https://africanjournalofbiomedicalresearch.com/index.php/AJBR
Afr. J. Biomed. Res. Vol. 27 (October 2024); 933-939

Review Article

Navigating the Landscape of Pancreatic Tumors: An In-Depth Analysis of Classification Methods.

Prakashini Koteshwar[1], Visakh T[2], Athira Rajeev[3], Shailesh Nayak S[4*]

[1]MBBS, MD, Professor, Department of Radio-diagnosis and Imaging, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, 576104, Karnataka, India
[2]MSc. MIT, Assistant Professor-Senior scale, Department of Medical Imaging Technology, Manipal College of Health Professions, Manipal Academy of Higher Education, Manipal, 576104, Karnataka, India
[3]MSc. MIT, Assistant Professor, Department of Radiodiagnosis and Imaging, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, 576104, Karnataka, India
[4]MSc. MIT, Assistant Professor, Department of Medical Imaging Technology, Manipal College of Health Professions, Manipal Academy of Higher Education, Manipal, 576104, Karnataka, India*

Abstract
Pancreatic tumors are, oncological diseases, considered one of the toughest types of cancers due to their malignancy and unfavorable prognosis. This piece deals with the complexity of pancreatic tumor classification and the multidisciplinary approaches used to arrive at a comprehensive framework and personalized care. The histopathological classification is a starting point, but the development of molecular techniques and radiological techniques and their utilization expands the scope of considerations in clinical practice. Genomics testing allows for molecular classification of pancreatic ductal adenocarcinoma (PDAC) through the identification of discrete subtypes with varying therapeutic yields. Radiology in the process of adding radiomics to it, can highlight the tumor parameters from an objective point of view. IHC fuses the others and helps to generate the picture of protein expression patterns. Integration of comprehensive IHC markers with genomic profiling and machine learning enables better stratification accuracy and treatment individualization. With these strategies working hand-in-hand, the optimism is high that there will be better outcomes for pancreatic cancer patients through tailored treatment approaches. This refrains the significance of a coordinated effort involving many disciplines in the attempt to deal with the complexity of Pancreatic Cancer and treatment.

Keywords: Pancreatic Tumors, Classification, Histopathology, Molecular Profiling, Radiological Imaging, Immunohistochemistry

**Author for correspondence: Email: shailesh.nayak@manipal.edu*

Receiving Date: 30/09/2024 Acceptance Date: 21/10/2024

DOI: https://doi.org/10.53555/AJBR.v27i3.3184

INTRODUCTION

Pancreatic tumors are the arch enemies of oncologists and are termed for their aggressive nature and abysmal endpoint Although there have been significant successes by way of innovative diagnostic and therapeutic interventions, pancreatic cancer to date is one of the deadliest malignancies worldwide, its five-year survival rate being a feeble 10% [Siegel et al., 2020]. The subtle setup of these pancreatic tumors is attributed to the complexity of their heterogeneity, posing obstacles to both the classification and treatment of these tumors as a whole. This creates an urgent need for basic techniques that can provide us with a deep comprehension of pancreatic cancer and, thereby, improve patient results. This call for action involves the initiation of complex mechanisms able to identify a number of the molecular, pathophysiological, and clinical aspects of pancreatic cancer. Through the reckoning of a

discrete subtype and a mechanism of cancer progression, such classification systems put the ground to curative treatment that will consider individual peculiar traits of every patient. Moreover, they offer invaluable insights into prognostic stratification and the identification of novel therapeutic targets, thereby fostering advancements in the management of this formidable malignancy.

Understanding Pancreatic Tumors

Pancreatic cancers, heterogeneous and malignant neoplasms, are the disease of the pancreas, an organ important for digestion and regulation of blood sugar levels. A wide variety of pancreatic neoplasms is encountered from this cancer, which is the most aggressive and common type (PDAC) with Pancreatic ductal adenocarcinoma (PDAC) accounting for about 90% of these neoplastic cases. Moreover, there is a saying that PDAC comes late in the game and it is a pretty fast track to death, which leads to its high mortality rates. The rest of the pancreatic tumors are formed from different subtypes that have unique features and outcomes. A significant part of this classification is neuroendocrine tumors (PanNETs), cystic tumors, and rare histological variants. PanNETs, mainly characterized by the fact that they proliferate at a slow pace and without generating severe symptoms, are typically considered to be less aggressive types of cancer. Nevertheless, it should be recognized among the group of PanNETs, that there is a faction that presents more hazardous characteristics, thereby their management is more difficult.

