

肺动脉栓塞检测的可视中国人蒙特卡罗模拟分析

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摘要 肺动脉数字减影血管造影技术是现阶段临床检测肺动脉栓塞的主要手段,但该技术是一种有创的检查,且易对血管及周围组织造成损伤。在目前的心血管医学研究中,肺动脉栓塞的无创检测具有一定挑战性。本课题组运用蒙特卡罗方法模拟研究了光在人体胸部组织中的传输规律,探讨了近红外光谱技术在肺动脉栓塞无创检测中的可能性。结果表明:在 2.8~3.1 cm 的光源与探测器距离下,检测到信号对肺动脉部位激活的灵敏度可达到 0.073% 的峰值;不同栓塞水平下的归一化光照强度差异显著,且二者之间呈线性关系($R^2=0.998$, $p<10^{-5}$)。这些结果表明,近红外光谱技术在肺动脉栓塞定量检测中具有巨大潜力。本研究为无创光学方法诊断肺动脉栓塞提供了参考。

关键词 医用光学; 肺动脉栓塞; 近红外光谱技术; 蒙特卡罗模拟; 无创检测

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1 引言

肺动脉栓塞(PE)是一种临床和病理生理综合征,通常伴随心血管疾病发生^[1]。肺动脉栓塞的发病率仅次于冠心病和心血管疾病中的高血压,死亡率排名第三,临床观察急性肺动脉栓塞死亡率不低于心肌梗死^[2]。目前,最准确的肺动脉栓塞检测方法是肺动脉数字减影血管造影(DSA)^[3],准确率接近 100%。然而,这种检查方法具有侵入性,易对血管或周围组织造成损伤。此外,检查后经常出现并发症,从而限制了 DSA 的应用。因此,肺动脉栓塞的无创监测仍是心血管医学面临的一项挑战。

近红外光谱(NIRS)^[4]技术基于氧合血红蛋白(HbO₂)和脱氧血红蛋白(Hb)的光谱特征^[5]来定量测定组织中血红蛋白氧饱和度,从而实现疾病的诊断。自 20 世纪 70 年代发明以来,NIRS 技术凭借非接触、无创和在线快速监测等优势被用于一系列临床人体研究^[6]。NIRS 技术可以检测到深度高达几厘米处的物体,足以穿透胸部到达肺动脉^[7]。然而,研究人员尚未对人体肺动脉区域的光子迁移进行深入研究。无创光学技术在临床肺动脉栓塞检测方面具有广阔的应用前景。

之前的研究显示,在出现肺动脉栓塞时通常会首先发生血液动力学异常,其次是发生与低氧血症相关的特征性事件。血流动力学的变化为直接检测低氧血症下的肺栓塞提供了生理基础^[8]。目前,近红外光在肺动脉中的迁移规律尚不清楚,因此无法确定光源和检测器的放置位置、光源和探测器的间距(L_{SD})以及空间灵敏度分布(SSD)。这也是实现肺动脉栓塞无创监测应用于临床亟待解决的问题。

肺动脉栓塞检测研究是在三维结构上模拟的,中国数字化可视人体(VCH)数据集^[9-10]是开展模拟的最佳选择。VCH 数据集是一种个性化的三维异质结构模型,在众多研究中发挥着重要作用^[11-12]。精确的组织建模可以增加光子迁移在更广泛应用中的效用。本团队开发了一个用于模拟光子在体素化介质中传播的软件程序(MCVM)^[11],通过该程序可以更好地评估 VCH 胸部模型中光子传播与 L_{SD} 之间的关系。目前,MCVM+VCH 已被成功用于研究脑^[13]、乳腺^[14]和心脏^[8]中光子的传输分布,而且众多研究已证明了 MCVM+VCH 方法的可靠性。

本课题组采用 VCH 数据集中的胸部组织模型来提高胸部结构建模的精度,并结合三维体素化介质进行蒙特卡罗模拟,建立量化、可视化的光子迁移人体胸

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部模型,并计算了一系列 SSD、部分路径长度因子 (PPF)^[15] 和差异路径长度因子 (DPF)^[16]。结果显示,肺栓塞程度与检测到的信号强度之间有很强的线性关系。本研究验证了无创光学检测肺动脉栓塞的潜力,为其临床落地提供了可行性。

