Tumour Heterogeneity Profiling and Molecular Subtype Classification: AI-Enhanced Systems for Precision Oncology Drug Development Personalisation

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1. Introduction to Personalized Cancer Drug Development

Cancer drug development and treatment strategies have undergone a revolution in the past two decades. New technologies have propelled oncology research, providing doctors and scientists with tools to delve deeper into individual patient tumors and create revolutionary treatment strategies. To date, tumor mutations and patient-specific characteristics have been largely ignored in the design of cancer treatment strategies. The current standard of care for diagnosing, characterizing, and treating cancer often entails a one-size-fits-all approach where multiple patients receive the same therapy, regardless of whether it is likely to benefit them or lead to damaging side effects. The use of these technologies to obtain a comprehensive view of cancer biology has paved the way for truly personalized cancer treatment strategies, tailoring treatments based on individual patient and tumor profiles, also known as precision or personalized medicine.

Decades of research in the field of cancer biology, in conjunction with technological advancements, have contributed to an acceleration in the development of targeted and personalized cancer medicine and an increased understanding of the power of the immune system in treating cancer. Over time, our ability to match individuals to targeted therapies has expanded to include an increasing number of criteria such as gene expression, protein expression, cancer stem cell markers, tumor mutational load, tumor-infiltrating lymphocytes, and more. As a result, cancer treatment strategies for individual patients are now radically personalized and can include combinations of molecularly targeted therapies, chemotherapy, cancer immunotherapy, and radiation therapy to increase the breadth and depth of the immune response and increase the efficacy of the therapies. As cancer treatment options have expanded, it has also become

increasingly important to consider how to use various types of biomedical data together to help make treatment decisions.

1.1. Overview of Traditional Cancer Treatment Methods

Introduction Cancer has historically been treated with three standard modalities: chemotherapy, radiation therapy, and surgery. All three evolutionarily based and well-defined methodologies have been the foundation of managing cancer for decades. In chemotherapy, various intravenous, oral, or topical agents are used to eradicate rapidly dividing cancer cells. Radiation therapy also targets rapidly dividing cells, leveraging the fact that cancer cells grow more quickly than most normal cells. Using technology like external beam machines and brachytherapy, high doses of radiation damage the cancer cell's DNA, halting their ability to reproduce. The third traditional approach to managing cancers is resection or surgery, which physically removes the primary tumor and surrounding tissue. When combined, these three methodologies offer the best odds for successful cancer management. Historically, chemotherapy, radiation therapy, and surgery have been the most suitable treatments for a wide array of cancer types. However, apart from their generally toxic side effects, they are all reliant on population-based clinical trials, and their results are quite variable. Even if seemingly alike by microscope and projection vector, different patients could have a wildly different experience with any of these treatments, and often the unique response of the individual is unknown before treatment begins. While these three methodologies have indisputably been major factors in the decrease in global cancer mortality rates over the last two decades, the critical factors responsible for the reported decrease in overall cancer mortality over the past forty years have been changes in health policy, early detection, and new treatments. Individuals are not identical, and cancer patients are one of the most variable groups of all. Much of this variability is in the biological makeup of the patient, and sometimes the genetic composition of the tumor. Impersonal reliance on standard, population-based treatments overlooks these important variables.

1.2. Rise of Personalized Medicine in Oncology

The rise of personalized medicine in oncology represents a paradigm shift in the treatment of chronic and life-threatening diseases such as cancer. The development of oncogenomics and noteworthy increases in practical genomics in particular have spurred personalized strategies. It is now increasingly believed that all health issues

should be viewed in the context of an individual's hereditary makeup. Cancer is not just the consequence of a series of random, bad-luck cells but is driven by genetic mutations. New genome therapies are today approved as well as a long list of "conditionally authorized" cancer therapies, which operate based on phenotypic rather than overall survival in some situations.

