

Advancements in biomedical sensing through integrated optical endo-microscopy systems

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Abstract:

Monitoring physiological changes in living organisms presents significant challenges, necessitating the use of specialised analytical tools. Fibre-optic probes provide a minimally invasive means for detecting physiological signals from precise locations within the body. Advancements in fibre probe-based sensing and imaging are crucial to biomedical fields, achieving transformative outcomes through interdisciplinary collaboration. Key attributes of fibre optics for *in vivo* imaging and sensing include their compact dimensions and inert glass composition, enabling minimally invasive clinical applications and deep tissue, non-destructive probing. Moreover, approximately one in twelve adults suffer from chronic obstructive pulmonary disease (COPD) or asthma, with acute exacerbations of chronic lower respiratory diseases (CLRDs) being the leading causes of mortality and morbidity. Effective methods for detecting exacerbations and cases within populations are vital for advancing prevention research. This study demonstrates the potential of integrating biomedical and fibre-optic research in an educational and engaging manner for non-specialist audiences. It aims to enhance understanding of lung diseases using novel techniques based on optical endo-microscopy (OEM). The study has improved engagement activities, bridging theoretical concepts with practical applications. These activities include the development of cost-effective educational tools adapted from medical OEM technologies, facilitating the dissemination of advanced scientific knowledge to a broader audience.

Keywords: biomedical sensing, chronic lower respiratory diseases, fibre-optic probes, *in vivo* imaging, minimally invasive techniques, optical endo-microscopy.

Classification numbers: 1.3, 2.3, 3.6

1. Introduction

The educational needs of contemporary distance learners and educators must be addressed to overcome modern challenges. Leveraging technology can significantly enhance the comprehension of fundamental principles while fostering problem-solving, analytical, and expert thinking skills [1]. Health and disease states originate from molecular processes within the complex and heterogeneous environments of living organisms [2]. Imaging and sensing these processes present significant scientific challenges due to the anatomically defined compartments in the human body, which are difficult to access using minimally invasive or non-invasive techniques. Consequently, many fundamental physiological events and processes remain incompletely understood [3].

Understanding these processes often necessitates reconstructing them from isolated snapshots, requiring repeated measurements and long-term monitoring of individuals [3]. This approach results in a fragmented understanding of molecular pathways and events. Progress in fibre-optic sensing and imaging technologies is inextricably linked to biomedical disciplines; transformative outcomes are achievable only through interdisciplinary convergence [4, 5]. These technological advancements must meet several criteria, including the ability to image or sense: a) within ultra-small volumes; b) at specific locations in the body; c) *in vivo*; d) within relevant timelines; e) with high sensitivity, specificity, and selectivity; and f) using deployable devices when necessary. Fibre-optic probes have the potential to satisfy many of these conditions, playing a crucial role in *in vivo* imaging and sensing [6, 7].

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Fibre-optic platforms support imaging modalities crucial for *in vivo* bio-analysis [8]. These probes are well-developed technologies employed in various industrial and research applications, leveraging their immunity to electromagnetic interference, high bandwidth, extended interaction length, lightweight nature, long-distance sensing, and multiplexed sensing capabilities [9]. The small footprint and inert glass composition of fibre-optic probes enable minimally invasive or non-invasive clinical implementations and non-destructive probing deep within tissues. Consequently, light-based sensing and imaging technologies are well-suited for repetitive measurements of molecular events in anatomical locations in pre-clinical models. Fig. 1 illustrates how an object can be sensed by optical cable probes by positioning it on an optical table and connecting the probe to a computer system [10].

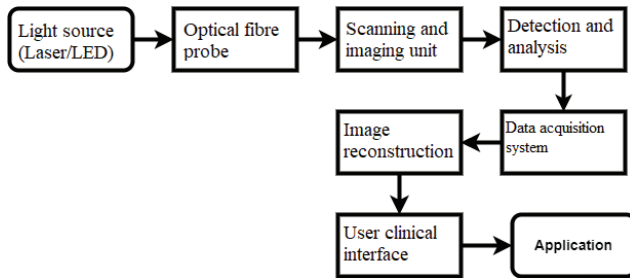


Fig. 1. Block diagram representation of optical endo-microscopy.

