Commentary

Optical Mapping Methods for Treating Cancer in Low- and Middle-Income Countries like India

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Abstract

Cancer presents substantial challenges globally, particularly in low- and middle-income countries (LMICs) such as India, where resources are limited. This study explores the potential of optical imaging technologies for cancer diagnosis in low-resource settings (LRS) within India. It assesses the benefits, prospects, and obstacles associated with their adoption. Optical imaging offers advantages including non-invasiveness, automated diagnosis, and cost-effectiveness; however, its widespread implementation faces constraints such as high initial costs, inadequate infrastructure, a shortage of skilled personnel, and integration challenges with existing healthcare systems. Addressing these challenges necessitates strategies involving capital investments, skill enhancement, and infrastructure development. Affordable and user-friendly optical imaging systems tailored for LRS have been developed, and the application of artificial intelligence (AI) shows promise for improving cancer diagnosis in LMICs like India. This study reviews the latest advancements in optical imaging technology and underscores the need for further research and collaboration to enhance cancer treatment in India and other LMICs.

Keywords: Optical imaging, Cancer treatment, Fluorescence imaging, Bioluminescence imaging, Raman spectroscopy, Optical coherence tomography, Cancer surgery, Treatment monitoring

Introduction

Cancer is a significant global issue, particularly affecting individuals in low- and middle-income countries (LMICs) such as India. As the incidence rate of malignancies in LMICs rises, it's crucial to develop early detection and screening programs for better treatment and prognosis.[1,2]. Insufficient infrastructure and lack of trained personnel hinder cancer screening and early detection initiatives, especially in LRS. This leads to late-stage diagnosis, ineffective interventions, and care continuity loss. Optical imaging, with its real-time imaging capabilities, noninvasiveness, automated diagnostic performance, and cost-effectiveness, has emerged as a promising tool for cancer detection and diagnosis.[3]. Optical imaging in low-resource regions (LRS) faces challenges such as high upfront costs, inadequate infrastructure, shortage of experienced personnel, technical support, maintenance requirements, data management issues, and integration difficulties with existing healthcare systems. To overcome these obstacles, a multidimensional approach involving capital expenditures, skills creation, infrastructure development, and coordination with key parties is needed. Recent developments in optical imaging systems for LRS offer low-cost, high-quality, and

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user-friendly features, aiming to provide accurate cancer diagnosis while overcoming resource, infrastructural, and fiscal constraints. Combining artificial intelligence with optical imaging modalities opens new opportunities for global cancer detection. In low-resource regions, affordable, battery-powered alternatives have been developed to minimize expenses and infrastructure requirements. Automated algorithms may become less important in the future, making expertise less important. This research investigates current breakthroughs in low-cost optical imaging technologies for cancer detection in LRS, highlighting the benefits, possibilities, and challenges that still need to be addressed.

LITERATURE REVIEW

- Zhang et al. (2020) [4] reviewed that Hyper spectral imaging (HSI) is a non-invasive technology that uses spectroscopy and conventional imaging to gather spectral and spatial information from tissues. It assumes that individual tissues have discrete spectral fingerprints, which differentiate between normal and cancerous tissues. HSI offers label-free histological examination and real-time intraoperative assistance, making it a promising tool for tumor diagnosis and detection.
- Sung et al. (2021b) [2] evaluated the International Agency for Research on Cancer's GLOBOCAN 2020 forecasts show that around 10.0 million cancer deaths and 19.3 million new cases occurred worldwide in 2020. Female breast cancer has surpassed lung cancer as the most commonly diagnosed malignancy, with 2.3 million new cases. Lung cancer remains the most frequent cancer, with 1.8 million deaths (18%). Other common causes include colorectal, liver, stomach, and female breast cancers. In transitioned versus transitional nations, total incidence was two to three times greater for both sexes, but mortality varied by less than two fold for males and scarcely altered for women. Transitional nations exhibited higher mortality rates from female breast and cervical cancers. The worldwide cancer burden is expected to reach 28.4 million cases in 2040, a 47% increase from 2020, possibly worsened by increased risk factors linked to globalization and a developing economy.
- Pierce and Richards-Kortum (2010b) [3] reviewed that cancer incidence and death rates are increasing globally, with emerging nations bearing a higher burden. Optical diagnostic methods like diffuse optical tomography, wide-field auto fluorescence imaging, co focal microscopy, and optical coherence tomography are being explored for early cancer detection. However, their primary application is in developed countries' medical institutions. Researchers have developed low-cost, portable versions of these devices using early clinical tests.
- Shao et al. (2022) [5] demonstrated that traditional diagnostic techniques often lead to over diagnosis of thyroid nodules, which is the primary cause of thyroid cancer. Treatment options for a plastic thyroid carcinoma are limited to surgery and 131I radiation therapy, both of which have severe side effects. Optical imaging, using features like absorption, refraction, and scattering, could accurately and non-invasively treat thyroid cancer by examining the structure and function of cells, tissues, organs, or the entire body. While the potential of optical imaging in thyroid cancer surgical navigation is significant, further research is needed.
- Xia et al. (2021) [6] showed that optical coherence tomography (OCT) is a non-invasive, high-resolution imaging technology with a penetration depth of 1-2 mm and a resolution of 1-10 μm. It is extensively utilized in ophthalmology, but it may also be employed in many other medical areas, including cancer. OCT has been proved to be a valuable method for identifying gastrointestinal, prostate, breast, skin, and oral malignancies. It offers the benefit of being able to acquire high-resolution, cross-sectional pictures of tissues in real time without the requirement for sample fixation or preparation. Additionally, it may be used with other optical imaging modalities, such as fluorescence, to offer extra information for cancer diagnosis.