Crucially, "a key insight from the drug industry is that genetic abnormality is not only essential for the advancement of malignancy, but in addition offers precious information as to which the investigation people ought to think about and the therapy agents they might most likely do so successfully." These tailored therapies have accomplished significantly greater results with much lower percentages of recipients than the general populace, thus changing the process of treatment from a time-consuming (and sometimes dangerous) trial-and-error sequence to one that is immediate and individualized. This approach is ideal for the strategies behind genomics, particularly enhanced genomics. Clinical study settings need to become adaptable based on this new evaluation paradigm. As this curriculum will quickly elucidate, systems are now investigating oncogenic targets to drug resistance, suggesting that targeted therapies will be made viable either by stratifying patients into those with rare genetic abnormalities or by directing participants in a clinical trial.

2. Role of Machine Learning in Cancer Drug Development

Machine learning, typically a type of artificial intelligence, is being used, along with other enhanced technologies, to shift cancer drug development towards creating more patient-specific medications. Although these innovations have many different goals, they are all part of a broader effort to advance personalized and more effective cancer therapies. Personalization is a more modern approach that decides the optimal therapy more often based upon an individual’s gut microbe, genetic makeup, and type of cancer that they have. In machine learning, sophisticated algorithms pick through extensive datasets to spot trends and patterns that might have been overlooked during manual analysis. This process can also account for features that are not as readily understood, such as pixels in a pathology slide. The primary goal of using machine learning in the field of cancer research includes being able to guess which patients may benefit from a therapy, how they are likely to unfold once treated, what molecules or switches should serve as a potential new medicine target, and how best to plan and design clinical trials.

When different types of data are integrated, machine learning plus panomic themes can also potentially shed light on specific mechanisms behind the biology of cancer. In short, these technologies have many use cases relevant to oncology clinical development and subsequent treatment.

2.1. Fundamentals of Machine Learning

Machine learning is a subfield of artificial intelligence (AI) that studies software systems that learn from experience to gradually improve their performance in solving tasks. Three main types of training exist: supervised, unsupervised, and reinforcement learning. Supervised and unsupervised learning could be effective in cancer research. In supervised learning, a model is learned from input-output data pairs. In unsupervised training, only the input data are available to the algorithm, which is asked to infer their structure. A reinforcement learning agent learns from the environment feedback produced by the action it performs in the environment. Another central concept is that of an algorithm or model, depending on the nature of the approach. The model is the function learned from the data, while the learning algorithm details the scheme by which the model is learned.

There are two types of models: generative models, which learn the joint distribution of the data; discriminative models, which learn the conditional probability of the output from the input. In the terminology of supervised learning, the inputs are the features, and the feature space is the set of possible values of these features. The inputs are often referred to as features or predictors in statistical terms. A predictor is some value computed in terms of known data that is of interest in a prediction problem. Feature selection applies to the entire setup. In the case of a discriminative model, the features are often patient-specific information extracted from various sources. Knowing how to effectively select features for input, remove redundant features, and create an efficient feature model is important in the context of complex diseases such as cancer, i.e., when a small number of predictors identifies possible cases or best predicts patient outcomes. Because models contain unpredictable patterns, the performance of a model can be artificially accumulated over time. Therefore, while a model may store predictions for given samples, this does not guarantee that it will generalize to new samples. Several strategies are often used to ensure generalization, including inner and/or outer validation, cross-validation, and blind testing. A reliable general model should capture

the true relationships up to noise and not the noise patterns. When learning from data, especially in the context of health data, it is also important to take into account ethical considerations, including the possibility of producing biases in the outcomes or interpretations of the model. Responsible AI in healthcare should prioritize fairness, security, privacy, and the well-being of the patients.

2.2. Applications of Machine Learning in Oncology

Applications of machine learning in oncology. Machine learning has many applications in oncology, most of which can be grouped under two broad headings: empowering cancer research and bespoke cancer therapy. Cancer research is increasingly becoming a data-driven science. Data analytics offer new ways of interpreting experimental and clinical findings that are otherwise hidden. Examples of large-scale analyses that are only made possible using machine learning include prognostic and predictive modeling. AI and machine learning are also being used to stratify patients by predicting patient outcomes. It is also used to identify predictive biomarkers.