COPD is a progressive illness caused by an abnormal inflammatory response in the airways to gases and particles. This inflammation leads to progressive airflow limitations, resulting in hypoxaemia and alveolar hypoxia. COPD is recognised as a systemic disease and is projected to become the third leading cause of death worldwide by 2020 [11]. Systemic effects are precipitated by hypoxia and inflammatory cytokines released during the disease, often associated with smoking. Reported comorbidities of COPD include nutritional problems, weight loss, autoimmune disorders, diabetes, osteoporosis, sleep apnoea, depression, and cardiovascular diseases. Inflammation and hypoxaemia reduce choroidal and retinal blood flow, further complicating the management and treatment of COPD patients.

Fibre-optic sensing and imaging technologies have the potential to revolutionise the understanding and management of diseases such as COPD. By facilitating minimally invasive, high-resolution imaging and real-time monitoring of physiological processes, these technologies can provide deeper insights into the molecular mechanisms underlying disease progression and response to treatment [12].

As a result, they are invaluable tools in both clinical and research settings, contributing to the advancement of medical science and the improvement of patient outcomes.

OEM is an emerging imaging tool used in both pre-clinical and clinical settings. In pulmonary optical endo-microscopy, abundant collagen and elastin enable structural imaging through autofluorescence generated by laser excitation at 488 nm [8]. The fibre optics used in lung applications have a diameter of 1.4 mm, facilitating the exploration of the digital pulmonary tract and the assessment of respiratory bronchioles. Clinically, OEM is employed for detecting lung cancer and accessing distal lung regions. Additionally, OEM is used in organs such as the urological tract [4-6].

These outcomes optimise, test, and design phases to develop novel activities that enhance knowledge in the field [9]. Over a year, the team has advanced co-production processes to demonstrate the use of fibre optics in biomedical applications. In this manuscript, we propose a novel and easy-to-implement teaching session and educational tool in the field of optical fibre and biomedical engineering, focusing on the use of optical fibres in biomedical sciences for molecular imaging and sensing in the distal lung.

The current manuscript is organised into six sections. Section 1 introduces the manuscript. Section 2 reviews the literature. Sections 3 and 4 present the methodology and result analysis, respectively, while Sections 5 and 6 discuss the conclusions and future scope of the proposed model.

2. Review of existing literature on the proposed model

The following section provides an overview of existing literature relevant to the proposed mode.

2.1. Advances in fibre-optic probes for biomedical applications

Fibre-optic probes have become a cornerstone in biomedical sensing and imaging due to their minimal invasiveness and high sensitivity. These probes enable real-time monitoring of physiological parameters and biochemical markers within living tissues. For instance, research by Z. Zhang, et al. (2018) [1] highlights the use of fibre-optic probes for continuous monitoring of pH and oxygen levels *in vivo*, demonstrating their capability for real-time physiological assessments. Such advancements are crucial for the development of diagnostic tools that provide immediate and accurate information about a patient's health status.

2.2. Integration of optical endo-microscopy in clinical diagnostics

OEM merges high-resolution imaging with the minimally invasive properties of endoscopy, offering enhanced visualisation of internal tissues. A study by S. Prompalit, et al. (2018) [2] demonstrated that OEM could effectively detect early-stage cancers in the gastrointestinal tract, providing clinicians with detailed images of cellular structures without the need for extensive surgical procedures. The integration of OEM into clinical diagnostics represents a significant advancement in early disease detection and patient care.

2.3. Challenges in *in vivo* imaging and sensing

Despite technological advancements, several challenges persist in the field of *in vivo* imaging and sensing. One primary difficulty is accessing specific anatomical regions in a minimally invasive manner while obtaining clear and accurate images. For example, B.M. Quandt, et al. (2017) [3] discuss how the complex structure of lung tissue complicates imaging efforts. Their work illustrates how OEM can overcome some of these challenges by providing high-resolution images that aid in the early detection of diseases such as COPD and lung cancer.

2.4. Impact of chronic obstructive pulmonary disease on biomedical research

COPD is a significant global health issue, with increasing prevalence and mortality rates. COPD is characterised by chronic inflammation and progressive airflow limitation. Understanding the molecular mechanisms of COPD is essential for developing effective treatments. C. Broadway, et al. (2016) [4] explored the role of inflammatory cytokines in COPD progression and suggested that targeted therapies could mitigate inflammation and improve patient outcomes. This research underscores the importance of continuous monitoring and early intervention in managing chronic diseases.

2.5. Educational applications of fibre-optic technology

Incorporating fibre-optic technology into educational tools can significantly enhance learning outcomes in biomedical engineering. By providing hands-on experience with cutting-edge diagnostic tools, students can bridge the gap between theoretical knowledge and practical application. A. Goorsenberg, et al. (2020) [5] developed an educational module that uses fibre-optic sensors to teach principles of biomedical imaging. This approach improved student engagement and understanding, demonstrating the potential of fibre-optic technology in academic settings.

