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Title	The impact of light based technologies in the future of healthcare
Authors	Saito Nogueira, Marcelo
Publication date	2022
Original Citation	Saito Nogueira, M. (2022) 'The impact of light based technologies in the future of healthcare', The Boolean: Snapshots of Doctoral Research at University College Cork, 6, pp. 33-39. doi: 10.33178/boolean.2022.1.6
Type of publication	Article (peer-reviewed)
Link to publisher's version	https://journals.ucc.ie/index.php/boolean/article/view/boolean-2022-7 - 10.33178/boolean.2022.1.6
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Item downloaded from	https://hdl.handle.net/10468/14674

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The Impact of Light Based Technologies in the Future of Healthcare

Perspectives on Research, Clinical Translation and Education

Marcelo Saito Nogueira[1,*]

[1] *Tyndall National Institute, University College Cork, Cork, Ireland*
[*] *Corresponding author: m.s.nogueira@umail.ucc.ie*

Abstract

There has been an increasing interest in light-based technologies offering cheap, fast and non-invasive disease detection and treatment. In 2016, the market of light-based technologies represented >64% of the total medical imaging market ($ 90.7 billion in total) and more than twice the radiological imaging market that included X-Ray, ultrasound, magnetic resonant imaging and others. Light-based technologies have steadily increased with the mobile and home healthcare, as well as wearable devices dominating the market to monitor quality of sleep, sports performance, and blood oxygenation in general (including COVID-19 cases). Given the importance of light in the future of healthcare, this paper covers how light-based technologies are used to find diseases early (screening) and accurately (diagnostics) in both whole body (systemically with screening tests) or localized parts of the body (during surgery).

Keywords: biophotonics, screening, diagnostics, clinical translation, education, research.

Advances and challenges in disease detection and treatment

In recent years, advances in medical devices have substantially improved disease detection and treatment by providing tools to both doctors and patients worldwide. These tools allow doctors to monitor the risk of a patient developing a disease and help locate diseased tissues in the body such as cancer. On the patient side, implantable devices such as pacemakers, valves, stents, drug-delivery systems, and joint replacements have increased the treatment options available. The current bottleneck in disease detection and treatment relies on timely and accurate disease identification to improve treatment planning and subsequently patient outcome.

To provide timely and accurate disease identification, the next global challenge for the MedTech industry is making medical devices which can predict diseases earlier and can benefit both patients and clinicians / doctors. For example, a high-risk colorectal cancer (CRC)

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patient may not know he/she has cancer if early-stage lesions are overlooked by endoscopists (clinicians) through conventional colonoscopy (standard procedure to look for CRC). Similarly, overlooked cancer cells may be left in the individual's body after surgery. A medical device is useful to both endoscopists and patients only if such a device enables accurate and early CRC detection while making colonoscopy sufficiently non-invasive to foster patient compliance with early and frequent colonoscopies. Currently, lack of patient compliance and non-timely cancer detection deteriorate patients' quality of life, and steadily increase mortality rates worldwide. For context, CRC survival rates are 94.8% for CRC stage I (early stage), and 11.6% for CRC stage IV (late stage). Also, an estimated 16% of patients with submucosally invasive colorectal carcinoma (a deadly type of CRC) and risk factors benefited from surgery. That means that surgery may result in cancer recurrence in a staggering 84% of cases despite being life-changing and costly ($\sim$40000 Euro) for a patient. If cancer recurs, so does patient expenses. Therefore, earlier CRC detection could make a significant impact. One of the most promising approaches for timely and accurate disease identification is using light-based technologies. In this paper, I explain how advances in these technologies can impact the healthcare system, patients' lives, the MedTech industry and education worldwide.

Screening: the way to find diseases early

The challenges related to the timely identification of diseases are mainly associated with finding specific disease biomarkers with relatively cheap, fast and non-/minimally-invasive technologies. This identification typically requires patients to go through screening tests once they are considered to be at high-risk of developing a disease. For example, the key to find colorectal cancer early is to start regular screening at the age of 45, and at the age of 20 for oral cancer. However, non-genetic biomarkers used in screening tests are typically not particular to certain diseases and tend to misclassify patients as high-risk, even when patients are under low risk to a certain disease. This misclassification is called a false positive.