Diagnosing pancreatic tumors is usually carried out by performing a combination of imaging studies (such as computed tomography and nuclear magnetic resonance imaging) and biopsy which can be done with a fine-needle aspiration or a core- needle biopsy. When a diagnosis is certain, selecting a treatment plan will be influenced by a variety of aspects including tumor stage, location, and the health of the patient. Surgery is the principal remedy for localized PDAC and PanNETs with a few cases using chemotherapy and/or radiotherapy alone or with the surgery.

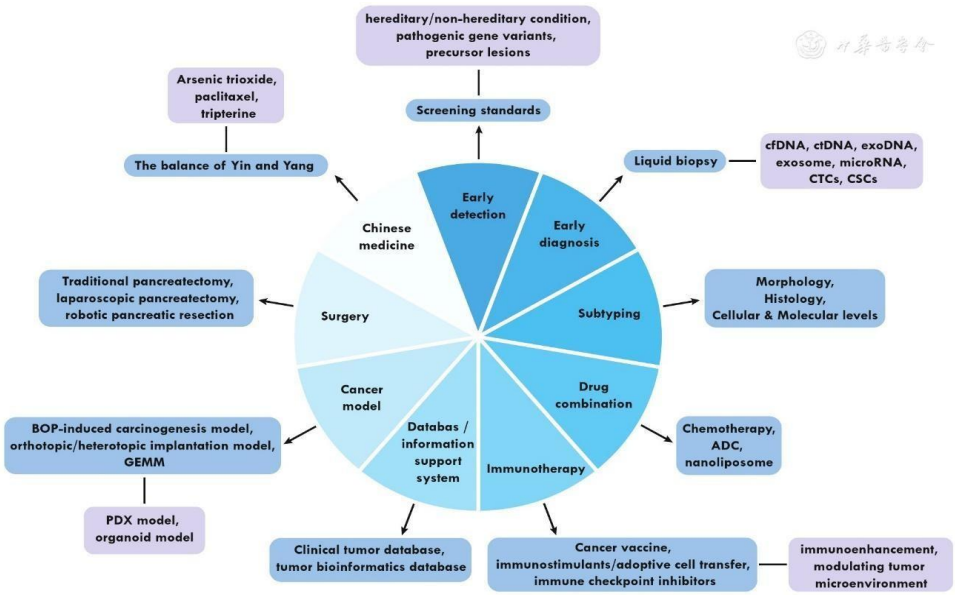
Healthcare has integrated advanced detection and therapeutic processes from the development of novel diagnostics and treatments. Yet the situation remains poor for patients with pancreatic tumors. PDAC carries a devastating prognosis and is related to the lowest five-year survival rate (approximately 10%) because of its rapid growth potential and tendency to spread throughout the body. The PanNETs have a much better prognosis with survival being dependent on the grade and stage of a tumor and its response to treatment.

The tumors of the pancreas are very diverse, and the ductal adenocarcinoma of the exocrine duct is the most common and aggressive one of them. While PanNETs generally have a more indolent course, their prognosis can vary significantly. Advances in early detection and treatment options are crucial in improving outcomes for patients with pancreatic tumors, but much more research is needed to address the complexities of these diseases and enhance patient survival rates.

Challenges in Classification

The classification of pancreatic tumors is a complex job as it is because of tumor diversity in terms of histopathologic features, molecular profiles, and clinical behavior of carcinoma. Conventional classification has always had features like histological characteristics, such as tumor classification, differentiation, and anatomical location. Nevertheless, these systems usually overlook the genetic diversity which is the very subject of tumor development, and that makes the cancer unresponsive to treatment.

During recent years, we have seen an increase in incorporating molecular subtyping into the subclassification categories. This revolution was stimulated by the observation that methylation profiles are critically implicated in the onset and progression of pancreatic cancer. The most common genetic mutations, expression changes and epigenetic modifications are associated with the different subtypes of pancreatic cancer [Collisson et al., 2011].



