A Novel Wireless Wearable Fluorescence Image-Guided Surgery System

Kunshan He, Yamin Mao, Yu An, Shixin Jiang, Jinzuo Ye, Chongwei Chi* and Jie Tian*, *Fellow, IEEE*;

Abstract**—Segmentectomy using indocyanine green (ICG) has become a primary treatment option to achieve a complete resection and preserve lung function in early-stage lung cancer. However, owing to lack of appropriate intraoperative imaging systems, it is a huge challenge for surgeons to identify the intersegmental plane during the operation, leading to poor prognosis. Thus, we developed a novel wireless wearable fluorescence image-guided surgery system (WFS) for fast and accurate identification of intersegmental planes in human patients. The system consists of a handle, light source, Google glass and laptop. Application software is written to capture clear real-time images and Google glass is adopted to display with augmented reality. Twelve *in vivo* studies of pulmonary segmentectomy in swine by intravenous injection of ICG were conducted to test the performance of the system. A distinct black-and-white transition zone image was observed and displayed simultaneously on the Google glass in all swine. The results demonstrated that surgeons using WFS can effortlessly and quickly discern intersegmental planes during the operation. Our system is enormously potential in helping surgeons to precisely identify intersegmental planes with mobility and high-sensitivity.**

I. INTRODUCTION

Lung cancer is one of the primary causes of cancer-related death all over the world. Nowadays, lobectomy is the regular treatment for lung cancer. However, from the trails of the Japan Clinical Oncology Group 0802 study and the Cancer and Leukemia Group B 140503 study, segmentectomy has become a more effective treatment for certain small, early-stage lung cancer [1-3]. To achieve complete segmentectomy, it is vital to detect the intersegmental plane precisely. Conventionally, the resected segment inflation method is used to delineate segmental lines by temporarily re-inflating the lung by clamping and unclamping the corresponding bronchus. However, this method usually obstructed the view of the target segment and it is not suitable for patients with emphysema. Therefore, a novel technique by transbronchial or intravenous injection of indocyanine green (ICG) [4-6] has drawn the attention of relevant researchers. Nevertheless, serious absence of high-quality intraoperative fluorescence imaging system has severely hindered the further development of this method.

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Kunshan He, Key Laboratory of Molecular Imaging, Chinese Academy of Sciences, Beijing, China (e-mail: hekunshan@fingerpass.net.cn).

Chongwei Chi and Jie Tian, Key Laboratory of Molecular Imaging, Chinese Academy of Sciences, Beijing, China (Corresponding authors, phone: 8610-82618465; fax: 8610-62527995; email: tian@ieee.org).

Although plenty of instruments, like magnetic resonance imaging (MRI), has been applied to assist surgeons in tumor preoperative diagnosis, there remains a serious lack of intraoperative tumor surgery devices, especially fluorescence imaging systems [7]. To address these challenges above, an intraoperative navigation technology with near-infrared (NIR) fluorescence imaging methods has become a heated-discussion international point [8-11]. Lots of imaging systems have been developed recently. But these systems mainly achieve human-computer interaction by the computer screen display, which may divert surgeons' attention from surgery field.

Recently, a wearable real-time fluorescence imaging and display system, named the fluorescence goggle, has been developed for locating tumor margins instantly [12]. However, clinical practicality of the goggle system is not optimal because it blocks the surgeon's vision. Therefore, we developed a novel wireless wearable fluorescence image-guided surgery system (WFS), which combined the mobility of the goggle system and the sensitivity of other imaging systems.

Our special design makes WFS capable of being readily used in real-time intraoperative image-guided surgery. Firstly, NIR light exited by a light source transmits through a filter, illuminates the target and then is collected by the NIR camera installed in the handle. An application is written to capture real-time images. Finally, the result is displayed on the Google glass in real-time mode at video-rate capacity of 20 frames per second, which is achieved by synchronizing the Google glass with the laptop. The sensitivity and mobility of our system are evaluated in pre-clinical ICG experiments. In conclusion, the results manifest that WFS is qualified of providing surgeons with real-time intraoperative images to precisely and objectively identify intersegmental planes.