2 研究方法

2.1 由 VCH 数据集构建的胸部模型

在 VCH 数据集建立的胸部模型上进行模拟。

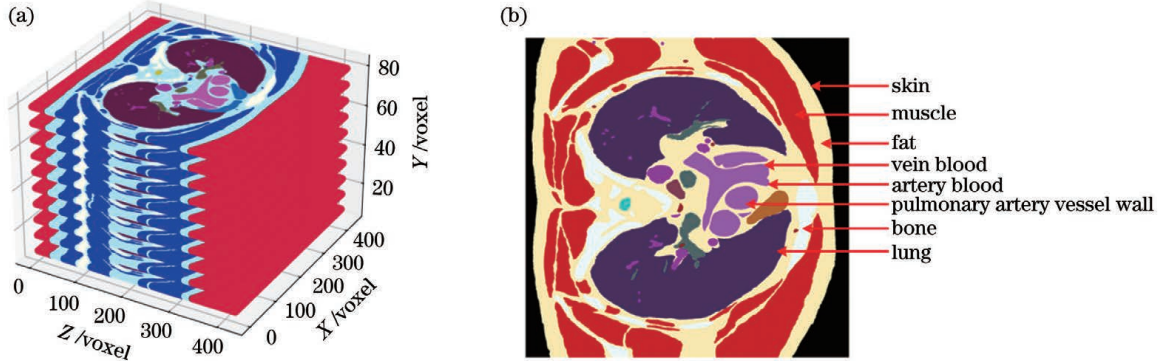


图 1 VCH 胸部模型描述。(a)由 $436 \times 420 \times 80$ 个体素的三维矩阵构建而成的胸部模型;(b)胸部模型分为 8 部分
Fig. 1 Description of VCH thoracic model. (a) Thoracic model built with 3D matrix of $436 \times 420 \times 80$ voxels; (b) thoracic model is divided into 8 tissue parts

2.2 蒙特卡罗模拟

蒙特卡罗模拟可用于推断光在胸部组织 VCH 数据集中的传播。针对三维体素化介质,本文使用的蒙特卡罗建模算法已在之前的文献中进行了详细描述^[11]。具体来说,当光子包(或单个光子)进入组织后,它会随机散射或被组织介质持续吸收,直至死亡。对探测器采集的存活光子进行分析可以获得有价值的信息,如强度和传播路径长度^[17]。在本研究中,光源被放置于第二和第三前肋骨之间,检测器被连接到光

VCH 数据集是全身冰冻切片的一组彩色照片,收集自一具病理变化较小的中国男性尸体(一具捐赠尸体)。在本研究中,使用 VCH 切片的 80 张摄影图像从上到下映射出肺动脉及其附近的胸部组织,首次建立了 $436 \times 420 \times 80$ 个体素的胸部摄影模型(如图 1 所示)。其中,每一个体素被定义为尺寸为 $0.4 \text{ mm} \times 0.4 \text{ mm} \times 0.4 \text{ mm}$ 的立方体。整个模型按组织分为 8 部分,包括皮肤、肌肉、骨头、皮下脂肪、肺、肺动脉、动脉血和静脉血。

源水平左侧的皮肤上,轴方向如图 2 所示。输入光为 800 nm 红外光,其他设置参数与之前的研究相同,如表 1 所示^[18]。每次模拟都会弹出 10^6 个光子。在每个水平上重复模拟 10 次,用平均光子通量表示光的传播结果。此外,还生成了两个文件(Absorption 和 Outphoton),这两个文件分别记录吸收光子数和输出光子分布。根据这两个文件,计算得到了一系列光子传输特性,计算结果如表 1 所示,其中 n 是介质的折射率, μ_a 是吸收系数, μ_s 是散射系数, g 是各向异性因子。