- Sinha et al. (2021) [7] stated that near-infrared (NIR) fluorescence imaging is a promising tool for cancer diagnosis and treatment due to its ability to penetrate tissue with greater penetration and less scattering. It has been used for intraoperative guidance during cancer surgery, non-invasive tumor identification, and characterization. NIR fluorescence imaging can also be combined with other imaging modalities like PET and MRI for more accurate cancer diagnosis and staging. Various NIR fluorophores have been developed to target specific cancer biomarkers or physiological processes.
- Al Rawashdeh et al. (2021) [8] showed that surface-enhanced Raman spectroscopy (SERS) is a promising method for cancer detection and diagnosis. It uses the Raman scattering signals from molecules on nanostructured metallic surfaces to detect biomolecules associated with cancer. SERS-based approaches have been developed for identifying cancer biomarkers in biological samples, with excellent sensitivity and specificity. SERS offers quick, label-free, and non-destructive cancer biomarker detection at the point of care, and can be combined with other diagnostic methods for more accurate cancer detection and staging.

OPTICAL MAPPING TECHNIQUES FOR THE DETECTION OF CANCER

Macroscopic Imaging

Macroscopic optical imaging uses light at multiple wavelengths to illuminate target regions beyond a few centimeters, providing real-time, non-invasive monitoring of tissue characteristics across a vast area, providing a complete picture of the questionable area [6]. The science of macroscopic imaging has evolved enormously thanks to important developments. With better imaging capabilities, macroscopic imaging modalities have become more accessible and may allow for more inexpensive imaging procedures. Furthermore, the interpretation of macroscopic photographs has been done utilizing DL approaches, which has the potential to boost diagnostic performance and minimize dependence on human interpretation [7]. Multimodal macroscopic imaging, which combines auto fluorescence imaging (AFI), multispectral imaging (MSI), and narrow-band imaging (NBI), has improved diagnostic accuracy and imaging capabilities, potentially providing more comprehensive tissue assessments [6]. Macroscopic imaging has proven useful in resource-constrained contexts, particularly in early cancer diagnosis in low-resource settings (LRS). The global burden of various cancers can be treated using optical imaging, and the limitations in early diagnosis impact patient therapy. Design parameters for optical imaging technologies are highlighted, and the potential for early cancer detection in LRS when combined with computer-aided diagnostics is highlighted. Biomedical Imaging focuses on real-time image processing, AI integration, multimodal imaging, low-cost and portable devices, and imaging in rural and low-cost areas.

White Light Imaging

White light imaging (WLI) has become more accessible and affordable due to advancements in optics, sensors, and Smartphone cameras. WLI offers improved picture quality from less costly imaging equipment, such as digital colposcopy. In the past, clinicians used standard-of-care exams with colposcopes and film cervicograms. However, recent developments in optics and camera sensors have led to the development of affordable, digital, portable colposcopes. A study in Peru found that Pocket Colposcopes perform similarly in identifying precancerous and cancerous cervical lesions [8].