II. MATERIALS AND METHODS

A. *Wireless wearable fluorescence image-guided surgery system design*

WFS was developed by the Key Laboratory of Molecular Imaging of Chinese Academy of Science based on our previous studies [13-15]. To optimize the performance of WFS, the whole system was composed by the following four modules: light source module (LSM), signal acquisition module (SAM), image processing module (IPM), and wearable display module (WDM). The framework diagram was illustrated in Figure. 1 and the picture of WFS were illustrated in Figure. 2.

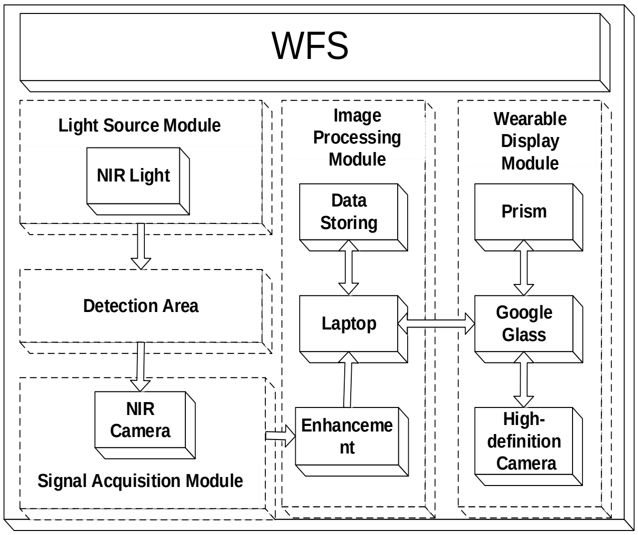

Figure 1. The framework diagram of WFS

Figure 2. The picture of WFS. There are four parts as follows: a handle, NIR excitation light source, Google glass and laptop.

LSM. LSM includes a NIR excitation light source (center wavelength 785nm, maximum power 2W), which is used to excite fluorophores to emit light of a different wavelength.

SAM. SAM consists of a handle, fluorescence filter (wavelength 810-870 nm), C mount lens (f/1.4 12.5 mm) and NIR charge-coupled (CCD) device camera. The function of this module is to capture distinct NIR images of surgery field.

IPM. IPM includes a laptop and an application software named MFVC (Molecular fluorescence View Capture) installed in the laptop. With the aid of MFVC, this module mainly performs image enhancement, mage transmission and data storage automatically.

WDM. WDM is composed by the Google glass (the developer Explorer units version 2), which is connected with the laptop through Wi-Fi. Thus, the Google glass can realize video synchronization with the laptop. So the result can be displayed on the prism screen instantly [16]. Moreover, the high-definition camera is capable to take photos and record videos conveniently by voice control.

B. Google glass video synchronization design

Google glass was initially released by Google in February 2013. The device is composed by many parts, such as a small prism screen mounted directly above the right eye, a camera and a central processing unit. Wearing it, subscribers can easily watch movies, take photos and access the Internet etc. Moreover, a combination control method of head gestures, voice commands and touch commands is adopted. However, it fails to realize video signal synchronization with the computer. So we design a program installed in Google glass to achieve this function. The procedure is showed in Figure. 3.