2.6. Auto-detection and removal of uninformative frames in optical endo-microscopy

The nature of OEM data in clinical settings often includes a significant number of uninformative frames. These frames may result from various factors, such as motion artefacts or pure noise, and must be identified and removed to enhance the quality and efficiency of clinical assessments. A study by A. Perperidis, et al. (2016) [10] focused on the automatic detection and removal of these uninformative frames while preserving those containing valuable structural information.

In this study, the researchers employed grey-level co-occurrence matrix (GLCM) texture measures to distinguish between informative and uninformative frames. GLCM is a statistical method that analyses texture by examining the spatial relationships of pixels, providing insights into contrast, homogeneity, and other texture-related properties of the frames.

The study treated the identification of motion artefacts and pure-noise frames as two distinct issues. Motion artefacts, caused by patient movement or device instability, can obscure structural details, while pure-noise frames contain little to no useful information. By addressing these issues separately, the researchers developed a more targeted and effective approach. Using pulmonary OEM frame sequences of the distal lungs, the study developed and evaluated detection algorithms.

The algorithms demonstrated impressive performance, achieving a sensitivity of 93% and a specificity of 92.6%. Sensitivity refers to the algorithm's ability to correctly identify uninformative frames, while specificity indicates its effectiveness in preserving informative frames. The robust and accurate detection algorithms developed in this study have significant implications for the use of OEM in pulmonary imaging. By automatically filtering out uninformative frames, these algorithms enhance the overall quality of the data, allowing clinicians to focus on frames containing meaningful structural information. This improvement not only streamlines the diagnostic process but also reduces the time and effort required for manual frame selection.

2.7. Challenges and proposed solutions

(1) Uninformative frames

Issue: OEM data often includes uninformative frames caused by motion artefacts or noise, which can diminish the efficiency and accuracy of clinical assessments.

Solution: Implement advanced algorithms, such as those employing GLCM texture measures, to automatically detect and remove uninformative frames. This approach ensures the preservation of frames containing valuable structural information.

(2) Miniaturisation and integration

Issue: Miniaturising components while maintaining high performance and integrating various functionalities into a compact OEM system remains a significant challenge.

Solution: Advances in microfabrication techniques and materials science can facilitate the development of smaller, more efficient components. Incorporating MEMS-based scanners and GRIN lenses can enhance imaging performance without increasing the overall size of the device.

(3) Complexity of data analysis

Issue: The complex and voluminous data generated by OEM systems require sophisticated analysis techniques to extract meaningful information.

Solution: Integrate artificial intelligence (AI) and machine learning algorithms to assist in real-time image processing, pattern recognition, and anomaly detection. These technologies can improve diagnostic accuracy and reduce the workload on clinicians.

(4) Invasiveness and patient comfort

Issue: Despite being minimally invasive, OEM procedures can still cause discomfort and pose certain risks to patients.

Solution: Further miniaturise OEM probes and enhance their flexibility and biocompatibility. Develop non-contact or non-invasive imaging techniques to complement existing OEM methods, thereby reducing invasiveness and improving patient comfort.

(5) Regulatory and standardisation hurdles

Issue: Securing regulatory approval and achieving standardisation for new OEM technologies can be time-consuming and costly.

Solution: Engage in early and continuous collaboration with regulatory bodies to ensure compliance with standards and facilitate smoother approval processes. Conduct comprehensive validation studies to demonstrate the safety and efficacy of the technology.

2.8. Alternative solutions

(1) Nanophotonic sensors

Description: Employ nanophotonic sensors to enhance the sensitivity and specificity of OEM systems. These sensors can provide higher resolution and more detailed images, facilitating improved diagnosis and monitoring of diseases.

Benefit: Nanophotonic sensors can detect subtle molecular-level changes, offering a non-invasive and highly accurate diagnostic tool.

(2) Sustainable and green technologies

Description: Develop OEM systems using sustainable materials and energy-efficient technologies. For example, biodegradable materials can be used in probe construction, and low-power light sources can be incorporated.

Benefit: Reducing the environmental impact of OEM systems aligns with global sustainability goals and minimises the carbon footprint of medical devices.

(3) Hybrid imaging techniques

Description: Combine OEM with other imaging modalities, such as ultrasound or MRI, to provide complementary information and improve diagnostic accuracy.

