

# The Role of Digital Biomarkers in Cancer Research and Patient Care

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## ABSTRACT

Classical biomarkers have been traditionally used to evaluate changes in the homeostasis of the human body. With the emergence of digital technologies, new opportunities have come up to continuously monitor patients during the course of illness and therapy. Improved computational methods have enabled researchers to track and analyze patient's health related data. While previous works have focused on the role of digital biomarkers in cardiovascular and neurological diseases, we aim to address the role of digital biomarkers in cancer research. Therefore, we provide a comprehensive review on the use of digital biomarkers in clinical trials and patient care, regulatory environment and future directions in this promising field.

**Abbreviations:** EMR: Electronic Medical Record; FDA: Food and Drug Administration; SaMD: Software as a medical device; SiMD: Software in a Medical Device

## Introduction

The impact of digital technologies on clinical trials and patient care is rising [1]. As in many other fields the major drivers for the wide adoption of digital technologies in health care are quick scalability and constantly decreasing costs [2]. In addition, this development is supported by improving computational power and new approaches to analyze great amounts of data by machine learning [3]. Biomarkers have traditionally been characterized as single time point assessments used to generate objectively measurable indicators of physiological changes of the human body. Biomarkers are currently employed in clinical trials [4] and influence clinical decision making [5]. Digital biomarkers are a emerging class of biomarkers that source their data from digital sensors or computational tools [6]. They can be composed of multiple hardware and software components and allow a continuous and remote assessment of patients [7]. So far, the impact of digital biomarkers on cancer research has not been intensively studied. Therefore we aim to provide an overview of the most important developments, regulatory burdens and future directions of digital biomarkers.

## FDA Regulation

Digital biomarkers are regulated by the Food and Drug Administration (FDA) under the device section [8]. The FDA has undertaken significant efforts to deal with the upcoming new categories of medical devices and drugs aimed to track patient's health and disease. Traditionally, software was considered to be part of a hardware component and was classified as Software in a medical device (SiMD). But in light of the new technological developments, software can stand alone and is termed Software as a medical device (SaMD). To speed up market entry for new software the FDA has created a "precertification program". Therefore, rather than seeking for approval by the FDA, companies can register every new software or software update and undergo a precertification process to quickly release software and updates on a regular base. Amongst those companies are major tech corporations as Apple, Fitbit, Samsung and Verily, but also pharmaceutical companies as Johnson & Johnson and Roche as well as Tidepool, Pear Therapeutics and Phosphorus [9].

## Current Digital Biomarker Landscape in Cancer Research and Patient Care

Digital biomarkers can be generated from various sources like body sensors, image processing or from health platforms and electronic medical records (EMR). The use of wearable body sensors, termed wearables, is not only widespread in healthy people, but is also increasingly employed in cancer trials to track the physical activity, vital parameters and sleeping profiles [10]. In fact, wearables play an important role in oncology as they allow physicians to track their patients in a real world setting. So far, most clinical trials assessing activity have focused on breast and lung cancer patients [11]. Recently, it could be demonstrated that wearables can predicted performance scores in patients with advanced malignancies [12]. Ingestible sensors on the other hand aim to transmit time medication was taken as well as data on physiological changes of the digestive system. They can potentially be used to control therapy adherence and although they have not entered clinical routine in oncology first trials are ongoing [13].

Image processing and analysis performed by advanced analytic tools such as machine learning can also generate innovative digital biomarkers. In radiology, for instance, image recognition, followed by analysis is currently changing clinical routine in areas such as stroke diagnostics [14]. Further, first attempts are being undertaken in breast cancer screening using mammography images [15]. In pathology new biomarkers are being tested to determine the PD-L1 expression in cancer tissue [16]. In dermatology cancer diagnostics rely mostly on the morphology of lesions detected by dermatologists. However, a newly developed neuronal network can predict the malignancy potential of skin lesions more efficiently than trained dermatologists [17].

Health platforms and electronic medical records are the third important source for digital biomarkers. However, a major obstacle to access and analyze data from medical records is that this data is mostly not electronically accessible. The company Flatiron Health for instance has overcome this hurdle by capturing structured and unstructured medical data from oncologic patients. This method is able to generate predictive scores from electronic health record [18].

## Discussion

Digital biomarkers are currently changing cancer research and start to get adopted in clinical decision-making. They can derive from body sensors, image processing or health platforms and electronic records and will have a substantial impact on clinical trials and patient management. Remote control of patients seems to be an interesting feature with wearables. In this case, biomarkers will not be limited to single-point measurements as traditionally performed during hospital visits, but will provide continuous measurements. Validation of biomarkers that rely on algorithms created by machine learning will remain a challenge. Since they can rely on a so called "blackbox" approach it is unclear what data the algorithms actually analyzes [19]. In addition, transferring biomarkers tested in certain subgroups to normal patient collectives can lead to wrong results.

As in traditional trials the information an algorithm generates from a training cohort is not necessarily true for the average patient population. Machine learning based biomarkers are trained by a training set of data, but the data can be biased as well and thereby the biomarker [20]. Therefore, a continuous validation process and post marketing studies might be required rather than a single time point validation.

## Conclusion

The impact of digital biomarkers on cancer research and patient care is rising. However, novel technologies require new validation methods and regulatory burdens remain an issue that has to be addressed thoroughly by the approval authorities. Potentially, digital biomarkers will deliver more accurate diagnostic and prognostic markers for cancer patients. This will be possible alongside with costs reduction for the healthcare system and increasing access of patients to a high quality of care.

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