The advancement of technology in LRS is largely driven by the ability to obtain high-quality digital pictures, enabling new methods for image interpretation through telemedicine or machine learning. A study in India validated a portable colposcope called Gynocular, which accurately diagnosed precancerous lesions by reviewing 495 pictures from 94 patients in real time and individually [9]. The use of digital image acquisition (DL) in real-time cancer detection has made it feasible, especially in point-of-care systems. However, the interpretation of these photos still requires experience. DL can minimize the need for clinical expertise. An automated algorithm, MobileODT, was developed using digital colposcopy pictures and digitized cervicograms. This algorithm was trained, confirmed, and tested using data from 9462 women in five independent studies [10]. The top-performing algorithm for cervical image classification demonstrated repeatable and reliable results for the target group, and a similar method was used to create a Smartphone endoscope and DL algorithm for identifying cervical lesions [11]. A study of 20 patients demonstrated that a simple Smartphone endoscope can effectively screen for cervical cancer in low-resource settings, confirming its potential.

Multispectral and Multimodal Macroscopic Imaging

MSI, AFI, and NBI have superior imaging capabilities compared to WLI, providing more data on tissue features and highlighting relevant qualities like vascularization, reduced auto fluorescence, and increased optical scattering. Integrating data from multiple imaging modalities can enhance clinical diagnosis and decision-making [12]. In a number of clinical scenarios, this multimodal technique has the potential to greatly enhance cancer diagnosis, biopsy guidance, and treatment decision-making. Filters and diffraction grating components are examples of specialized optics required for spectrum scanning activities, and MSI usually requires huge, bulky gear. Developments in electronics and optics, such as the swift rise of Smartphone technology, have made it feasible to proceed toward integration into platforms that are suited to point-of-care. Multiple Smartphone systems have implemented MSI, highlighting its promise for low-resource applications [13-17]. Oral Scan is a low-cost commercial technology that employs MSI and was tested in India to screen for and diagnose oral cancers. The analysis of this MSI device suggests that it has the potential to be applied as an adjuvant in LRS for biopsy guiding and lesion assessment [12].

Microscopic Imaging

The ability for real-time, non-invasive, exact point-of-care diagnostics has been established by the merging of computer-aided algorithms with in vivo microscopy (IVM). This method may be able to overcome a variety of difficulties with standard-of-care histology, which are particularly critical in LRS. These challenges include increased expenses, patient risk from invasive biopsies, erroneous diagnosis from simply looking at limited portions of suspected lesions, and large infrastructure and skill needs [18]. Three current projects that encourage the usage of IVM in LRS are highlighted:

- employing computer-aided techniques to increase imaging capabilities and facilitate the interpretation of clinical data;
- developing technological design to improve system portability and decrease costs, as well as field deployment for clinical performance assessment in LRS;
- the inclusion of multimodal, multiscale imaging to boost diagnostic potential. This section reviews and discusses key advancements in several areas of in vivo microscopic imaging with the objective of advancing LRS cancer screening, diagnosis, and therapy. Although the major emphasis of this review is on in vivo imaging methods, it is interesting to highlight the recent breakthroughs in ex vivo imaging techniques for histopathology, including artificial intelligence-based analysis and digital pathology [19].

Cathepsin Imaging

Cancer cells release more protease cathepsin than do healthy cells. It is thought that tumors activate cathepsins, altering the tumor microenvironment and facilitating the development and spread of cancer. For cathepsin-based cancer imaging, two medications—LUM015 from Lumicell and VGT-309 from Vergent—are undergoing clinical trials. Cathepsins activate the imaging probe LUM015 when they are present. Because it is Cy5-labeled, FI in vivo can assess tumor margins during surgery by using the Lumicell LUM Imaging System (Wellesley, MA, USA). Smith et al. (2018) [20] looked at the usage of LUM015 in breast cancer patients in a phase 1 study. It was shown to split tumors as expected and to be devoid of risks [20]. Breast density had no effect on the outcomes, and the tumor could be distinguished from normal tissue in both premenopausal and postmenopausal women. Owing to the favorable pharmacokinetics and biodistribution found, sarcoma and breast cancer clinical studies are underway.

Matrix metalloproteinase (MMP) Imaging

Extracellular matrix proteins are broken down by proteins called MMPs during normal tissue remodeling. They are secreted in an inactive form and then activated by extracellular proteases. These proteins—more especially, MMP-3—are thought to play a part in the growth of malignancies. MMP-3 activity is increased in several cancer types. To scan breast and other malignancies, AVB-620, a protease-activatable fluorescence imaging agent, was developed. When AVB620 is tagged with Cy5 and Cy7, it may be located using fluorescence detection [21]. Tissue retention and a ratiometric fluorescence color shift result from MMP hydrolyzing AVB-620; these effects may be seen with simultaneous recording of fluorescence and white light using camera systems. Through an ex vivo study, Miampamba et al. (2017) [21] examined the biological activity of this drug in human malignancies. Following homogenization and incubation with AVB-620, fluorogenic responses were assessed between the patient's tumor tissue and nearby healthy breast tissue. Tumor tissue dissolved two to three times faster than similar healthy breast tissue, resulting in a test with a 96% sensitivity and an 88% specificity.Phase 1/2 human studies are now being conducted on 22 AVB-620.