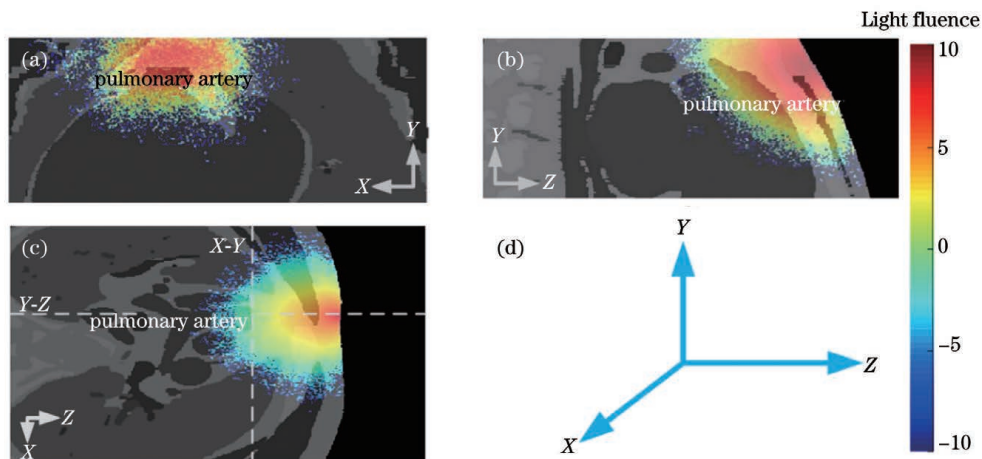


图 2 X-Y-Z 视场下胸部组织中的光通量分布。(a)X-Y 平面上的光通量;(b)Y-Z 平面上的光通量;(c)X-Z 平面上的光通量;
(d)本研究中使用的三维空间坐标系

Fig. 2 Light fluence distributions in thoracic tissue under X-Y-Z field of view. (a) Light fluence in X-Y plane; (b) light fluence in Y-Z plane; (c) light fluence in X-Z plane; (d) three-dimensional space coordinate system used in this study

本研究通过改变动脉血和静脉血之间的关系来改变血氧饱和度,进而根据动脉血氧饱和度(SaO_2)和静

脉血氧饱和度(SvO_2)的变化设计了三个疾病级别来模拟患者。实验共分为 4 组,包括轻度(I级)、中度

表 1 800 nm 波长下胸部组织的光学特性

Table 1 Optical properties of thoracic tissue at 800 nm

Tissue type	n	μ_a / cm^{-1}	μ_s / cm^{-1}	g
Fat	1.33	0.083	134	0.910
Skin	1.37	0.20	73.7	0.715
Lung	1.40	1.00	95.0	0.910
Bone	1.43	0.11	291	0.936
Muscle	1.40	0.54	66.7	0.930
Pulmonary artery vessel wall	1.40	0.92	103	0.930
Arterial blood	1.40	2.33	522	0.990
Venous blood	1.40	2.38	440	0.990

(II 级)和严重(III 级)疾病的三个患者组,以及正常人的对照组。参数详情如表 2 所示。

表 2 SaO₂ 和 SvO₂ 在每个实验组中的参数设置

Table 2 Parameters of SaO₂ and SvO₂ for each experimental group

Group	SaO ₂ / %	SvO ₂ / %
Level I	93	71
Level II	91	67
Level III	89	63
Normal	95	75

2.3 SSD

本研究的目的是实现肺动脉组织的血液动力学检测,通过对血液成分进行分析得出低氧血症的程度,从而间接达到监测肺动脉栓塞的效果。所以,在体表检测到来自肺动脉组织的光子是本研究的关键。在这需要用到一个指标,即 SSD。SSD 反映的是组织在检测光中贡献的变化量,可通过式(1)计算获得。

$$\text{SSD}(\mathbf{r}_S, \mathbf{r}_D, \mathbf{r}_m) = F(\mathbf{r}_S, \mathbf{r}_m) \times F(\mathbf{r}_D, \mathbf{r}_m), \quad (1)$$