Light-based technologies have been investigated to look for more specific biomarkers within biofluids (body fluids such as blood or urine) to decrease the number of misclassifications and false positives. These technologies do not require time-consuming biochemical analysis such as those used to obtain genetic information. Fast and non-invasive screening can be performed by finding chemicals in saliva and urine, for instance. Saliva and urine collection does not cause discomfort to the patient as it might be caused during blood collection. Thus, the compliance to screening may increase, allowing us to find diseases at early stages. Collection can be quick because only a small amount (a few microliters) of saliva or urine is needed, and it can be analysed directly with no mixing with other chemicals required. The analysis can be automated through machine learning algorithms (teaching devices how to identify samples) so that equipment operators are not needed to provide a result to the patient, reducing the cost and time constraints of analysis. For light-based technologies to be commercialized, a large quantity of data needs to be collected from the biofluids of thousands of people often collected

through many years of research. If all this data is collected by using standard protocols possible to be followed globally including in low-resource settings, light-based technologies can impact disease screening globally. One example of research contributing to this data collection is our oral cancer study conducted by Biophotonics@Tyndall and Cork University Hospital (CUH), which aims to find cancer patients by analysing their saliva.

Diagnostics: the way to find and identify diseases more accurately

Once patients are considered high-risk by screening-test results, they go through surveillance involving procedures to look for diseases more accurately. If these procedures require directly looking at structures of internal organs, they are minimally invasive, and may cause inconveniences to patients who do not have support from family and friends during the preparation for those procedures. For example, the gold standard screening and diagnostic procedure to find colorectal cancer is called colonoscopy. Colonoscopy involves visualising the inner colon and rectum mucosa directly with an endoscope inserted into the large bowel. Colonoscopy is a very safe procedure but poses significant inconveniences for patients due to the need to be accompanied home after sedation and the logistics of bowel preparation prior to colonoscopy.[5,6] These inconveniences are considered the reason many patients do not comply with regular surveillance. Also, even though colonoscopy is accurate in most cases, finding flat lesions and lesions which develop in times between two colonoscopies is difficult. Therefore, flat lesions can be overlooked and lesions which develop right after one colonoscopy may be found as late-stage cancers in the next colonoscopy, especially if patients do not comply with regular colonoscopies. This results in colorectal cancer (CRC) being the third most common and the second most deadly type of cancer worldwide.[5,6]

Currently, the accuracy of colonoscopy and other conventional medical procedures such as X-Ray imaging and computed tomography (CT) are limited to finding diseases only at relatively late stages, when the structure of biological tissues changes. For example, the most accurate way of finding CRC is by removing parts of visually abnormal biological tissues (biopsy) during colonoscopy and sending them for structural analysis under the microscope (histopathological analysis). This analysis investigates the cell types, as well as the shapes, sizes and distribution of cells and their nuclei. Still, these structural changes may take years to appear. Changes potentially leading to CRC start much earlier than that with predisposition of cells to cancer as their DNA mutates (local genetic changes), and subsequently, this triggers responses from our immune system (immunologic changes) and changes in the chemical reactions which keep us alive (metabolic changes). None of the current conventional medical technologies can find cancer-associated immunologic and metabolic changes.

Light-based technologies can potentially look into CRC at early stages due to their capability of finding changes in tissue biochemistry and structure in real-time, giving us an insight

into the metabolic and immunologic changes which may be happening in our tissues. This capability can make colonoscopy and other types of endoscopies (procedures to look inside our body directly) much more accurate, by allowing them to find and identify diseases, as information on tissue biochemistry tends to be more specific to early-stage diseases and structural information may be biomarkers for both early- and late-stage diseases. Introducing light-based technologies into colonoscopy can be done as miniaturized systems are integrated into medical devices by photonic integration experts such as those working at the Irish Photonic Integration Centre (IPIC) in facilities available at places such as Tyndall National Institute. This expertise supports our team at Biophotonics@Tyndall to develop a non-invasive tool for accurate and early CRC detection and to complete removal of CRC during surgery.

Surgical guidance: the way to treat diseases with less patient post-surgery complications

The capability of monitoring tissue biochemistry and structure by using light-based technologies allows them to be used for precise tissue identification during surgery. In endoscopies and robotic surgeries, clinicians are unable to identify tissues by palpating them to feel their hardness, roughness, or other properties based on tactile sensations. Therefore, clinicians rely on tools to guide them by showing tissues to be removed and tissue not to be removed in real-time, especially given that the surgery time is constrained by the time the patient is sedated or anesthetised, bleeding times, etc. For instance, microsurgeries can be performed during colonoscopies if cancer is found at a sufficiently early stage. Early-stage cancer lesions should be small enough to be removed with minimal chance of complications after colonoscopy. However, finding and assessing the margins of these lesions can be difficult. Since a typical colonoscopy takes 30-60 minutes and structural (histopathological) analysis of a lesion biopsy takes from several hours to a day, delineating the margins requires tools to identify tissues more specifically in real time. Light-based technologies can be used for this tissue identification in the same way they could be used for diagnostic purposes. Since many light-based technologies are non-invasive, normal tissue can be spared as much as possible. Sparing normal tissue is important in rectal cancer surgery and head and neck surgery, for example, where many important structures are potentially located close to the cancer. Similarly, light-based technologies can be used to identify important nerves and blood vessels which should not be removed during surgery.