(Source - Xu *et al.* 2022)

Nonetheless, the integration of molecular data into classification systems is not without challenges among which there are many. Therefore, one considerable problem is the diversity of opinions regarding which molecular characteristics are important and how many of them should be included in the list. Furthermore, technological advancements have resulted in the finding of emerging molecular subtypes - which on the other hand, increase the difficulties of classifying them.

To this end, the scientists are working towards the creation of more complex systems of classification that take the account both structural and genomic peculiarities. These integrated systems aim the draw a more mature model that will accurately portray pancreatic tumors and their clinical behavior. In general, the tissue classifications of pancreatic tumors are still in the process through teamwork. If the histological and molecular information are combined, researchers expect to design more and more advanced diagnostic and treatment protocols for pancreatic cancer.

Advancements in Classification Methods

Major progress has been witnessed in recent years in the areas of creating classifications for pancreatic tumors, which borrows from the recent preeminence of genomics, transcriptomics, and imaging modalities. Molecular profiling research over time has identified distinct molecular subtypes of PDAC that are uniquely different in their pathological and clinical peculiarities [Moffitt et al., 2015]. Similarly, efforts to characterize PanNETs have led to the identification of prognostically relevant molecular markers, facilitating risk stratification and personalized treatment approaches [Marinoni et al., 2014].

Genomic and Transcriptomic Profiling

Genomic and transcriptomic profiling has indisputably contributed to uncovering the complex molecular basis of pancreatic tumors and has allowed us to draw compelling mosaics of multiple intertwined mechanisms activated by which tumors can emerge and acquire resistance to therapies. This scientific quest is important as it enables the physician to conversely develop effective remedies and enhance the wellness of patients.

One of the most important picks in the field of molecular biology that has been found is the identification of common single nucleotide polymorphisms and chromosomal disorders in pancreatic ductal adenocarcinoma (PDAC). Multiple genes, such as KRAS, TP53, CDKN2A, and SMAD4, are related to PDAC [Waddell et al., 2015]. These mutated genes provide insight into the molecular changes that lay the foundation for and help drive the growth and advancement of PDAC. Modification of the KRAS gene, for instance, has been under research with the system showing the ability to signal the cells that lead to their excessive proliferation, a cancer mark.

To mention, the PanNETs studies proved the MEN1, DAXX, and ATRX gene mutations occur randomly with many more cases suggesting the possible role of epigenetic mechanisms in PanNET pathogenesis [Jiao et al., 2011]. Moreover, the mTOR signaling pathway mutations are known, and this opens up an idea about the cellular processes that interact with the development or progression of PanNETs. The data mentioned here shows the range of the molecular markers of different disease stages and cancers in the pancreas, and it also reinforces the targeted therapy approach.

The advancement of next-generation sequencing techniques and methods has proved to be of great significance in disclosing the genomic intricacies of pancreatic carcinomas. These types of techniques can empower scientists to take a complete genome- wide survey of the underlying genes and the mechanisms that are triggered during the tumor initiation and the resistance to treatment. In terms of a completely integrated view of 'tumor biology, the combination of genomic and transcriptomic information furnishes us with data on gene expression patterns as well as on repressing networks, which offers us a mean of a holistic view.

The genomic and transcriptomic profiling of pancreatic tumors has significantly advanced our understanding of the disease, uncovering key genetic alterations and signaling pathways that underpin tumorigenesis and therapeutic resistance. This knowledge serves as a foundation for the development of novel targeted therapies and precision medicine approaches, with the ultimate goal of improving patient outcomes in pancreatic cancer.

Integration of Multi-Omics Data

Multi-omics technologies constitute an ensemble of different "omics" approaches ranging from genomics to proteomics, transcriptomics, and epigenomics and have proven to be an efficient tool in oncology research. These technologies provide an overall view and reveal details at the molecular level of the tumor microenvironment, increasing our ability to know and understand cancer-driving mechanisms. By merging data from all the screens, the researchers can get an empirical picture of the complicated link between the different cellular structures and pathways governing cancer cell changes.