式中: $F(\mathbf{r}_S, \mathbf{r}_m)$ 表示的是光源位置下的组织体素 \mathbf{r}_m 在位置 \mathbf{r}_S 下的光通量; $F(\mathbf{r}_D, \mathbf{r}_m)$ 表示的是探测位置组织体素 \mathbf{r}_m 在位置 \mathbf{r}_D 下的光通量。收集所有体素的 SSD 值后,将所有体素的 SSD 值相加,计算整个模型的 SSD 值。某组织的 SSD 值与总 SSD 值的比值表示该组织在检测光中的参与度,详细信息可以参考文献[19]。

3 结果分析

3.1 光通量分布

如方法部分所述,本文绘制了光通量分布图,以指示光子在胸部组织中的存在(如图 2 所示)。在 X-Z、X-Y 和 Y-Z 三个视图中的任何一个中都可以观察到光子穿透组织到达肺动脉:从 X-Z 视图中可以观察到 800 nm 光穿过胸骨进入胸腔,如图 2(c)所示;从 Y-Z 光通量分布图中可以观察到光子在主肺动脉处散射,如图 2(b)所示;在 X-Y 光通量分布图中,皮肤表面 O 点距肺动脉表面的直线距离为 82 个像素点,每个像素点的真实距离为 0.4 mm,所以距皮肤表面 33 mm 处的 X-Y 光通量分布证明了光子可以穿透组织到达肺动脉,如图 2(a)所示。

图 3(b)显示了 X-Z 视图中第 40 层的代表性光通量分布。研究表明,光的强度设置为光子在体内传播至少 37 mm。当光子依次穿过皮肤、脂肪、肌肉、脂肪、肺动脉、静脉血组织时,对数尺度下的光子影响强度逐渐降低,如图 3(a)所示。同样,在正常尺度下,光影响强度也会急剧下降。当深度增加到肺动脉表面时,强度为 45 voxel;在 36 mm 深度处,强度降至 1 voxel,此时探测位置位于肺动脉内的静脉血。这些数据表明,在胸骨前部放置光源时,800 nm 光子可以传输到 36 mm 深度处的肺动脉。此外,当光子到达肺动脉血管壁时,光强度低至入射时的 1/22000。

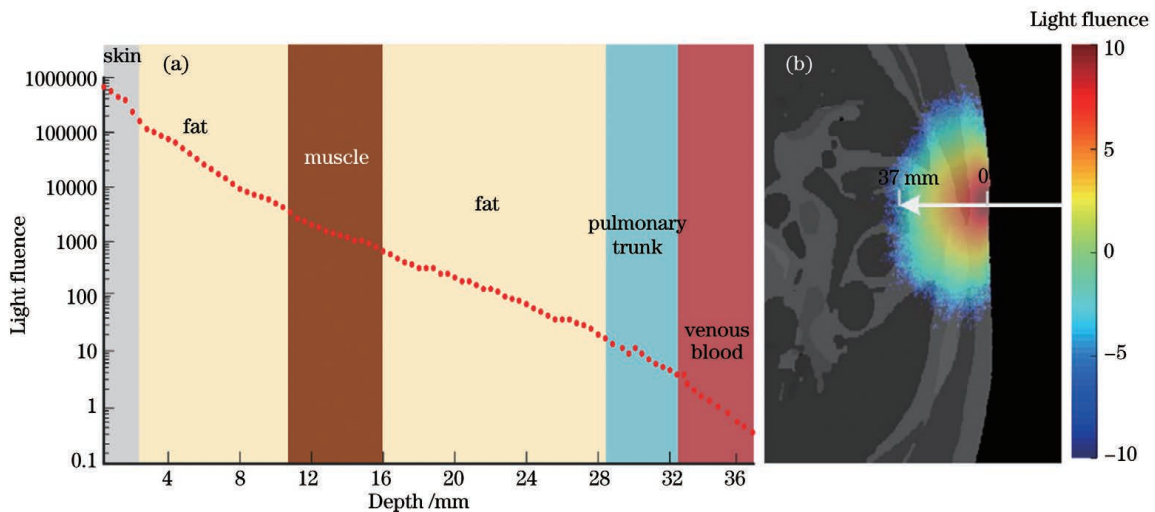


图 3 光通量在组织深度上的变化。(a)光通量从皮肤到静脉血(第 40 个切片)的变化;(b)第 40 切片上的光通量分布
Fig. 3 Variation of light fluence in tissue depth. (a) Variation of light fluence from skin to venous blood (the 40th slice); (b) light fluence distribution on the 40th slice