Integrative analyses of genomics are performed in order to gain insights into the characteristics of individual tumors. Through analyzing the patterns and changes in tumor genomes, these machine learning models can be used to identify fundamental molecular characteristics of a patient's tumor, such as gene expression patterns, tumor infiltration of immune cells, and a tumor's mutation landscape. By combining various data types, machine learning techniques can integrate an even larger amount of data to generate a more comprehensive profile of the biology of cancers. Integration of diverse data types can result in ultra-high-dimensional data matrices that emphasize the need for machine learning algorithms that can handle complex data types. Increasingly, machine learning is being used to identify compounds that could be used to develop new drug therapies. Machine learning models applied to drug-related datasets are trained to identify novel compounds that could be suitable for clinical trials. Parameters that can be screened include drug effect size, drug half-maximum inhibitory concentration, and drug-protein interactions. In some cases, these predictive models can be used to synthesize new compounds.

3. Integration of Tumor Genomics and Patient Data

Combining information on tumor genomics with clinical and computational patient data is key to delivering on the promise of personalized oncology. Genomic alterations in

tumors create molecular peculiarities that can be leveraged for targeted therapies in precision oncology. Opening up genome sequencing enables efficient discovery of new genomic aberrations across patients, and their targeted identification may guide treatment personalization. As such, genomic profiles are now events-based entries in drug personalization.

However, for translating genomics into a clinical setting, there is more information than identifying single driver aberrations. A complete strategy for identifying precision treatments entails knowing the panel of drugs specific to the patient along with the possible alterations that would lead to an anti-tumor effect. As with any data-driven market activity, data sources need to be broadened from a given tumor to clinical routine data to include the most meaningful predictors of patient responsiveness: clinical history and demographic variables to learn or infer the depth of drug response. This dialogue among the tumor, the therapy, and the individual is poised to become the foundation of cancer research for the next decade. It is now a matter of how to solve the integration problem. In principle, the available data could be linked from many systems to enable a truly holistic view of the patient, their tumor, their therapy, and their environment. Modern technological devices allow for faster, more reliable linking of data across systems, creating an interesting environment to foster the integration of clinical and other omics informatics. However, several challenges need to be met: the form of the data, its storage, and the communication between endpoints, the identification of meaningful events, the use of reliable methodologies, and statistical frameworks accounting for patient outliers. Moreover, it is pivotal to assure data integrity and to handle missing data or more generally, incompleteness. Indeed, these hurdles should be addressed before we push for radical advancements in patient personalization, because the implications are deep. Already, combining genomics with clinical events records is setting the ground for continuous monitoring and treatment personalization, leading to a disease-free regimen at all times - which is the very cradle of precision medicine.

3.1. Importance of Genomic Profiling in Cancer Treatment

In the era of personalized medicine, it is well established that not all patients with the same cancer histology are alike. Genomic profiling has been of utmost importance in non-oncology treatments for many decades, and lately, it has been realized that it is also

of pivotal importance in cancer treatment. Genomic profiling can help in identifying specific mutations and alterations within a given patient's tumor. The genetic landscape of the patient's tumor is characterized and, thereafter, treatment plans can be tailored for the patient. Genomic profiling is very important in the sense that the information derived can help in the design of an effective treatment plan. In addition, there is a greater likelihood of minimizing any unnecessary side effects that are usually associated with conventional therapies. It can also help in the selection of patients for specific clinical trials. With the advent of next-generation sequencing technologies, it has become easier and cost-effective to obtain genomic data. Characterization of the genomic data has gained vital importance in designing treatments for patients. This approach is more personalized and is based on the fact that no two patients are alike, even with the same cancer pathology.

