories and cutting-edge technologies. This instrument holds great potential to become an essential visual monitoring system in future targeted surgeries. The optical performance of the notch filter within the fluorescence endoscope plays a pivotal role in determining the clarity and precision of identifying fluorescence images of lesions, thereby influencing the endoscope's efficacy in supporting diagnostics and advancing precision medicine in clinical practice. Consequently, research into critical technologies related to notch filter for fluorescence endoscopy and the development of high-performance filter products demonstrate significant clinical application prospects and scientific significance. By aligning the operational principles of the fluorescence endoscope with the spectral profiles of corresponding fluorescent reagents, we can define the technical specifications for notch filter. Based on the theory of optical film, we have designed a notch filter utilizing K9 substrates, characterized by the deposition of notch coating and anti-reflective coating on both sides. The design of the notch coating was achieved by optimizing the matching of high and low refractive index coefficients, which is based on an in-depth comparison of the merits and drawbacks of Rugate filters, Rugate filters with step-change refractive index, methods for matching high and low refractive index coefficients, and other notch structures. Moreover, we employed Essential Macleod software in conjunction with various optimization synthesis methods to achieve high passband transmission, minimal ripple, excellent blocking property for the excitation light source, as well as a steep transition from the excitation spectrum to the emission spectrum. This approach ultimately enables efficient suppression of the excitation light and efficient capture of fluorescence signals, playing a crucial role in accurately identifying lesions. To ensure precise control, a plasma reaction magnetron sputtering coating device is selected after simulating and analyzing the standard deviation of film thickness. The coating process involves ultrasonic cleaning and drying of substrates to maintain cleanliness, followed by heating the vacuum chamber to 200 ℃ and maintaining a constant temperature for 30 minutes to remove gas. This is followed by ion bombardment of substrates for 120 seconds to activate the surface. The deposition rates for Nb_2O_5 and SiO_2 are both set at approximately 0.5 nm/s for coating applications. To ensure complete oxidation of the sputtered film, we employ an oxygen partial pressure sensor (λ-sensor) to monitor the deposition process and measure oxygen content. The system is equipped with an Optical Monitoring System (OMS) film thickness control system that uses a combination of Backward, Offset, and Forward algorithms to accurately calculate and correct the stop position of film thickness. This approach enables precise control over sensitive layer thickness in complex film systems, thereby reducing the impact of errors on the overall spectrum. By carefully selecting substrates with wavefront aberration control and implementing stringent coating process control methods, we ensure that the wavefront aberration remains below $\lambda/4$ @632.8 nm, effectively minimizing optical system aberrations. After two rounds of meticulous process optimization, the filter's average transmittance within the passband exceeds 97%, while maintaining an exceptional blocking capability of OD6 and a wavefront aberration below $\lambda/4$ @ 632.8 nm, meeting the demands for precision applications in medical and minimally invasive surgery.

Key words: Fluorescent endoscopes; Filter; Notch film; Near-infrared fluorescence; Indocyanine green

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