3.2 优化源探距离

本研究还探索了光源到探测器的距离(以下简称“源探距离”,记为 L_{SD})的最佳值,并引入 4 个指标来研究源探距离。这 4 个指标分别为 DPF、PPF、PPF 与 DPF 的比值、肺动脉吸收光子的占比。DPF 是将光子传输的平均路径与 L_{SD} 联系起来的比例因子,表征的是所有组织体素的影响;PPF 表征的是某一组织体素的影响。因此,肺动脉组织的 PPF_{pa}(pa 为 pulmonary artery 的简写)反映的是检测光对肺动脉组织的灵敏度,而 PPF_{pa} 与 DPF 的比值表示的是肺动脉组织对检测光的贡献。如图 4(a)所示,DPF 随着 L_{SD} 增大呈指数增长。图 4(b)显示了 PPF_{pa} 随 L_{SD} 增大的变化,可见:随着 L_{SD} 在 2.5~2.9 cm 范围内增大,PPF_{pa} 迅速增大,之后 PPF_{pa} 急剧下降。图 4(c)

显示,PPF_{pa} 与 DPF 的比值受 L_{SD} 的影响,即:随着 L_{SD} 在 2.0~3.1 cm 范围内增大,PPF_{pa} 与 DPF 的比值逐渐增大,然后急剧下降。另由图 4(c)可以看出, L_{SD} 在 2.0 cm 和 3.1 cm 之间时出现了一个峰值,为 0.073%。通过比较图 4(b)和 4(c)可以发现,当 L_{SD} 从 2.0 cm 增加到 2.8 cm 时,PPF_{pa} 以及 PPF_{pa} 与 DPF 的比值均逐渐增加到最大值,之后随着 L_{SD} 从 2.8 cm 增加到 3.1cm,PPF_{pa} 以及 PPF_{pa} 与 DPF 的比值都急剧下降。图 4(d)给出了不同 L_{SD} 下肺动脉吸收光子的占比。肺动脉吸收光子的占比在初始阶段缓慢增大,在 L_{SD} 达到 3 cm 附近时趋于平稳并达到最大值,最大值为 4.6%;之后随着 L_{SD} 继续增大,光子吸收呈快速下降的趋势。从理论仿真结果来看,最佳 L_{SD} 应在 2.8~3.1 cm 范围内取值。