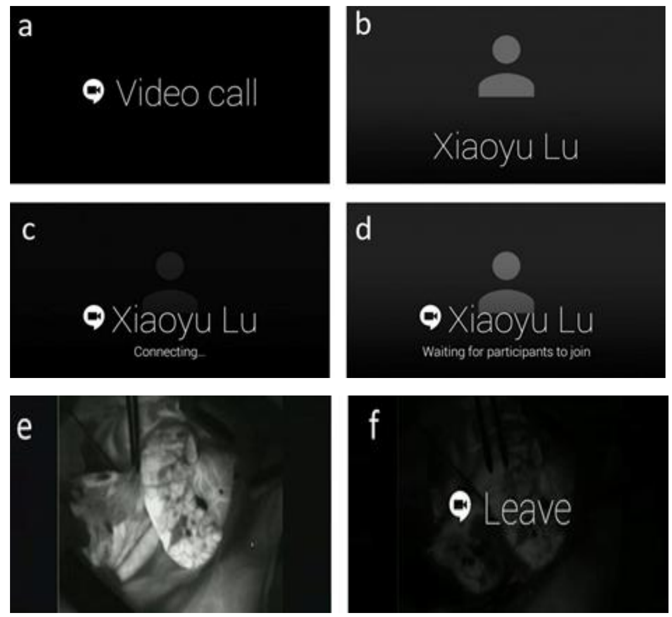

Figure 3. The procedure of Google glass video synchronization with our laptop named Xiaoyu Lu. (a) Surgeons wearing Google glass and opening the video synchronization interactive interface. (b) Choosing a computer (like Xiaoyu Lu) with which to synchronize. (c, d) Establishing the connection and waiting for response. (e) Success in synchronizing with Xiaoyu Lu. (f) Interrupting the connection and waiting for the next instruction.

C. MFVC (Molecular fluorescence View Capture)

MFVC is a multifunctional application software written by ourselves, which is mainly intended for NIR image capture, image co-registration, image fusion and reconstruction for molecular tomography on the basis of our previous work [17-20]. It can adjust many optical parameters continuously and record a video easily. In this study, it is mainly used for image capture and image enhancement. The interface of MFVC is showed in Figure. 4.

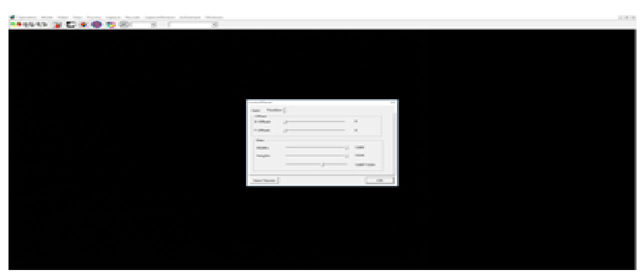

Figure 4. The interface of MFVC

D. Contrast agents

ICG is generally adopted in most pre-clinical and clinical studies because it is authorized for human use [21-24]. We purchase ICG from Yichuang Pharmaceutical Limited Liability Company (Dandong, China). Notably, the ICG dose of 0.5 mg/kg was adopted as a normal concentration in the latest clinical study of intravenous injection [4].

E. Pulmonary segmentectomy in swine

Before the pre-clinical experiment, some fundamental performance parameters of WFS are measured. By trials, the clearest images could be obtained when the handle of WFS was placed 28cm above the surgery field. At this point, the NIR excitation light from the light source cloud illuminate a surgical field as much as 200 mm × 200mm. Besides, there are excellent technical specifications of the developer Explorer units version 2 as follows: 640×360 Himax HX7309 LCoS display, 16 GB storage, 5-megapixel camera, and capable of 720p video recording etc. All of these made WFS possible to achieve the ideal experiment outcome and established the sound basis for the further research and application.

The swine studies were approved by the Peking University People's Hospital. We assigned twelve Yorkshire swine with a mean weight of 30 kg to one of two groups. Firstly, the swine was anesthetized by inhalation of Sevoflurane. Its signs of life were monitored by the care workers during the surgery. Then we placed the swine in a lateral decubitus and operated thoracotomy on it. After the pulmonary artery of the target segment was ligated with silk in each of the swine, ICG with a concentration of 0.2 mg/kg or 0.6 mg/kg was injected into the marginal ear vein according to their group assignment. The handle of WFS was placed 28cm above the surgery field. After five seconds, fluorescent images could be observed clearly on the prism screen under NIR light in each of the swine. Finally, sparing of intersegments was performed using electric cautery. The experimental lung was resected to conduct pathologic analysis.

III. RESULTS

We conducted experiments in swine to measure the sensitivity and mobility of WFS in accurate identification of intersegmental planes. Twelve swine were equally divided into two groups. Group A was injected 0.2mg/kg ICG into the marginal ear vein and Group B was injected 0.6mg/kg ICG. Five seconds later after injection, the black-and-white transition borders among the targeted segment and the non-targeted segments were easily recognized visually in all the swine. Real-time videos were displayed on the prism screen during the surgery as shown in Figure. 5.