Today, we understand the molecular pathology behind many cancers; this has resulted from the recent technological advancements in sequencing technologies such as whole exome sequencing, whole genome sequencing, and, later, the most utilized sequencing technology in the era of personalized medicine, RNA sequencing, and DNA amplicon sequencing and cancer trusomes. Many specific genomic mutations have been termed actionable mutations. These mutations may potentially inform the use of clinical trial drugs that may be more efficacious as these drugs are designed for the specific mutations. Actionable mutations or drug-targeted mutations are identified in the tumor, and thereafter a particular drug targeted for the specific drug target is used. If the patient responds to this therapy, it is termed a "personalized therapy" as it has been postulated based on the presence of exclusive "personalized" mutations. This individualized approach offers a greatly enhanced likelihood of improved patient outcomes contrary to the best standard therapy offered. In essence, today, the patient is the center of decision-making in personalizing cancer therapy. These advances in molecular medicine have revolutionized cancer treatment plans in recent years. Here, we review genomics and genomics at a glance, including some real-life case scenarios in various cancers, what useful actionable mutations are known to be tumor "drivers" and suitable for targeting in designing personalized therapy. However, it should also be stated that a dearth of translatable drug targets exists, and they need to be developed further. Consequently, actionability rates for the knowledge gained through sequencing

may vary widely on account of the high throughput of genomic data and the advanced complexity in computational modeling and consequently in predicting.

3.2. Challenges and Opportunities in Integrating Genomic and Clinical Data

Randomized clinical trials compare standard cancer treatments against experimental agents and randomize patients to one of the treatment arms in order to determine the effectiveness of a new treatment for a group of cancer patients. The result of a clinical trial may indicate an increase in the likelihood of a meaningful benefit along with many potential side effects due to treatment. However, the results of these treatments may not benefit all cancer patients, and many patients may not be eligible for clinical trial participation. As a new conceptual model of cancer emphasizes a multi-omic approach, integrating information from cancer genomics, transcriptomics, proteomics, metabolomics, and clinical data are key elements for effective personalized treatment of cancer. Clinical data outcomes can provide insight beyond the standard surrogate markers and may facilitate our ability to link an individual's tumor to specific and relevant data.

Despite the potential value of integrating genomic and clinical data in cancer therapy, several challenges still exist to avoid scoping and determine if this topic has reached an inflection point. The barriers to integrating genomic data with clinical outcomes are indeed multifaceted. Data silos between genomic, proteomic, and clinical data often exist, making data integration difficult. Clinical data have not been standardized among biobanks. Personal data protection is a major hurdle for data-sharing efforts for ethical reasons, particularly for identifying potential patients who need possible additional treatments. Determining which genomic alterations have clinical significance beyond benign germline polymorphisms is difficult. Furthermore, identifying those critical genomic alterations relevant for individual patient treatment involves a myriad of possible combinations, making analysis more complex. One recent report demonstrates that patients harboring the same driver mutation tend to exhibit diverse clinical outcomes. Fully understanding the complex molecular changes in individual cancers is critical for providing clear and precise decision-making about the application of targeted therapies. Although this area is currently under active exploration and development, there are currently no recommended or standard methods available. Finally, within many clinical institutions, integration between genomic and clinical data varies and may

occur too late in the decision-making process to affect treatment strategy. However, both the difficulty and potential of integrating genomic and clinical data into treatment strategies are recognized. Hybrid devices and machine learning methods of artificial intelligence that integrate algorithms for fast and accurate analysis of genomics, proteomics, and other omics technologies can help to bridge this gap. Also, there are commercial software solutions to provide integrated workflow data. With evolving technologies, integrating these two fields can help close the missing link in cancer biology: the interaction between genomic pathways and individual patients associated with both static and dynamic phenotypic clusters in patient responses. Improvement in the ability to link genome alterations and fusion proteins to patient responses and outcomes has a larger potential for stratifying patients into risk categories and determining treatment plans than surrogate response criteria based on protein levels. This area, however, is still under development, and some are just now using it within retrospective data sets. It has been shown that introduction to semi-quantitative proteomics expressions of proteins could have potential utility equivalent to mutational status. Integration of omics data with electronic health records can enhance our ability to use AI to provide more accurate prognosis or identify which patients will benefit from treatment. It is hoped that one day interdisciplinary teams of geneticists, oncologists, computer scientists, AI experts, bioinformatics professionals, data curators, and others will collaborate to provide novel treatments and insights to this long-active area.