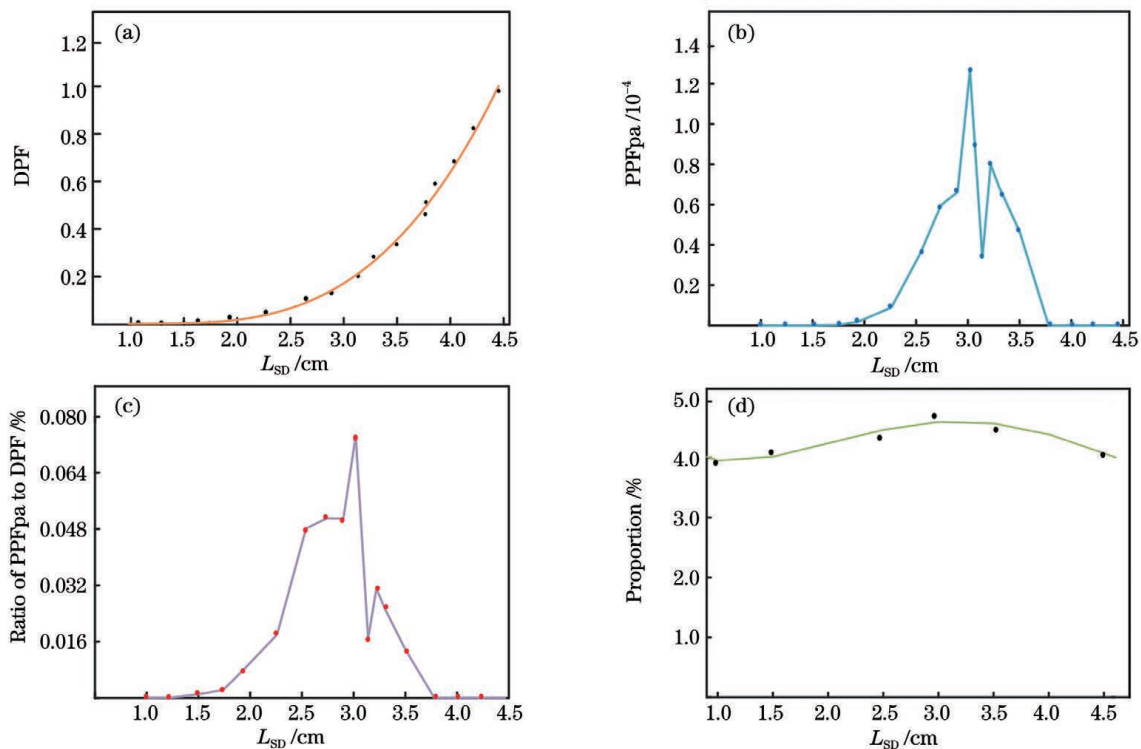


图 4 DPF、PPF_{pa}、PPF_{pa} 与 DPF 的比值随 L_{SD} 的变化以及肺动脉吸收光子的占比。(a)DPF 随 L_{SD} 增大呈指数级增长;(b)PPF_{pa} 随 L_{SD} 的变化;(c)PPF_{pa} 与 DPF 的比值随 L_{SD} 的变化;(d)肺动脉吸收光子的占比

Fig. 4 Variation of DPF, PPF_{pa}, ratio of PPF_{pa} to DPF with L_{SD} . (a) DPF exponential growth with the increase of L_{SD} ; (b) variation of PPF_{pa} with L_{SD} ; (c) variation of ratio of PPF_{pa} to DPF with L_{SD} ; (d) proportion of photon absorption in pulmonary artery

3.3 肺栓塞对 SSD 的影响

4 次仿真输出的吸收文件取均值,得到 SSD 的矩阵数据(r_s, r_D, r_m),每种组织的 SSD 是本组织中每个体素的 SSD 的累积和,如表 3 所示。SSD 可以间接反映肺栓塞的级别^[20]。健康人、I 级患者、II 级患者和 III 级患者肺动脉的 SSD 占比分别为 0.0131%、0.0129%、0.0127%和 0.0126%。虽然这些值相对于脑部研究中目标组织的 SSD 占比 5.56%^[21-22]要低得多,但是理论上仍然处在目前光电检测技术可以检测的范围内。本课题组在之前的研究中采用的

是半径为 1 cm 的雪崩光电探测器探头(OPT101 型号光源),其可探测到 SSD 占比低至 $10^{-6} \sim 10^{-7}$ 量级的信号^[6],所以本次实验测得的 0.002% 的 SSD 信号理论上仍然在现有设备的可测范围内。当肺栓塞严重时,SSD 占比降低。本研究对不同程度肺栓塞的动静脉血和肺组织的 SSD 占比进行了评估,结果表明,随着肺栓塞程度加剧,肺组织和静脉血的 SSD 占比逐渐降低,而动脉血的 SSD 占比几乎为零。这一结果表明,静脉血和肺组织对检测灵敏度具有一定影响。

表 3 不同等级的肺动脉栓塞下每种组织的 SSD 占比

Table 3 Proportion of SSD of each tissue at different levels of pulmonary embolism

Level of pulmonary embolism	Proportion of SSD / %							
	Fat	Skin	Lung	Bone	Muscle	Pulmonary trunk	Arterial blood	Venous blood
Normal	67.398	11.34	0.002	15.92	5.34	0.0131	0	0.004
Level I	67.638	11.21	0.002	15.84	5.31	0.0129	0	0.004
Level II	67.588	11.27	0.002	15.89	5.25	0.0127	0	0.003
Level III	67.867	11.19	0.001	15.65	5.28	0.0126	0	0.002