Then the signal-to-background ratio (SBR) and the total fluorescence lasting time were measured. Using ImageJ (Image Processing and Analysis Application in Java), the corresponding SBR of the two groups (Group A and Group B) were 9.00 ± 0.70 and 8.96 ± 1.23 respectively, which indicated that the sensitivity of WFS was fairly high. Moreover, the NIR fluorescence images of Group A lasted as long as ten minutes and those of Group B lasted up to fourteen minutes until the SBR was 1. Both the results of the two groups indicated that WFS was outstanding enough to help surgeons identify intersegmental planes. Above all, the pathologic analysis result conformed our conclusion.

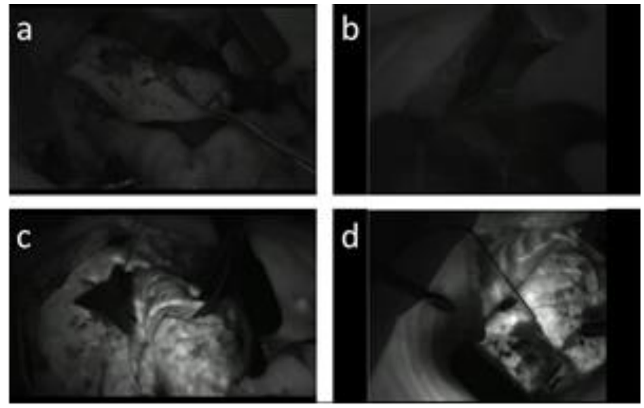

Figure 5: The results of intraoperative pulmonary segmentectomy in swine. (a) Before injection 0.2 mg/kg ICG of Group A; (b) Before injection 0.6 mg/kg ICG of Group B. (c) After injection 0.2 mg/kg ICG of Group A; (d) After injection 0.6 mg/kg ICG of Group A

IV. DISCUSSION

In recent years, segmentectomy has become a secure and effective treatment of early-stage lung cancer, especially in patients with emphysema. In some cases, it is superior to lobectomy [1-3]. When operating pulmonary segmentectomy, it is critical to precisely identify the intersegmental plane, which is difficult for surgeons without suitable interventions. Thus, a novel technique by transbronchial or intravenous injection of ICG to discern intersegmental planes has promoted the development of segmentectomy. It can efficiently avert needless resection, lower the costs and reduce complications [25-27]. Besides, this method can also be adopted to determine the margin of tumors. However, owing to lack of intraoperative fluorescence imaging system, the progress is limited.

At present, many instruments, such as positron emission tomography (PET) and Ultrasound (US), have been widely applied to diagnose tumors preoperatively. Nevertheless, few devices can be used intraoperatively, especially fluorescence imaging systems. Not to mention, there are rare wearable fluorescence imaging systems. Therefore, we developed a novel Wireless Wearable Fluorescence Image-Guided Surgery system named WFS, which could absolutely free surgeons' hands without influencing the routine surgical procedure and make surgeons fully concentrate on the surgical site to achieve the best effect of surgery.

To test the mobility and sensitivity of WFS, we conducted serials of experiments. Twelve swine were evenly divided into two groups, which were injected 0.2mg/kg and 0.6mg/kg apart into the marginal ear vein. The satisfactory outcomes prove that WFS is dominant in identifying intersegmental planes during surgery. The real-time imaging and high SBR are essential for further clinical studies. Besides, the large surgical field (200 mm × 200mm) and the unique wireless wearable display capacity make WFS more attractive and potential.

Recently, our researchers have initiated the clinical translational research. In the future, we expect to employ this novel system in diverse surgical oncology to help more patients get rid of the pain of the cancers.

V. CONCLUSION

Summarily, we have designed a novel wireless wearable fluorescence image-guided surgery system for segmentectomy. The result of this study demonstrates that this system has major advantages in identifying intersegmental planes. Further, we will conduct clinical experiments to validate and optimize our system.

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[1] M. Okada, T. Koike, M. Higashiyama, Y. Yamato, K. Kodama, and N. Tsubota, "Radical sublobar resection for small-sized non-small cell lung cancer: a multicenter study," Journal of Thoracic & Cardiovascular Surgery, vol. 132, pp. 769-775, 2006.