Genomics, in particular, shows what types of genetic alterations are present in the tumor, e.g., mutations (point and small changes in the genome, respectively), copy number variations, or structural rearrangements. Transcriptomics alternatively provides information on gene expression profiles that manifest at the tumoral level hence revealing which gene is active or inactive in the given tumor. Proteomics signifies the proteins present in a tumor, depicting the amount of such proteins, modifications in them, and their interactions. Epigenomics studies such hereditary influences, as DNA methylation and histone modifications, which may show how genes are expressed. However, the underlying DNA sequence will remain unchanged. The interplay of these multiple omics techniques yields an advanced and complete interpretation of the molecular basis of pancreatic tumorigenesis which is the base for the development of new treatment plans. As an example, researchers have succeeded in the field of multi-omics in subtyping pancreatic cancer with diverse prognostic and clinical traits. This insight is valuable to clinicians when constructing treatment regimens accordingly. It is a means to an end and a boost to the care provided, thereby, improvements in outcomes and reducing side effects. Simultaneously, improvements in computational biology along with machine learning algorithms have made possible the analysis and appraisal of the data that is gathered from thousands of organisms. As an illustration, machine learning algorithms like

those can be taught to recognize trends and, perhaps, predict complex molecular patterns in pancreatic cancer data so that the discovery of many molecular signatures could be made. These molecular signatures may be applied as diagnostic markers for the prognosis of patients and the assessment of drug response providing the foundation for more personalized medicine treatment choices.

The collaboration of multi-omics technologies, computational biology, and machine learning has revolutionized our understanding of pancreatic tumorigenesis. By leveraging the vast amounts of omics data available, researchers can develop more accurate predictive models for patient prognosis and treatment response, ultimately improving outcomes for pancreatic cancer patients. The integration of these technologies holds great promise for refining existing classification schemes and uncovering novel therapeutic targets, ultimately leading to more effective treatments for this deadly disease.

Role of Imaging Modalities

Molecular profiling, as such, is considered a pinnacle in understanding the pathways and characteristics of pancreatic tumors, intrinsically. However, by using different imaging modalities comprehensively and accurately, disease evaluation and management need to integrate all of them because each of these modalities offers specific information about tumor morphology, staging, and treatment planning.

Among other significant imaging techniques, CT is the main one as it produces incredible cross-sectional images of the pancreas and other tissues located in the area. The high level of microscopy is how precise visualization of tumor morphology such as size, location, and proximity to nearby blood vessels is possible. Meanwhile, CT scans are very useful for the evaluation of vascular encasement and infiltration, the key component in the decision to operate or not based on the resectability principle and the nature of surgery.

MRI is an excellent additional tool that provides better soft tissue resolution and for imaging in multiple planes, than CT. This modality facilitates the differentiation between the tumor and the surrounding vascular and essential structures, so we need to be extremely careful in our preoperative planning. For instance, the assessment of tumor vascularity and diffusion properties uniquely dissociates between malignant and benign lesions and treatment responses to the process.

The Positron emission tomography (PET) imaging, more exactly with the Computed Tomography (PET-CT), gives relevant functional information by evidence of areas that have higher metabolic activity. This allows the detection of distant metastases and facilitates staging by serving as a foundation for the adoption of neoadjuvant chemotherapy and surgery for those who are eligible. In addition to this, PET-CT serves as an important tool in determining the treatment progress and detecting disease recurrence, contributing to patient monitoring and management.

In essence, the combined use of high-resolution techniques like CT, MRI, and PET-CT together in the classification, staging, and management of pancreatic tumors is rather valuable. These imaging techniques, among others, are of critical importance in patient care procedures because they provide accurate diagnosis, appropriate treatment planning, and monitoring of patients according to their progress level (Al-Hawary et al., 2014).

Current Classification Methods for Pancreatic Tumors

There is no denying the fact that pancreatic tumor genesis poses the most complicated problem for oncology: they are extremely heterogeneous, highly malignant, and often not responsive to treatment. Through classification transformation, pathological, molecular, and radiological features have been introduced to provide a currently complete view of the underlying cause of cancer. This periodic, multi-dimensional method gives a complete picture of the tumor's characteristics, which will help in prognosis, choosing the best treatment, and early patient care.