4. Case Studies and Success Stories

Case Study 1: Our journey started in 2020. In January 2020, a 39-year-old patient with metastatic perivascular epithelioid cell tumor (PEComa) who had not responded to the standard treatment underwent comprehensive sequencing to study their cancer. This analysis revealed a fusion gene believed to be indirectly associated with responding to an investigational drug, dactolisib. Dactolisib inhibits the mTOR protein in the mTOR pathway, and results of chemotherapy or immunotherapy with normal treatments were negative. The patient's treating clinician reached out to develop a clinical trial that would utilize the patient's genetic information to qualify for personalized drug treatment with dactolisib. The study was launched in collaboration with a clinical coordinator. Within 2 months, three sites were activated. Contributions were made to the refurbishment of a pre-approved drug supply of dactolisib that had been highlighted in the clinical trial protocol. The full dose of dactolisib was gradually increased and

taken from each patient. After the first on-treatment evaluation, the patient in the first dose level had a 71% reduction in total tumor volume following three cycles of therapy. Objective responses have also been observed in two other patients at this dose level. This study is currently underway.

Case Study 2: A phase 3 evaluation of atezolizumab or placebo in combination with the platinum-based chemotherapy drug cisplatin/gemcitabine in a total of 1213 cisplatin-eligible patients with locally advanced or metastatic urothelial cancer who have not been previously treated with systemic therapy. Patients were randomized in a 2:1 ratio to receive either cisplatin/gemcitabine in combination with atezolizumab or a placebo. The phase 3 clinical trial found that men live longer when treated with a combination of a PD-L1 inhibitor and standard chemotherapy compared to just receiving chemotherapy, findings that led the PD-L1 inhibitor to win regulatory approval. In a secondary endpoint of overall survival, patients who received atezolizumab in combination with chemotherapy lived longer compared to those who did not receive atezolizumab plus chemotherapy. The upper end of the atezolizumab plus chemotherapy arm reached 18.8 months; however, it should be noted that statistical significance was not met.

4.1. Real-World Examples of AI-Enhanced Cancer Drug Development

Machine learning and genomics have shown promise in identifying targets and treatment responders for which no patient will progress for years. Programs have been launched in a multi-organization effort to combine the data from academic cancer centers, biopharma data, and data curated from patient records to train machine learning algorithms to anticipate who will respond to which treatments. Details are lacking in the neuroendocrine tumor case study example, but the breast cancer case study highlighted the patients' ability to be co-therapy-free after having progressed on most chemotherapy options, and the number of predicted months that they would see their disease stabilize or shrink was over double the 2 months predicted by using an online tool. In addition, sponsors are comparing the effectiveness of the standardized treatment regimens recommended for Phase II trial participants with the results observed in the actual Phase II trial participants.

At the same time, collaborations between technology companies and healthcare are beginning to bear fruit, altering the standard treatments patients receive. The trial includes collaborations between multiple healthcare and industry partners for machine

learning-based combination therapy strategies for platinum-resistant ovarian cancer patients. For a patient with extensive-stage small cell lung cancer, a case study highlights over three additional years of survival. With reports estimating a survival of 8.0 months, including additional therapeutic options beyond the third-line settings, a 40-year-old male with lung adenocarcinoma saw his quality of life and performance status worsen. AI predicted a progression-free survival of 'several years.' AI developed combination treatment strategies and made them available for off-label use. Surviving 43 months following diagnosis, he showed progression at month 39 and has been placed into hospice care. Entries and exits from both studies are made in the real world. These results are certainly cherry-picked at this stage from thousands of passionate and gifted oncologists—efforts that are needed. Nonetheless, these real-world cases offer a 'proof of concept' for the alignment of regulators, patients, clinicians, payers, and sponsors to work with organizational involvement as an internal check and balance. Subsequently, this end-user utilization of AI is based on deep learning networks presented: proposals that leverage this study or other initiatives will need to undertake compared traditional methodologies versus that proposed in well-designed studies and report progression-free survival, adverse events, and quality of life—and not just 'confidence.' The development studies showing AI superiority will be subject to public communication.