[2] R. J. Keenan, R. J. Landreneau, R. H. M. Jr, D. Singh, R. Macherey, S. Bartley, et al., "Segmental resection spares pulmonary function in patients with stage I lung cancer," Annals of Thoracic Surgery, vol. 78, pp. 228-233, 2004.

[3] T. Koike, Y. Yamato, K. Yoshiya, T. Shimoyama, and R. Suzuki, "Intentional limited pulmonary resection for peripheral T1 NO MO small-sized lung cancer," Journal of Thoracic & Cardiovascular Surgery, vol. 125, pp. 924-8, 2003.

[4] N. Misaki, S. S. Chang, H. Igai, S. Tarumi, M. Gotoh, and H. Yokomise, "New clinically applicable method for visualizing adjacent lung segments using an infrared thoracoscopy system," Journal of Thoracic & Cardiovascular Surgery, vol. 140, pp. 752–756, 2010.

[5] Y. Sekine, E. Ko, H. Oishi, and M. Miwa, "A simple and effective technique for identification of intersegmental planes by infrared thoracoscopy after transbronchial injection of indocyanine green," Journal of Thoracic & Cardiovascular Surgery, vol. 143, pp. 1330-5, 2012.

[6] O. Shiaki, S. Kenji, M. Yoshikazu, M. Takeshi, T. Yukio, and T. Kazuya, "New technique for lung segmentectomy using indocyanine green injection," Annals of Thoracic Surgery, vol. 95, pp. 2188-2190, 2013.

[7] A. M. De Grand and J. V. Frangioni, "An operational near-infrared fluorescence imaging system prototype for large animal surgery," Technology in Cancer Research & Treatment, vol. 2, pp. 553-562, 2003.

[8] G. M. Dam, Van, T. George, L. M. A. Crane, N. J. Harlaar, R. G. Pleijhuis, K. Wendy, et al., "Intraoperative tumor-specific fluorescence imaging in ovarian cancer by folate receptor-α targeting: first in-human results," Nature Medicine, vol. 17, pp. 1315-9, 2011.

[9] J. R. Vorst, Van Der, H. Merlijn, J. S. D. Mieog, K. E. Rooij, De, E. L. Kaijzel, C. W. G. M. L?Wik, et al., "Near-Infrared Fluorescence Imaging of Liver Metastases in Rats using Indocyanine Green," Biomedical Chromatography Bmc, vol. 174, pp. 266-71, 2011.

[10] Y. Yuasa, J. Seike, T. Yoshida, H. Takechi, H. Yamai, Y. Yamamoto, et al., "Sentinel lymph node biopsy using intraoperative indocyanine green fluorescence imaging navigated with preoperative CT lymphography for superficial esophageal cancer," Annals of Surgical Oncology, vol. 19, pp. 486-493, 2012.

[11] L. M. A. Crane, G. Themelis, R. G. Pleijhuis, N. J. Harlaar, A. Sarantopoulos, H. J. G. Arts, et al., "Intraoperative Multispectral Fluorescence Imaging for the Detection of the Sentinel Lymph Node in Cervical Cancer: A Novel Concept," Molecular Imaging & Biology Mib the Official Publication of the Academy of Molecular Imaging, vol. 13, pp. 1043-1049, 2011.

[12] L. Yang, Z. Yi-Ming, A. Walter, T. Zhao-You, F. Jia, S. Hui-Chuan, et al., "First in-human intraoperative imaging of HCC using the fluorescence goggle system and transarterial delivery of near-infrared fluorescent imaging agent: a pilot study," Translational Research the Journal of Laboratory & Clinical Medicine, vol. 162, pp. 324–331, 2013.

[13] C. W. Chi, J. Z. Ye, H. L. Ding, D. He, W. H. Huang, G. J. Zhang, et al., "Use of Indocyanine Green for Detecting the Sentinel Lymph Node in Breast Cancer Patients: From Preclinical Evaluation to Clinical Validation," Plos One, vol. 8, Dec 16 2013.