3.4 肺动脉栓塞对检测光强度的影响

在上述结果中,最佳的源探距离约为 2.9 cm。因此,将 L_{SD} 设置为 2.9 cm,以检测不同肺栓塞等级下体表处的光强。以正常状态下的检测光强度为标准进行归一化,然后以归一化的检测光强为因变量,不同的栓塞水平为自变量进行一元线性回归分析。分析结果表明,归一化光强度随着肺栓塞程度的增加而降低。因此,肺动脉组织部位的光子吸收随着肺栓塞程度的增加而增加。虽然更高水平的肺动脉栓塞吸收了更多的光子,但探测器仍能检测到逃逸的光子,证明了本文检测方法可用于肺栓塞检测。归一化光强的线性拟合函数为 $y = -0.00871x + 1.002 (R^2 = 0.998, p < 10^{-5})$ 。这种线性关系表明,用检测到的光强度可以近似估计肺栓塞水平^[23]。

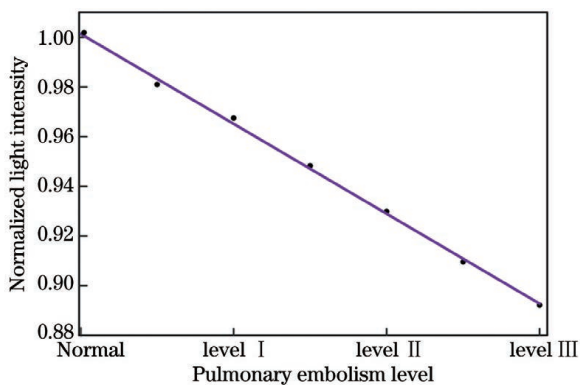


图 5 归一化光强度与肺栓塞水平的线性拟合

Fig. 5 Linear fitting of normalized light intensity and pulmonary embolism level

4 结 论

本课题组基于 VCH 数据集并采用蒙特卡罗模拟方法实现了肺动脉栓塞的无创光学监测。通过模拟光子在人体胸部组织中的迁移,得出胸腔组织中吸收光子的数量和光通量分布,这些证据表明部分光子可以到达肺动脉。此外,本课题组还研究了光源与探测器之间的优化距离,根据 PPF 和 DPF 两个路径长度因素,得出 2.8~3.1 cm 是最佳距离。通过肺动脉处的 SSD 和输出光子强度验证了肺动脉栓塞对光子检测的影响,结果表明,肺动脉处的 SSD 随着栓塞程度的增大而减小。研究还发现,检测光强度与栓塞程度

直接相关,严重栓塞对应着较低的光强度,这可以作为肺动脉栓塞程度的反映。总的来说,本研究证实了 NIRS 技术在床边连续监测肺动脉栓塞方面的巨大潜力。

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Visible Chinese Human for Pulmonary Embolism Detection of Monte Carlo Simulation Analysis

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Abstract

Objective Pulmonary embolism (PE) is a clinical and pathophysiological syndrome in which an endogenous or exogenous embolus occludes the pulmonary artery or its branches, causing pulmonary circulatory impairment that can lead to severe pulmonary infarction, usually accompanied by cardiovascular disease. Currently, the most accurate method for detecting PE is digital subtraction angiography (DSA) of the pulmonary arteries. However, this detection method is invasive and can easily damage blood vessels or surrounding tissues and often causes additional complications. Therefore, non-invasive, real-time, and accurate detection of pulmonary artery hemodynamics is highly desirable. Near-infrared spectroscopy (NIRS) is a simple, rapid, portable, and relatively inexpensive technique for non-invasive deep-tissue hemodynamic monitoring, which is based on the spectral characteristics of oxyhemoglobin (HbO₂) and deoxyhemoglobin (Hb), which are characteristics used to quantify tissue hemoglobin oxygen saturation for disease measurement. In recent years, an increasing number of research groups have chosen to use NIRS to monitor human diseases, and it has been validated for use in studies involving many tissue sites in the body. However, the study of photons in the human pulmonary artery site has not been conducted in depth. Therefore, the feasibility of using NIRS to detect pulmonary artery embolism is investigated in this study.