One of the main histopathological features is the tumor grading and staging. These features facilitate to assessment of how the tumor might react to the treatment. Molecular classification, unlikewise, goes deep into the genetics of the tumor pinpointing significant traits, that are used in establishing a targeted medicine selection, this is in line with the tumor behavioral assessment. Using Radiological ways with the latest imaging techniques helps to give more accurate information about the tumor location, size, and possibility of involved adjoining structures. Together these classifications will undoubtedly raise our comprehensiveness and efficiency of pancreatic tumor treatment, thus allowing for the best management of a patient's care plan.

Histopathological Classification:

The conventional imaging method used to detect a pancreatic malignancy remains quite a tedious and labor-intensive procedure, which involves a very careful observation of tissue samples carefully examined under a microscope, known as histopathological analysis. This approach is designed to find particular morphological features within the tissue that are flexible and trip being the characteristics of the tumor sub-type and gradation level. Pancreatic cancer generally has some subtypes that are attributed to early forms of diagnosis such as pancreatic ductal adenocarcinoma (PDAC), neuroendocrine tumors (NETs), and some notable ones that are termed as rare like acinar cell carcinoma.

Unlike other types of pancreatic cancers (other than pancreatic ductal adenocarcinoma, or PDAC), which account for the majority of pancreatic malignancies, PDAC has distinct histological features. Such characteristics usually consist of glandular differentiation, desmoplastic stroma (which is a fibrous tissue densely surrounding the tumors), and nuclear atypia (abnormality in size, shape, and staining pattern of cell nuclei). These features visualize an entire image of the tumor and its possible issues. On the other hand, histological changes also exist in NETs (neuroendocrine tumors) where a neuroendocrine differentiation is seen, thus manifesting in different kinds of histological profiles. These tumors may be compact, glandular, or trabecular, or partake complex of the morphology of the cells, which indicates their different origins and differentiation pathways. The making of the neuroendocrine markers mentioned is critical because you can determine where the given NET position lies within the whole spectrum of pancreatic neoplasms. Obviously, for such a long time many doctors have used histopathological attribution to diagnose pancreatic cancer but, at the same time, it possesses

some disadvantages. The cases with superimposed histological patterns or mixed histology might be hard to accurately sub-denomination this way. These kinds of arguments require more authenticated methods to be employed to avoid wrong diagnoses and prognoses.

As Collisson et al. (2019) state, this sets the need for the combination of complementary diagnostic approaches to achieve better pathology. Visits using several instruments including molecular profiling, immuno-histochemistry, and more advanced imaging modalities might provide lots of supportive data to help us determine the most precise characterization among pancreatic tumors. Through the multidisciplinary implementation of histopathological analysis and other techniques, physicians will be able to achieve higher diagnostic accuracy and choose appropriate treatment strategies to help patients. Classification of histopathological diagnosis is still the golden standard in the diagnosis of pancreatic tumors, but the drawbacks dictate the adoption of alternative approaches to fully grasp the genesis, behavior, and evolutionary potential of the tumor. Pancreatic cancer can be confirmed by employing combination approaches such as using new diagnostic techniques and histopathology for precise diagnosis and personalized treatment planning for the patients.

Molecular Classification:

With the advent of modern genomic profiling the novelty is sublime in the way that these methods enrich the diagnostic process in the sense that they allow a better understanding of the specific gene abnormalities causing pancreatic tumors. Molecular biomarkers helped professionals estimate the degree of similarity in the pathology of pancreatic ductal carcinoma (PDAC) and molecular classification revealed four subtypes of PDAC based on genetic alterations. These new biomarkers now greatly enhance our knowledge of the biological behaviors of the PDAC subtypes as well as the therapeutic susceptibilities of each. This grouping of PDAC, however, using genomic integration technologies, showed the subtypes showing quasi- mesenchymal, exocrine-like, and immunogenic features each with its particular response to therapy and prognosis. Moreover, molecular profiling serves as a crucial tool in pinpointing actionable mutations like KRAS, TP53, and SMAD4 alterations, which play pivotal roles in tumor development and progression (Bailey et al., 2016). By identifying these molecular signatures, clinicians can tailor treatment strategies to target specific genetic vulnerabilities, thus paving the way for personalized therapeutic interventions.