4.2. Impact of Personalized Approaches on Patient Outcomes

The move toward tailored therapies within cancer care has had a profound effect on patient outcomes. Therapies selected according to the molecular profile of the patient's tumor are significantly more efficacious when objective metrics such as progression-free survival and overall survival are compared. Such matched therapies show clear windows of improved outcomes and reduced adverse experiences, even in tumor types for which other predictive factors are not available, across a large population of patients. The use of molecular profiling to match patients to treatment increased the probability of achieving a positive progression-free survival as well as overall survival. In addition, after multivariable adjustment, the use of personalized treatment was associated with a lower likelihood of receiving a second line of cancer treatments than patients receiving unselected treatment.

Importantly, personalization of cancer therapy can result in statistically significant improvements in patient quality of life. Individual patient stories of improved

engagement, activity, and resolution of symptoms contribute significantly to the important "touch" of the approach, leaving a profound impact. Patient preference, patient-clinician engagement, and shared decision-making framed in the context of personalized treatment programs are needed, ultimately leading to greater patient satisfaction and engagement with their health and treatment programs. Not only is this emerging area of practice appropriate, it is already recognized as changing the standard of care in a proportion of the population. The increasing evidence of cost-effectiveness, resource utilization, and spurious waste hardwired into systems that do not prioritize patient pathology in treatment choices has also raised the need to fast track greater access and reimbursement systems that are sustainable so all may benefit. However, concerns about access remain, with some analyses suggesting no net value from greater access if equity issues are not addressed. The uptake of personalized medicine across various tumor types and patient cohorts has also revealed disparities, for example, being limited because of psychosocial factors such as fear, anxiety, and denial.

5. Future Directions and Ethical Considerations

Emerging Trends and Future Directions Precision medicine, the increasing accessibility of cloud-based big data analytics, and the development of continuous learning systems are the major trends shaping future AI-enhanced cancer therapy systems. These foundational elements interact with a range of other trends, such as an increasing focus on adaptive therapies and a better understanding of the complexity of cancer. These changes are beginning to shape the cancer research landscape. In order to use advancing knowledge about cancer biology in a way that is beneficial to patients and their caregivers, AI-enabled treatment planning and continuous patient monitoring must develop in tandem. Data from patient care can be leveraged for these two components—treatment planning and continuous monitoring—contributing to the development of real-time adaptive treatment strategies for the benefit of future patients.

Ethical Considerations The further development of AI will allow us to navigate increasingly complex ethical considerations. Issues to be addressed include: ensuring valid, informed patient consent when using AI-assisted interventions; data privacy, specifically around the increasing volume of data generated during each patient treatment; the question of physician autonomy in proposing interventions; and concerns about the negative influence of algorithmic bias on particular populations. These

considerations need careful attention from the relevant stakeholders to ensure responsible innovation. To help consider these challenges, dedicated research into the regulation of AI-enabled oncology will be crucial. It is crystal clear to me that legally and ethically robust frameworks will and should be established in response to cancer care using AI. Looking ahead, grouping the best minds across multiple sectors and geographies to address these challenges is imperative. Such multidisciplinary groups might include dedicated researchers from across the world, collaborating in harmonized research. This might include those from basic science, bioinformatics, engineering, healthcare technology, medical and clinical oncology, patient and multidisciplinary care, continuous learning systems and monitoring efficacy, as well as experts in research ethics, law, data governance, and regulation. The identification of substantial breakthroughs and challenges, together with a detailed roadmap into how the field of AI-enabled oncology may evolve, should be key objectives.