Fluorescent Nanoparticle Imaging

Various techniques have been developed to accurately identify cancer-invaded lymph nodes. These include cancer imaging probes using ultrasmall inorganic nanoparticles to target tumors. Elucida Oncology's C-Dots, tagged with Cy5.5 for fluorescence detection, have been used in phase 2 studies for malignant lymph node identification in head and neck and breast cancer.[22].

Chlorotoxin (CTX)-based Agents

Clinical trials are underway on peptide conjugates made from the scorpion Leiurus quinquestriatus venom, which have intrinsic tumor-binding capabilities and can attach to solid tumors and cancers, including gliomas, with BLZ-100 being one such compound that fluoresces in response to intracellular calcium [23]. Baik et al. (2016) [23] have discussed the preclinical testing of this medication in the diagnosis of head and neck squamous cell carcinoma (HNSCC). In xenografts, BLZ-100 proved to be an effective marker of HNSCC that was both sensitive and specific, allowing for the distinction between high-risk and low-risk dysplasia.24 Testing on humans is how BLZ-100 is being developed.

Fluorescent Antibody-based Imaging

The use of many cell-surface tumor markers has substantially aided in the pathologic identification of solid tumors. The following have shown to be the most important among them:

- Prostate-specific carcinoembryonic antigen (CEA) for colorectal, stomach, lung, and breast malignancies
- prostate cancer membrane antigen (PSMA) and ovarian cancer cancer antigen (CA125).
- Specific antibodies with high affinity have been developed and used in the area of diagnostic imaging for cancers like these.

68Ga-PSMA antibody PET scanning26 and 124I-CEA antibody PET scanning p25 are promising clinical imaging modalities. Fluorophores are being used to identify these antibodies, which are being proposed for use in surgeries and procedures. Additional antibodies targeting PSMA, including Tag-72, are also being studied.

CHALLENGES AND FUTURE DIRECTIONS

The effective use of optical imaging equipment for cancer diagnosis in low-resource settings (LRS) requires the resolution of many challenges. These challenges include:

Table 1: Challenges and Solutions for Implementing Optical Mapping Methods for Treating Cancer in Low-Resource Settings (LRS)

Cost	Optical imaging systems are challenging to implement in LRSs with limited resources due to their high initial costs	*Example:* OralScan Assessment: OralScan is a feasible alternative for LRS since it is reasonably priced in comparison to other optical imaging systems.
Skilled Staff	A primary barrier to a successful cancer diagnosis in LRS is the scarcity of skilled personnel trained in optical imaging methods.	*Example:* OralScan Assessment: By lowering the need for specialized training, paramedics and other healthcare professionals may utilize OralScan with little to no training.
Infrastructure	Lack of infrastructure and technical support impedes the implementation of optical imaging technology in LRS.	*Example:* OralScan Assessment: OralScan is appropriate for LRS with limited healthcare infrastructure since it needs nothing in the way of infrastructure improvements.
Connectivity and Data Management	Issues with data communication and administration are impeding the effectiveness of optical imaging integration with the current healthcare systems in LRS.	*Example:* OralScan Assessment: Despite connection issues, OralScan allows digital data exchange and storage, making it easier to integrate with current healthcare systems.
Integration Obstacles	Optical imaging technology must be integrated with the existing healthcare systems in LRS by overcoming administrative and technical challenges.	*Example:* OralScan Assessment: Because of its versatility and user-friendly interface, OralScan may more easily be integrated with modern healthcare procedures, overcoming both administrative and technological challenges.

Conclusion

Optical imaging technologies hold great promise for cancer diagnosis in low- and middle-income countries (LMICs) like India due to their non-invasive, real-time imaging capabilities and flexibility. However, they face challenges such as high upfront costs, lack of infrastructure, and integration issues with existing healthcare systems. To develop and deploy affordable, user-friendly optical imaging technologies, governments, academic institutions, and industry partners must collaborate. Capacity-building initiatives are essential for successful implementation and long-term viability. Collaborative research efforts from engineering, medicine, and public health teams are crucial for improving cancer therapy in LMICs and advancing the science of optical imaging. Overall, optical imaging technologies hold great promise for improving cancer diagnosis and detection, potentially leading to improved patient outcomes and a decrease in the global cancer burden.

Ethical Clearance: NA as no live subjects are present

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