This mesenchymal-like subtype (quasi-mesenchymal), for instance, may acquire resistance to traditional chemo, however, could potentially respond well to microtargeted treatments that affect specific molecular pathways that participate in its development. On the contrary, the immune dimension may result in potent immune responses under mimic immunotherapy, triggering the immune system of the host to eliminate the tumor cells. This mentioned, however, promotes more precise therapy efficacy and decreases the risk of unwanted effects associated with non-selective treatments. The molecular classification of pancreatic tumors reflects a complex framework of heterogeneity and therapy personalization in patient care. This method, which is very specific about the intricate interplay of genetic alterations, is a symptom of the new exact approach in the management of pancreatic cancer. It brings about improvement in the patient's outcomes and quality of life.

Radiological Classification:

Radiological imaging, which includes examination with the help of computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) is of paramount importance for staging of cancer and assessment of resectability as well as in treatment planning. It is the key component of diagnosing a tumor's morphological features, vascular patterns, and distant spread, essentially acting as a source of crucial information for treating specialists. The present conventional method of radiological classification, nevertheless, is not precise because of its shortcomings such as the lack of objective data and quantification, and therefore, nonexistent appreciation of differences. Now, radionic is entering the scene. Through the extraction of qualitative image characteristics that may be acquired from CT or X-ray scans, radiomic analysis enables a more precise diagnosis and prediction of prognosis. To put it in a nutshell, it does a more information-rich and data- based approach to the identification of cancer types.

In addition to that, recent improvements in machine learning algorithms allowed the radio genetic trait to be developed. Such signatures link the molecular subtypes with the imaging and clinical outcomes in patients. In his 1948 essay, George Orwell launched a scathing attack on totalitarian regimes, specifically positing the dangers of thought control and the idea of an Orwellian society. By rigorously analyzing his philosophy and stylistic choices, we will delve deeper into his warning against the prevalent trend The diagnosis and selection of treatment strategy have been upgraded significantly as a result of improvements in this area. Pcsits can make use of the treasury of these data to create more targeted treatments hence the outcome will improve. In its essence, the use of radiological imaging jointly with radionic analysis and machine learning caused its revolution promoting tumor assessment and planning treatment. It has paved the way for a more personalized and effective approach to cancer care. (Cassinotto et al., 2020)

Immunohistochemistry-Based Classification in Pancreatic Tumors

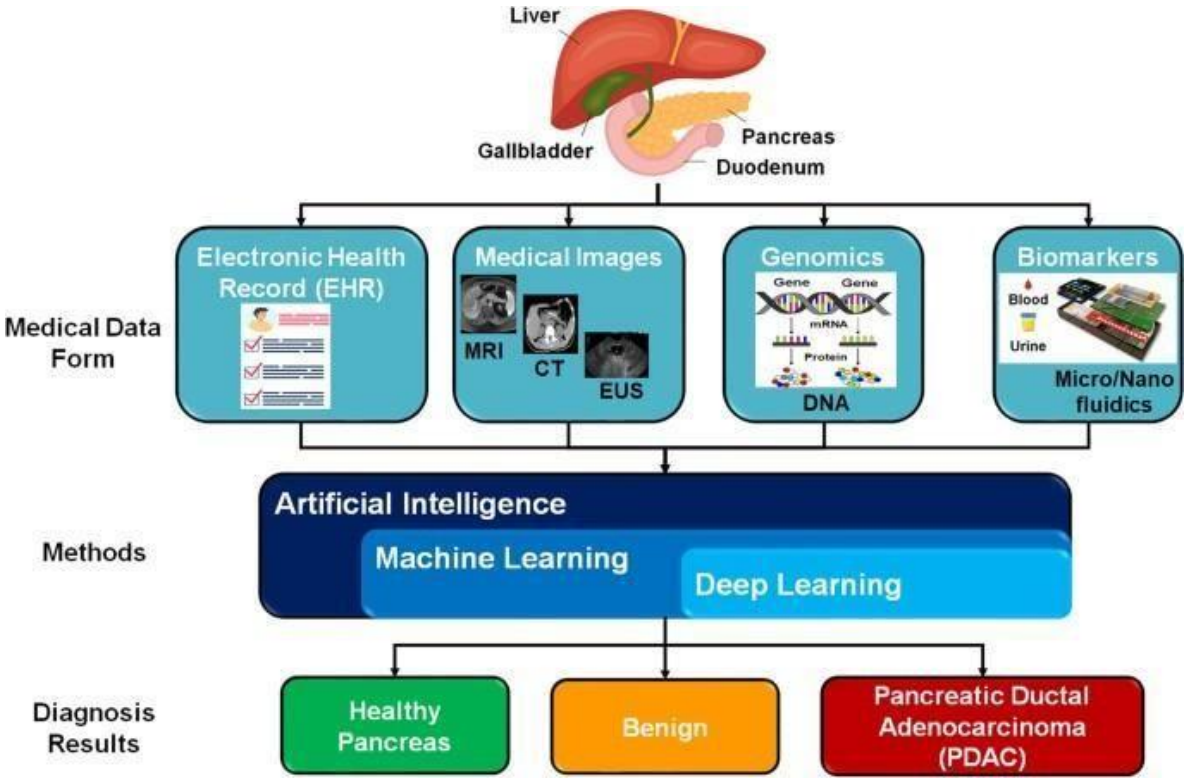
Immunohistochemistry (IHC) has come to be a quintessential tool for the assessment of pancreatic tumor molecular make-up that helps better comprehend the individuality of these patients and as a result, formulate personalized treatment programs. It is a basis technique that allows the detection of various tumor features and patterns of protein expression through the process of proteome analysis. Whether by detecting antigens localized in tumor tissues or characterizing cells at the molecular level, IHC has become a big contributor to our understanding of cancer and those entities connected to it. By doing such, it becomes possible for oncologists to assess even the minutest differences among pancreatic neoplasm types, which ultimately translates into customized treatment approaches. Through IHC clinicians can have the ability to predict the tumor composition based on the unique molecular profiles of each individual, thereby likely more accurate diagnostics can