Methods In this study, we used 80 photographic images from the Visual Chinese Human (VCH) dataset slices to map the thoracic tissue region of the pulmonary artery from top to bottom to build a 436 × 420 × 80 voxel thoracic photographic

model (Figure 1). Each voxel is defined as a $0.4\text{ mm} \times 0.4\text{ mm} \times 0.4\text{ mm}$ cube. The entire model is divided into eight parts based on tissue type, including skin, muscle, bone, subcutaneous fat, lung, pulmonary artery, arterial blood, and venous blood. The constructed model is then loaded into a software program developed by our team for Monte Carlo simulation of light propagation in Voxlated Media (MCVM). MCVM generates two files: a photon absorption data file and a photon escape data file at the body surface, from which we can calculate a series of evaluation metrics to better evaluate the relationship between photon propagation and the separation of the light source and detector (L_{SD}) in the VCH chest model.

Results and Discussions According to photon absorption data, photons pass successively through the skin, fat, muscle, adipose tissue, and pulmonary artery to the venous blood. The intensity when reaching the pulmonary artery is estimated to be 45 voxel (Figure 3), which is sufficient to demonstrate that photons can cross the thoracic cavity and penetrate the experimental region of interest. Four indicators are introduced to study the optimized light source and detector distance: differential optical path-length factor (DPF), partial path-length factor (PPF), the ratio of PPF to DPF, and the proportion of photon absorption in the pulmonary artery. DPF increases exponentially with the increase of L_{SD} , whereas the three other indicators (PPF, the ratio of PPF to DPF, and proportion of photo absorption in the pulmonary artery) trend upward and then downward, with the peak occurring in the 2.8–3.1 cm L_{SD} range (Figure 4). Based on the above results, we selected 2.9 cm to study the effects of different degrees of pulmonary embolism on SSD (Table 3) and on the intensity of light detected on the body surface (Figure 5). As pulmonary embolism progressively worsens, the percentage of SSD present in the pulmonary arteries decreases (0.0131%, 0.0129%, 0.0127%, and 0.0126% in healthy, Level I, Level II, and Level III subjects, respectively). The SSD proportions in arteriovenous blood and lungs were then evaluated for different degrees of pulmonary embolism. The results indicate that the proportion of SSD in the lung and venous blood gradually decreases as the degree of pulmonary embolism increases. However, the proportion of SSD in the arterial blood is almost zero. These results suggest that venous blood and lung tissue influence the sensitivity of the total assay. A one-dimensional linear regression analysis was performed by standardizing the light intensity of the measurement in the normal state and different embolic levels as independent variables. The results indicate that the standardized light intensity decreases with increasing levels of pulmonary embolism. Thus, the level of pulmonary embolism can be approximated using the detected light intensity.

Conclusions This study implements noninvasive optical monitoring of pulmonary artery embolism based on the Visible Chinese Human dataset and use of Monte Carlo simulations. By simulating light migration in human thoracic tissues, the number of absorbed photons and the light fluence distribution in the thoracic tissues are derived, and the evidence suggests that some of the photons can reach the pulmonary artery, indicating that the proposed technique is feasible. In addition, this study proposes an optimized separation distance between the light source and the detector and concludes that a separation of 2.8–3.1 cm may be optimal based on two path length factors, PPF and DPF. The effect of pulmonary artery embolism on photon detection is verified based on SSD estimates at the pulmonary artery and the output photon intensity. The results indicate that the SSD at the pulmonary artery decreases with increasing embolization. Furthermore, light intensity directly correlates with the degree of embolization, and the presence of embolization can significantly decrease the light intensity, therefore indicating the presence of emboli in the pulmonary artery. Overall, this study demonstrates the great potential of NIRS for continuous bedside monitoring of pulmonary embolism.

Key words medical optics; pulmonary embolism; near-infrared spectroscopy; Monte Carlo simulation; noninvasive detection