Benefit: Hybrid systems can offer a more comprehensive view of tissues, enhancing diagnostic capabilities and reducing reliance on a single modality.

(4) Educational tools and training

Description: Develop cost-effective educational tools and training programmes adapted from clinical OEM systems to enhance the understanding and application of these technologies among healthcare professionals.

Benefit: Improved training and education can lead to better utilisation of OEM systems, resulting in enhanced diagnostic accuracy and improved patient outcomes.

(5) Long-term monitoring and telemedicine

Description: Develop OEM systems capable of long-term monitoring and integrate them with telemedicine platforms for remote diagnosis and patient management.

Benefit: Long-term monitoring provides continuous data on disease progression, while telemedicine integration extends the reach of medical expertise to remote and underserved areas.

Summary of some studies in biomedical sensing and imaging technologies is shown in Table 1.

Table 1. Summary of studies in biomedical sensing and imaging technologies.

Reference	Study focus	Key findings
[10]	Auto-detection and removal of uninformative frames in OEM	Developed methods for detecting and removing uninformative frames with 93% sensitivity and 92.6% specificity using GLCM texture measures. Effective for pulmonary OEM frame sequences.
[11]	High-performance OEM systems for ex-vivo and in-vivo imaging	Demonstrated three-colour imaging capability for simultaneous multi-molecular target imaging at video rates. Cost-efficient and suitable for widespread clinical use.
[12]	In situ detection of bacteria using OEM	Enabled multiplexed, simultaneous, multi-colour <i>in-vivo</i> imaging in real-time. Combined a 3-in-1 optical fibre endoscope with molecular imaging agents for diagnostic decisions.
[13]	Correlation between NLR and pulmonary function in COPD patients	Showed that COPD negatively impacts OCT measurements. SC-OCT reflects inflammation intensity, and NLR predicts cellular damage in COPD patients.
[14]	Anxiety and respiratory rate in MRI patients	Evaluated anxiety levels and respiratory rates (RR) using fibre-optic sensors. Found significant anxiety reduction in subjects with decreased RR; no change in the stable RR group.
[15]	Smartphone-based optical fibre sensors for respiratory monitoring	Developed a cost-efficient sensor using smartphone components and POF for detecting breathing rates. Validated experimentally with effective results.
[16]	Optical fibre deformation sensor for respiratory measurement	Created a system using optical fibre sensors on an elastic belt to measure respiratory rate and depth quantitatively. Enhanced sensitivity through differential systems.
[17]	Chronic lower respiratory disease (CLRD) case detection	Validated protocols for classifying CLRD cases and exacerbations. Highlighted the importance of early detection for prevention research.
[18]	Synthetic fluorophores for molecular interrogation	Improved signal detection using a three-branched dendrimer scaffold for pathogen identification in human lungs.
[19]	Bayesian approach for bacteria detection in OEM images	Employed a Bayesian model to detect bacteria, showing strong correlation with bacterial counts. Developed a multi-colour endo-microscopy system for guidance and detection.
[20]	Low-cost wide-field fibre-optic OEM systems	Demonstrated a system for enhancing fluorescent signal differences without complex un-mixing. Effective in detecting bacteria in auto-fluorescent lung tissue.
[21]	Bronchoscopy and pulmonary nodule detection	Addressed discrepancies between pre-procedural CT scans and bronchoscopy. Proposed methods to reduce diagnostic inaccuracies.
[22]	Educational and interactive biomedical engineering	Highlighted the importance of public engagement and understanding in biomedical research. Focused on respiratory diseases and optical fibre endo-microscopy techniques.
[23]	Fibre-optic pressure sensors for clinical applications	Reviewed advantages of fibre-optic pressure sensors for in-vivo measurements. Discussed recent developments and application areas.
[24]	Hydrogel pH sensors for tissue monitoring	Developed a compact hydrogel pH sensor for precise tissue pH monitoring, achieving high accuracy.
[25]	Photonic estimations of oxygen and pH in lungs	Developed a flexible optrode miniature for photonic estimations, providing rapid and precise measurements. Suitable for integration with multiple sensors.

3. Methodology

The proposed system is described as follows: The OEM system has been designed to align closely with laboratory standards, ensuring reproducibility, cost-effectiveness, and durability (Fig. 2).

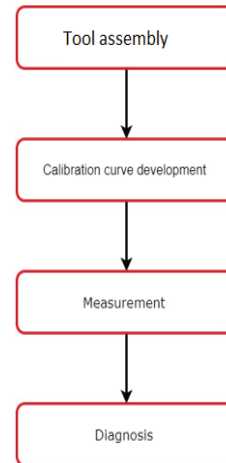


Fig. 2. Process flow of the proposed design.