5.1. Emerging Trends in AI-Enhanced Cancer Therapy

Cancer therapy is a rapidly evolving field. In addition to targeting cancer stem cells and immune-permissive chemistries, new anti-cancer regimens are shifting to precision medicine—serums or procedures that are best suited based on the individual characteristics of the patients or the cancer itself, or both. One transaction of tenured cancer therapy is the aggregated use of AI to fuel personalized care, ushering a treatment-as-unique-as-the-person paradigm across the entire patient journey – from detecting disease to disease management. The emergence of big data analytics, whereby omic, clinical, and imaging datasets for thousands of humans or human diseases can be plumbed to craft hypothesis-derived care recommendations, is now a crystalline vision. Clinical data analytics revealed new subtypes in disease and a deeper molecular image when correlated with clinical endpoints.

In the clinical imaging domain, the era of radiomics and digital pathology suggests advanced processing of 3D and 2D images for diagnostic testing, tumor characterization, biopsy guidance, and extent of disease evaluation. Machine learning algorithms are also being adapted to triage or pre-diagnose alterations associated with a developing health condition, often heralded by subtle changes at the cellular or molecular levels. Machine learning models scan chemoprofiles of stress and neoplastic cells cultured on the lab bench to predict response, relapse, or sensitivity to emerging molecules and drug

cocktails. Machine learning models have the propensity to bolster expertise in oncology. Wearables, mobile device applications, or apps that monitor tumor cell secretion proteins present in body fluids and track precipitous shifts in body chemistry are en route to becoming 'porch visits' in real-time bioanalytics. Technologies are here to pave the way for earlier screening of tumors in progress before their advent at a clinician's door. Do today's clinically available proven numbers curtail their credibility in fostering precision oncology upon clinical grounds? Yes, only if excellence in AI is to be plonked alongside insights from clinical science pathways. Emerging trends pattern the future of AI-guided oncology or AI-augmented oncology today.

5.2. Ethical Implications of Personalized Medicine

Ethical Implications in Personalized Medicine

In the context of oncology, the proliferation of AI algorithms presents new ethical challenges. As models are trained on an exponentially increasing amount of sensitive patient data, it becomes exponentially more important to ensure proper data storage and patient privacy. As with any pursuit in personalized medicine, patients must be able to trust that their healthcare workers have protected their information. This matter is only exacerbated when the data is related to their most sensitive health information. Moreover, since the growing field of AI in oncology is quickly evolving, individuals must give their fully informed consent about the use of any AI application that is proposed as part of their treatment. The themes of this special section call for a recognition of the potential pitfalls of the shift towards personalized healthcare, particularly in pediatric oncology, highlighting the potential for increased cost and health disparities in an era where hopeful parents are given additional options for their children. The emphasis on fairness, AI bias, and its potential extrapolation underscores the importance of cautious consideration when discussing the validity of evidence derived from AI-enabled personalized medicine. At the very core, the aim is to improve the lives of those suffering and to be fair and just in how care is dispensed.

When genetic screening is proposed to families and patients for the purpose of identifying personalized therapeutic targets, it must be made abundantly clear that participation is voluntary and will not compromise the quality and compassion with which conventional pediatric oncologic care is delivered. If the child's or family's priorities do not align with this intensive plan, then the personalization of care has the

potential to introduce unnecessary financial hardship as well as increase exposure to physical and emotional risk in their already vulnerable situation. However, away from the financial scope, the discussion of potential AI biases that could be misinterpreted is particularly relevant in a compromised pediatric population seeking a rare and innovative therapy that could deliver hope. For one, young children are often treated based on physician discretion through the provision of indirect consent given by their guardians as they lack the ability to independently provide informed consent. AI-based algorithms, with large libraries of data, may rely on and continue to generate influential data collected predominantly from white populations even in the voracious pace of innovation in childhood oncology. Indeed, the small number of non-Caucasian pediatric patients included in many studies highlights the disproportionality of AI-generated data in modern oncology. Furthermore, if that treatment yields remarkable outcomes, it should be accessible to all and not solely restricted to the population from which input data was generated. Inequity in the AI's data is indicative of the inequitable dissemination of the needed healthcare. Moreover, physicians seeking to push the boundaries of treatment even with extraordinary or risky measures may form a much more unjust and biased relationship that could compromise future care. Patient participants contain data that are, in many scenarios, personal and private. Parental consent may denote an uninformed agreement that the use of their children's health information is simply implied and their rights inferior to the potential health of the population, which would be unjust.