[14] C. Chi, Y. Du, J. Ye, D. Kou, J. Qiu, J. Wang, et al., "Intraoperative Imaging-Guided Cancer Surgery: From Current Fluorescence Molecular Imaging Methods to Future Multi-Modality Imaging Technology," Theranostics, vol. 4, pp. 1072-1084, 2014.

[15] C. Chi, Q. Zhang, Y. Mao, D. Kou, J. Qiu, J. Ye, et al., "Increased precision of orthotopic and metastatic breast cancer surgery guided by matrix metalloproteinase-activatable near-infrared fluorescence probes," Scientific Reports, vol. 5, 2015.

[16] O. J. Muensterer, M. Lacher, C. Zoeller, M. Bronstein, and J. Kubler, "Google Glass in pediatric surgery: An exploratory study," International Journal of Surgery, vol. 12, pp. 281-289, 2014.

[17] J. Ye, C. Chi, Z. Xue, P. Wu, Y. An, H. Xu, et al., "Fast and robust reconstruction for fluorescence molecular tomography via a sparsity adaptive subspace pursuit method," Biomedical Optics Express, vol. 5, pp. 387-406, 2014.

[18] Y. Jinzuo, D. Yang, A. Yu, C. Chongwei, and T. Jie, "Reconstruction of fluorescence molecular tomography via a nonmonotone spectral projected gradient pursuit method," Journal of Biomedical Optics, vol. 19, pp. 126013-126013, 2014.

[19] Y. An, J. Liu, G. Zhang, J. Ye, Y. Du, Y. Mao, et al., "A Novel Region Reconstruction Method for Fluorescence Molecular Tomography," IEEE transactions on bio-medical engineering, vol. 62, pp. 1818-1826, 2015.

[20] Y. An, J. Liu, G. Zhang, J. Ye, Y. Mao, S. Jiang, et al., "Meshless reconstruction method for fluorescence molecular tomography based on compactly supported radial basis function," Journal of Biomedical Optics, vol. 20, 2015.

[21] M. D. Kunihito Gotoh, T. Y. M. PhD, O. I. M. PhD, M. D. Hidenori Takahashi, H. E. M. PhD, M. Y. M. PhD, et al., "A novel image-guided surgery of hepatocellular carcinoma by indocyanine green fluorescence imaging navigation," Journal of Surgical Oncology, vol. 100, pp. 75–79, 2009.

[22] T. Ishizawa, N. Fukushima, J. Shibahara, K. Masuda, S. Tamura, T. Aoki, et al., "Real-time identification of liver cancers by using indocyanine green fluorescent imaging," Cancer, vol. 115, pp. 2491-504, 2009.

[23] L. Sampath, W. Wang, and E. Sevick-Muraca, "Near infrared fluorescent optical imaging for nodal staging," Journal of Biomedical Optics, vol. 13, p. 041312, 2008.

[24] B. E. Schaafsma, J. S. D. Mieog, H. Merlijn, d. V. J. R. Van, P. J. K. Kuppen, C. W. G. M. Löwik, et al., "The Clinical Use of Indocyanine Green as a Near-Infrared Fluorescent Contrast Agent for Image-Guided Oncologic Surgery," Journal of Surgical Oncology, vol. 104, pp. 323-32, 2011.

[25] M. J. Schuchert, B. L. Pettiford, P. Arjun, A. Ghulam, A. Omar, C. John, et al., "Anatomic segmentectomy for stage I non-small-cell lung cancer: comparison of video-assisted thoracic surgery versus open approach," Journal of Thoracic & Cardiovascular Surgery, vol. 138, pp. 1318–1325.e1, 2009.

[26] M. Schuchert, B. Pettiford, J. Luketich, and R. Landreneau, "Parenchymal-Sparing Resections: Why, When, and How," Thoracic Surgery Clinics, vol. 18, pp. 93-105, 2008.

[27] K. Takagi, Y. S. Hata, K. Tamaki, K. Fukumori, H. Otsuka, C. Hasegawa, et al., "Late onset postoperative pulmonary fistula following a pulmonary segmentectomy using electrocautery or a harmonic scalpel," Annals of Thoracic & Cardiovascular Surgery, vol. 16, pp. 21-25, 2010.