This setup can be readily adapted from the laboratory to clinical settings for human analysis. An educational tool was developed to complement the OEM system, utilising advanced optical fibres in the probe design.

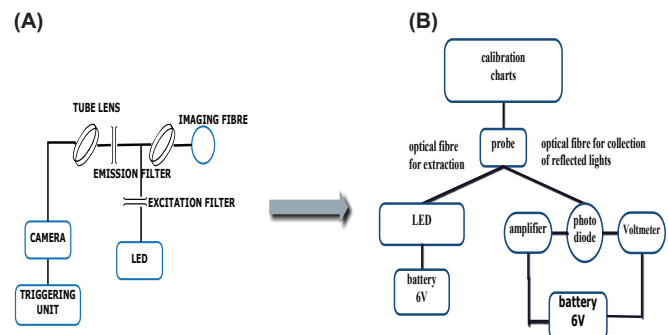


Fig. 3. (A) Schematic of the optical endo-microscopy setup, (B) Educational tool designed around an optoelectronic circuit.

In Fig. 3A, a schematic of the OEM setup is presented. A blue LED light is used to excite fluorophores, particularly structural molecules such as collagen, connective tissue, and elastin, which emit fluorescence in the green spectrum. This autofluorescence effect enables technicians to visualise the bronchial tree and excite exogenous fluorescent disease markers.

In Fig. 3B, the educational tool relies on a light source, a lung sample or calibration chart, and two optical fibres, which combine to create an efficient probe. These probes are employed for sample excitation and collection of light reflected from the lung sample. The measurement unit

includes an amplifier, photodiode, and voltmeter. The tool utilises three LED lights powered by a 9V battery, along with the amplifier-photodiode combination, enabling users to examine samples and take measurements.

The research demonstrated that the optoelectronic function kit could be easily reproduced using a simple circuit design. A voltmeter was used to display the output of the amplifier/photodiode combination. The probe consists of three-dimensional printed parts and two optical fibres that can be attached to the optoelectronic kit, making it portable. These include: a probe tip for securing the collection fibres and illumination at a 45-degree angle, covers to block unwanted light and position the illumination and collection fibres optimally in relation to the photodiode and amplifier combination, and clips to secure the kit board for convenient use (Fig. 4).

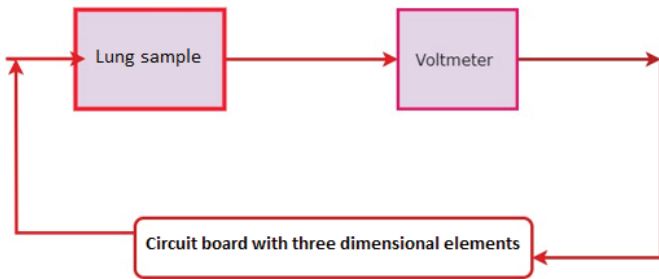


Fig. 4. Assembly of the experimental approach.

4. Results and discussion

The educational tool facilitated the transportation and collection of data on environmental changes, such as colour, which were analysed using light and represented as variable voltage readings. This enabled students to comprehend the calibration curve, which could be extended as a teaching model for understanding misdiagnosis and uncertainties.

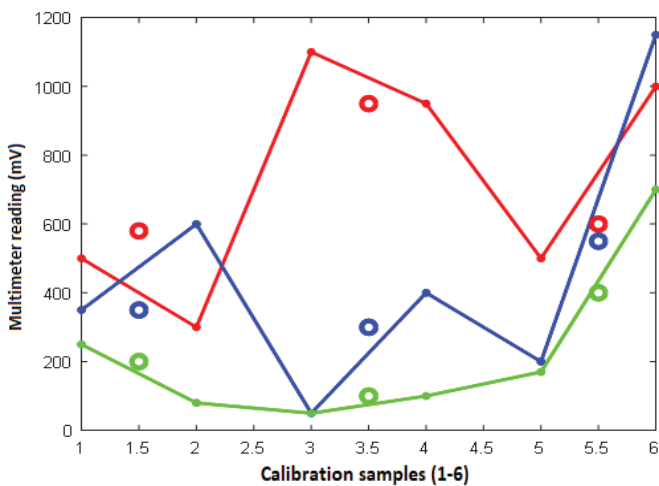


Fig. 5. Example calibration curves (lines).