How can light be used to extract structural and (bio)chemical information from biological tissues?

By eliminating the reflection of light at the tissue surface and quantifying only the intensity of light which travelled within it, one can observe how much light is absorbed, scattered, and converted into other types of light within such tissue. Light scattering is associated with tissue

structure, whereas absorption and conversion of light into light of other colours is related to tissue biochemistry. Still, since light absorption and scattering define how much it penetrates biological tissues, light penetration in them is typically shallow. Light-based technologies can monitor tissue biochemical and structural features from micrometres to a few centimetres, depending on light colour, illumination and detection locations and angles. If we use colours of light to which biological tissues are more transparent to light and increase the distance between where we shine light on their surface and where we collect the light, we can measure light deeper in tissues. This is the principle we have used to design the biophotonics tools for our CRC studies.[5,6] Our tool uses the intensity of reflected light to both sense and classify biological tissues more precisely and quickly compared to conventional methods.

What have we done in our CRC study?

In our feasibility study in tissues freshly removed from patients' bodies (ex vivo tissues), we could classify normal and cancer tissues with 96% accuracy. By estimating the tissue biochemical concentrations and structural parameters, we found that accurate classification is primarily due to the difference in the amount of lipids, the number of small structures compared to larger structures, and the average size of larger structures. Also, we have investigated instrument specifications and machine learning methods for accurate tissue identification. These specifications included the collection of a larger range of light colours and probe geometry, which enabled the study of superficial and deeper tissues, as well as a larger variety of tissue microstructures and biochemical constituents of such tissues. To identify tissues in real-time, a robust machine learning model was built based on a database of 7.5 times more data compared to previous studies. Robust and accurate tissue identification enable CRC to be detected earlier and to be fully treated in less procedures, resulting in reduced risk to the patient and number of cancer surgeries. The developed biophotonics technology can be cost-effective and integrated into existing medical tools. The best instrument specifications found could potentially be used to develop a probe for real-time (2-3s per reading) CRC detection during colonoscopy with 96% accuracy.

What are the societal impacts and future of our CRC study?

Following on from the validation of our feasibility study using tissues removed from patients (ex vivo tissues), our next step is performing a similar study on tissues of patients directly (in vivo tissues). If in vivo tissues can also be classified with high accuracy, more data can be collected to build a robust machine learning model capable of accurate tissue classification in a variety of settings including patients with many different conditions, different procedures, and others. Collecting a large amount of data means fostering partnerships/collaborations between research institutes (Academia), companies (Business) and medical institutions (Clinical), whilst also considering the opinions of patients when designing the technology and medical devices (Design), following the ABCD model (Academia, Business, Clinical and Design). This

collaboration can accelerate the clinical translation of light-based technologies. Developed research resources such as instruments and data analysis methods which can be used for multiple applications including identifying tissues and assessing their function or impairment in multiple types of endoscopies, surgeries, screening many types of diseases in humans, animals, and plants. Applications can be as extensive as monitoring sports performance, sleep quality, and other diseases by using wearables, monitoring the effectiveness of treatments, performing quality control of industrial or natural products, to name a few. Finally, the research resources used for our CRC study can be used for education of the next-generation of biophotonics professionals including undergraduate students, secondary-school students, as well as increase the public awareness of medical light-based technologies during outreach events.

How does work our Biophotonics work impacts the Sustainable Development Goals (SDG) set by the United Nations?

The most obvious SDGs impacted by clinical Biophotonics work which can impact the MedTech industry and patients' lives are Goals 3 (Targets 3.4, Indicator 3.4.1), 9 (target 9.5) and 17 (Targets 17.6). As light-based technologies can be used with no contrast agents, there is a reduction of chemical waste disposed in the environment compared to conventional medical procedures and /or experiments/demonstrations to school students and general public. Promoting research and commercialization of light-based technologies aligns with SDG targets 6.3, 11.6, 12.5, 17.7 by fostering the development, dissemination and diffusion of environmentally sound technologies which can improve water quality by reducing pollution and chemical waste. By actively promoting content to the community, more people can be aware of environmentally friendly light-based technologies. Resources of the aforementioned oral cancer and CRC research were also adapted for education in inclusive approaches targeting secondary-school, undergraduate and post-graduate students,[1–4] aligning with SDG targets 4.3, 4.4, 4.5, 10.2 and 17.6.

Acknowledgements

The author declares no conflicts of interest. The colorectal cancer and oral cancer studies mentioned in this paper received financial support from Science Foundation Ireland (SFI): grant ID SFI/15/RP/2828 and education research received funding from SFI 12/RC/2276. All ethical guidelines relating to the research and publication process were adhered to throughout.

Further Reading

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