be obtained and the way doctors make decisions can be affected. Therefore, it may be summarized that the IHC turns out to be the by far most critical evaluation tool for reliable diagnosis of pancreatic malignant tumors, which can subsequently not only lead to the achievement of much higher precision treatment of cancer patients but also constitute one of the key cornerstones of individualized treatment approaches for improved patient outcomes.

Emerging Techniques for Pancreatic Tumor Classification

Genomic Profiling- With IHC, information about the protein expression patterns is provided, providing the immunologic process needed for pancreatic tumors as seen from the molecular level. Nevertheless, It is Difficult to Have a Full Understanding of Pancreatic Cancer Development Without the Help of Genomic Profiling As a Complementary Tool, It Studies the Genetic Alterations that are Implicated in the Tumorigenesis Process of Pancreatic Cancer. Genomic information integration with IHC results increases the resolution of tumor typing and aids in the identification of clinically actionable mutations and important signaling pathways making disease progression easier to detect. Jones et al. (2018) and Collisson et al. (2019) are the scientists who stipulate that the genomic approach helps to stratify patients' pancreas tumors based on mutation profiles. The division between the subtypes is not only the explanation of the disease itself but also marks the path for personalized medicine where the treatment strategies are developed based on the molecular signature of each tumor. In light of this, blending the strengths of both techniques will pave the way for clinical agents to guide towards developing more effective and selective cancer treatments, which is good for pancreatic cancer patients.

Machine Learning-Based Classification: Machine Learning (ML) has brought about a paradigm shift in the classification of tumors, particularly in the context of pancreatic malignancies. Leveraging vast datasets, ML algorithms have been instrumental in unraveling complex molecular signatures that characterize different tumor types. In pancreatic cancer, this has led to the development of machine learning models trained on Immunohistochemistry (IHC) data, showing promise in enhancing diagnostic accuracy and prognostic stratification. A seminal study conducted by Chen et al. in 2020 is a testament to the potential of ML in the field of pancreatic tumor classification. By employing ML-based approaches, the researchers were able to discern subtle variations in protein expression patterns, allowing for the creation of robust classification models. These models not only accurately classified pancreatic tumors but also offered enhanced predictive power, which is crucial for optimizing treatment strategies and improving patient outcomes.