Calibration curves were created using six predetermined colour patches, with three readings per set, and plotted accordingly. Fig. 5 provides an example of the six colour patches (1 to 6) illuminated by green, red, and blue light. Calibration curve characteristics were observed within two ranges: 0 to 600 and 1200 mV. Calibration values were estimated differently for each sample to account for tool operation errors and power supply variations, ensuring an acceptable calibration curve. Measurements were taken from three lung samples, each containing a coloured patch not visible to the naked eye within a long tube. The lung sample colours were selected to fall between two points on the curve, aiding students in understanding lung diagnoses.

Lung A’s reading fell between samples 3 and 4, indicating a cancer diagnosis. Lung B’s reading fell between samples 5 and 6, suggesting pneumonia. Lung C’s reading fell between samples 1 and 2, representing a healthy lung (Fig. 6).

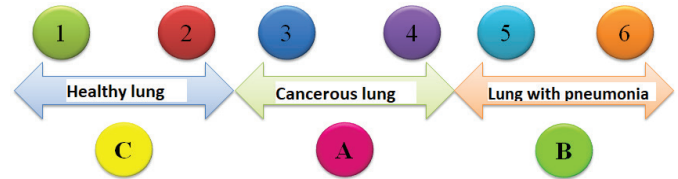


Fig. 6. Lung diagnosis measurements (circles).

Table 2. Comparative analysis of calibration curve of the existing and proposed system.

Existing system	Normal lung	500	300	1100	950	500	1000	580	950	600
	Cancerous lung	350	600	50	400	200	1150	350	300	550
	Pneumonia lung	250	80	50	100	170	700	200	100	400
Proposed system	Normal lung	350	550	1030	830	150	800	470	960	570
	Cancerous lung	500	230	0	60	65	930	350	60	580
	Pneumonia lung	200	50	0	590	350	650	100	280	450

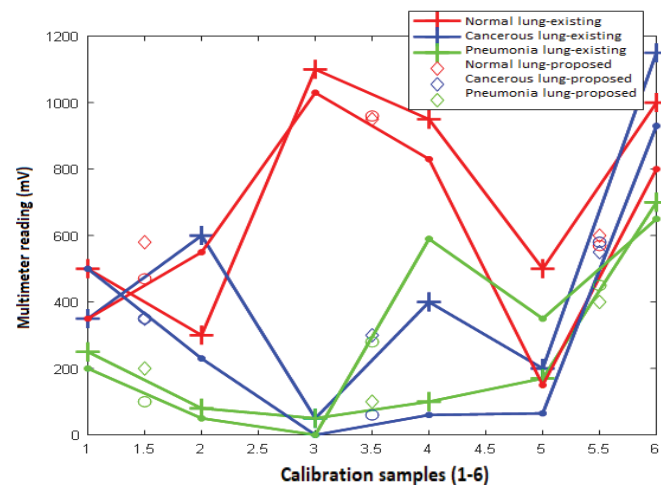


Fig. 7. Comparison of the calibration curves between the existing and proposed systems.

These measurements enabled participants to delve deeply into the research. A comparative analysis, as presented in Table 2 and Fig. 7, demonstrated the efficiency of the proposed method compared with existing approaches.

5. Conclusions

The OEM system exhibits substantial potential for extensive applications in multiplexing with disease-targeting labels [26-29]. This study emphasises the convergence of optical fibre technology and biomedical research, presenting it in an educational and interactive format accessible to diverse audiences. The primary objective is to advance understanding of lung diseases through novel methodologies in fibre-based optical endomicroscopy. This study introduces an enhanced engagement activity that bridges the gap between theoretical knowledge and practical application, incorporating an affordable educational tool adapted from clinical OEM systems. The OEM system is particularly significant in multiplexed imaging, enabling simultaneous detection of multiple disease markers in complex biological environments. By integrating fluorescent markers or contrast agents, the system facilitates high-resolution, real-time imaging of pathological processes at the cellular and subcellular levels. The compact design and high sensitivity of fibre-optic probes make them ideal for *in vivo* applications, enabling minimally invasive procedures, reducing patient discomfort, and providing valuable diagnostic information.

6. Future scope

Future advancements in OEM systems will focus on developing fifth-generation sensors with heightened sensitivity and specificity for early detection of molecular-level changes. These innovations will enable precise disease diagnoses.

Sustainable, bio-derived sensors will enhance biocompatibility and minimise environmental impact, ensuring safer integration with biological tissues. Concurrently, hospital-on-chip biosensors integrated into OEM platforms will miniaturise diagnostic capabilities, facilitating point-of-care testing and real-time disease monitoring.