6. Conclusion

The integration of machine learning technologies with routine genomic profiling in an AI-enhanced identification of cancer pathways and personalized point-of-care oncology tests have the potential to improve treatment outcomes in such patients. Such a system will ultimately allow drug and treatment predictions, monitor treatment resistance and provide a growing repository of worldwide cancer genotypes and phenotypes that will provide researchers with a learning ground to constantly improve upon the AI prediction systems. This trend is further demonstrated in such datasets, with a vast number of articles being published since the turn of the century on genotyped drugs in disease patients. With levels of investment from competitors confirming the importance of a deeper systems level AI integration, therefore, we can project that AI will simultaneously improve both our understanding and impact on human disease. In

conclusion, the advent of highly specific, targeted and effective therapies is an enormous advance of the field of oncology, and it is one that has been decades in the making. Genomic analysis has been used to develop companion diagnostics, to enable recruitment of matched patients to clinical trials, to identify responders or non-responders, and most recently, in the hope of providing context for drug repurposing or combination. In the case of a primary analysis of a study indicated that a product had a confirmed ORR of at least 57% and a median duration of response of at least 16.5 months in adults with ROS1 fusion-positive NSCLC who were treated with at least one prior ROS1 TKI. However, the conversion of disease endpoints into the benefit of overall survival is as yet an elusive art, and it is not easy to determine the stage at which to introduce a new challenging agent into the patient pathway. With the number of therapeutic breakthroughs in personalized care now expanding into the epithelia and sarcoma, and more than 2890 precision medicine studies enrolling patients, the future is a bright one, alongside the acknowledgment of the ongoing challenges surrounding profiling individual samples and the accurate translation of this data. AI has the potential to transform patient selection approaches that are both complex and time-consuming. The improvement in response rates demonstrated has the potential to bring about new, improved era in high-throughput medicine and to bring about a significant transition in the luminal breast cancer clinical landscape. Like all forms of change, the evolution of personalized medicine is not, and neither should it be, straightforward. The downside risks of bioinformatics constitute first-order constraints, which have slowed the deployment of multi-gene expression signatures, pan-cancer machine learning recognition to the clinic. The rule of thumb of these capabilities is in the high, often single system, where bioinformatic professionals dominate. Such professionals develop initial cut thresholds and the vast majority of their rules for use, as well as portfolio charging campaigns and individual test validation. More complex data, such as proteogenomic output, across diverse systems and longitudinal datasets, remain an emerging phenomenon in high-grade clinical medicine and there is therefore a lag to performance. Given both this, as well as the looming data protection challenges, process efficiencies and patient access requirements, which remain repositories for massive emerging investment interest and have implications stretching well into the next several decades, all of our effort must be to surmount these biologic and technical challenges in a collaborative spirit that connects disciplines. Eighteen years on, therefore, the

spectrum of breast cancer medicine is finally becoming more technically tailored. Emerging hypotheses with the potential to enhance this treatment landscape and reduce the workflow-to-clinical time include: visual interpretation learning, algorithm transparency, the need for data analysis and human behavior to happen in parallel, a greater focus on pediatric cancers and a growing point-of-care and primary care premise. In conclusion, we propose a transformation in individual treatment paradigms built not by doctors or biologically proficient individuals, or corporations, but via computer intelligence that is commercially independent or regulatory subsidiary. In doing such work, we will be mindful of emerging ethical principles which lie at the forefront of such an ascent. In going forward with this project, we argue not for sole investment in an established supervisor function to oversee these systems, but scientific investment in the ecosystem of agents studying and applying these supervised and unsupervised systems.