These developments will revolutionise clinical diagnostics, providing rapid, accurate, and personalised healthcare solutions, empowering healthcare providers to deliver proactive interventions and improve global patient outcomes.

CRedit author statement

Aditya Tandle: Data curation, Principal investigator, Writing original draft; Vrushali M. Shitole: Conceptualisation, Methodology, Formal analysis; Shilpa Choudhary: Investigation, Formal analysis; Mahesh V. Shitole: Methodology, Formal analysis; Akhilesh Kumar Pandey: Supervision, Funding acquisition, Data curation, Principal investigator.

COMPETING INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this article.

REFERENCES

- [1] Z. Zhang, Y. Zhang, L. Yao, et al. (2018), "A sensor-based wrist pulse signal processing and lung cancer recognition", *Journal of Biomedical Informatics*, **79**, pp.107-116, DOI: 10.1016/j.jbi.2018.01.009.
- [2] S. Prompalit, G. Fruhwirth, K. Rhode, et al. (2018), "Development of a non-contact device based on optical fibre technology for detecting respiration of small animals in imaging instruments", *IEEE Sensors*, DOI: 10.1109/ICSENS.2018.8589570.
- [3] B.M. Quandt, F. Braun, D. Ferrario, et al. (2017), "Body-monitoring with photonic textiles: A reflective heartbeat sensor based on polymer optical fibres", *Journal of The Royal Society Interface*, **14(128)**, DOI: 10.1098/rsif.2017.0060.
- [4] C. Broadway, D. Gallego, A. Pospori, et al. (2016), "Microstructured polymer optical fibre sensors for opto-acoustic endoscopy", *Micro-Structured and Specialty Optical Fibres IV*, *International Society for Optics and Photonics*, DOI: 10.1117/12.2227588.
- [5] A. Goorsenberg, K.A. Kalverda, J. Annema, et al. (2020), "Advances in optical coherence tomography and confocal laser endomicroscopy in pulmonary diseases", *Respiration*, **99(3)**, pp.189-204, DOI: 10.1159/000503261.
- [6] J.U. Lim, J.H. Lee, J.S. Kim, et al. (2017), "Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients", *International Journal of Chronic Obstructive Pulmonary Disease*, **12**, pp.2465-2475, DOI: 10.2147/COPD.S141295.
- [7] A.T. Hastie, F.J. Martinez, J.L. Curtis, et al. (2017), "Association of sputum and blood eosinophil concentrations with clinical measures of COPD severity: An analysis of the SPIROMICS cohort", *The Lancet Respiratory Medicine*, **5(12)**, pp.956-967, DOI: 10.1016/S2213-2600(17)30432-0.
- [8] A.K. Eldaly, Y. Altmann, A. Perperidis, et al. (2018), "Deconvolution and restoration of optical endomicroscopy images", *IEEE Transactions on Computational Imaging*, **4(2)**, pp.194-205, DOI: 10.1109/TCI.2018.2811939.

- [9] J. Li, B.C. Gibson, A.D. Greentree, et al. (2018), "Perspective: Biomedical sensing and imaging with optical fibres - Innovation through convergence of science disciplines", *APL Photonics*, **3(10)**, DOI: 10.1063/1.5040861.
- [10] A. Perperidis, A. Akram, Y. Altmann, et al. (2016), "Automated detection of uninformative frames in pulmonary optical endomicroscopy", *IEEE Transactions on Biomedical Engineering*, **64(1)**, pp.87-98, DOI: 10.1109/TBME.2016.2538084.
- [11] N. Krstajić, B. Mills, I. Murray, et al. (2018), "Low-cost high sensitivity pulsed endomicroscopy to visualize tricolor optical signatures", *Journal of Biomedical Optics*, **23(7)**, DOI: 10.1117/1.JBO.23.7.076005.
- [12] B. Mills, A.M. Fernandez, D. Norberg, et al. (2020), "Molecular detection of Gram-positive bacteria in the human lung through an optical fibre-based endoscope", *European Journal of Nuclear Medicine and Molecular Imaging*, pp.1-8, DOI: 10.1007/s00259-020-05021-4.
- [13] P.A. Ozer, N. Ogan (2020), "Correlation of neutrophil/lymphocyte ratio and pulmonary parameters with optic coherence tomography findings in stable chronic obstructive pulmonary disease", *The Clinical Respiratory Journal*, **14(4)**, pp.353-363, DOI: 10.1111/crj.13140.
- [14] Ł. Dziuda, P. Zieliński, P. Baran, et al. (2019), "A study of the relationship between the level of anxiety declared by MRI patients in the STAI questionnaire and their respiratory rate acquired by a fibre-optic sensor system", *Scientific Reports*, **9(1)**, pp.1-11, DOI: 10.1038/s41598-019-40737-w.
- [15] A. Aitkulov, D. Tosi (2019), "Optical fibre sensor based on plastic optical fibre and smartphone for measurement of the breathing rate", *IEEE Sensors Journal*, **19(9)**, pp.3282-3287, DOI: 10.1109/JSEN.2019.2894834.
- [16] H. Di, S. Sun, Y. Che (2017), "Respiration measurement using fibre-optic deformation sensor", *Journal of Modern Optics*, **64(6)**, pp.639-645, DOI: 10.1080/09500340.2016.1255367.
- [17] E.C. Oelsner, L.R. Loehr, A.G. Henderson, et al. (2016), "Classifying chronic lower respiratory disease events in epidemiologic cohort studies", *Annals of the American Thoracic Society*, **13(7)**, pp.1057-1066, DOI: 10.1513/AnnalsATS.201601-063OC.
- [18] A.R. Akram, N. Avlonitis, E. Scholefield, et al. (2019), "Enhanced avidity from a multivalent fluorescent antimicrobial peptide enables pathogen detection in a human lung model", *Scientific Reports*, **9(1)**, pp.1-10, DOI: 10.1038/s41598-019-44804-0.
- [19] A.K. Eldaly, Y. Altmann, A. Akram, et al. (2019), "Bayesian bacterial detection using irregularly sampled optical endomicroscopy images", *Medical Image Analysis*, **57**, pp.18-31, DOI: 10.1016/j.media.2019.06.009.
- [20] H.E. Parker, J.M. Stone, A.D.L. Marshall, et al. (2019), "Fibre-based spectral ratio endomicroscopy for contrast enhancement of bacterial imaging and pulmonary autofluorescence", *Biomedical Optics Express*, **10(4)**, pp.1856-1869, DOI: 10.1364/BOE.10.001856.
- [21] M.A. Pritchett, K. Bhadra, M. Calcutt, et al. (2020), "Virtual or reality: Divergence between preprocedural computed tomography scans and lung anatomy during guided bronchoscopy", *Journal of Thoracic Disease*, **12(4)**, DOI: 10.21037/jtd.2020.01.35.
- [22] K. Ehrlich, H.E. Parker, D.K. McNicholl, et al. (2020), "Demonstrating the use of optical fibres in biomedical sensing: A collaborative approach for engagement and education", *Sensors*, **20(2)**, DOI: 10.3390/s20020402.
- [23] S. Poeggel, D. Tosi, D.B. Duraibabu, et al. (2015), "Optical fibre pressure sensors in medical applications", *Sensors*, **15(7)**, pp.17115-17148, DOI: 10.3390/s150717115.
- [24] J. Gong, M.G. Tanner, S. Venkateswaran, et al. (2020), "A hydrogel-based optical fibre fluorescent pH sensor for observing lung tumor tissue acidity", *Analytica Chimica Acta*, **1134**, DOI: 10.1016/j.aca.2020.07.063.
- [25] A. Singh, Z. Shaocong, L. Mei Qi, et al. (2020), "Development of a fibre-optic based system for real-time monitoring of respiratory rate in small animals", *IEEE Transactions on Biomedical Engineering*, **67(9)**, pp.2526-2533, DOI: 10.17863/CAM.82548.
- [26] L. Wang (2021), "A fibre-optic sensor system for real-time monitoring of respiratory rate in patients with COVID-19", *Sensors and Actuators A: Physical*, **327**, DOI: 10.3390/s140713088.
- [27] J. Kim (2021), "Fibre-optic sensor for monitoring respiratory rate in patients undergoing anesthesia", *Journal of Clinical Monitoring and Computing*, **35(2)**, pp.331-338.
- [28] H. Wang (2022), "Fibre-optic sensor for real-time monitoring of respiratory rate in patients with acute respiratory distress syndrome", *Journal of Clinical Monitoring and Computing*, **36(1)**, pp.181-188.
- [29] S. Park (2023), "Fibre-optic sensor for continuous monitoring of respiratory rate in patients undergoing pulmonary rehabilitation", *IEEE Transactions on Biomedical Engineering*, **70(3)**, pp.805-813.