(Source: Karar *et al.*, 2023)

The significance of this study lies in its ability to demonstrate how machine learning, particularly when trained on molecular data such as IHC, can revolutionize tumor classification paradigms. Such advancements are critical in the clinical setting, where accurate and reliable tumor classification is essential for guiding treatment decisions and improving patient care. Chen et al.'s study serves as a noteworthy example of the transformative potential of machine learning in the realm of tumor classification, particularly in the context of pancreatic cancer. As our understanding of the molecular underpinnings of cancer continues to evolve, the integration of machine learning into diagnostic and prognostic workflows holds

tremendous promise for improving patient outcomes and advancing personalized medicine.

Conclusion

The classification of pancreatic tumors presents a multifaceted challenge, necessitating a multidisciplinary approach that integrates histopathological, molecular, and radiological techniques. The traditional histopathological classification, although foundational, has limitations in capturing the underlying molecular heterogeneity of tumors. Molecular classification, on the other hand, delves deeper into the genetic makeup of tumors, offering insights into biological behaviors and therapeutic susceptibilities. The advent of genomic profiling has enabled the subdivision of pancreatic ductal adenocarcinoma (PDAC) into distinct subtypes, each with unique responses to treatment and clinical outcomes. Meanwhile, radiological imaging has transformed with radiomic analysis, providing a more objective and data-driven approach to tumor characterization. Immunohistochemistry (IHC) stands at the intersection of these classification methods, giving valuable insights into protein expression patterns. By leveraging genomic profiling and machine learning-based classification, IHC enriches the precision of tumor classification, facilitating the detection of actionable mutations and crucial signaling pathways implicated in disease progression. The synergy between IHC, genomic profiling, and machine learning-based classification holds the promise of personalized treatment strategies tailored to the unique molecular signature of each patient's tumor. Integrating histopathological, molecular, and radiological classification approaches, supplemented by immunohistochemistry and machine learning, provides a comprehensive framework for understanding pancreatic tumors. This multidisciplinary approach enhances diagnostic accuracy and lays the groundwork for personalized treatment strategies, ultimately improving outcomes for pancreatic cancer patients.

References:

Al-Hawary, M. M., Francis, I. R., Chari, S. T., et al. (2014). Pancreatic ductal adenocarcinoma radiology reporting template: Consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. Radiology, 270(1), 248-260.

Bailey, P., Chang, D. K., Nones, K., Johns, A. L., Patch, A. M., Gingras, M. C., ... & Thomas, J. (2016). Genomic analyses identify molecular subtypes of pancreatic cancer. Nature, 531(7592), 47-52.

Cassinotto, C., Chong, J., & Zogopoulos, G., et al. (2020). Radiomics in pancreatic cancer: Early experiences and future perspectives. Abdominal Radiology, 45(8), 2352-2368.

Chen, J. Y., Hsu, C. Y., Liu, Y. C., Liang, C. W. (2020). Identification of driver genes in pancreatic cancer by a novel machine learning framework. BMC Bioinformatics, 21(10), 1-12.

Collisson, E. A., Sadanandam, A., Olson, P., & Gray, J. W. (2011). Subtypes of pancreatic ductal adenocarcinoma and their differing responses to therapy. Nature Medicine, 17(4), 500-503. Collisson, E. A., Bailey, P., & Chang, D. K., et al. (2019). Molecular subtypes of pancreatic cancer. Nature Reviews Gastroenterology & Hepatology, 16(4), 207-220.

Hruban, R. H., Goggins, M., Parsons, J., & Kern, S. E. (2000). Progression model for pancreatic cancer. Clinical Cancer Research, 6(8), 2969-2972.

Jones, S., Zhang, X., Parsons, D. W., Lin, J. C., & McLellan, M.

D. (2018). Core signaling pathways in human pancreatic cancers revealed by global genomic analyses. Science, 321(5897), 1801- 1806.

Jiao, Y., Shi, C., Edil, B. H., et al. (2011). DAXX/ATRX,

MEN1, and mTOR pathway genes are frequently altered in pancreatic neuroendocrine tumors. Science, 331(6021), 1199-

1203.

Marinoni, I., Kurrer, A. S., Vassella, E., et al. (2014). Loss of DAXX and ATRX are associated with chromosome instability and reduced survival of patients with pancreatic neuroendocrine tumors. Gastroenterology, 146(2), 453-460.e5.

Moffitt, R. A., Marayati, R., Flate, E. L., et al. (2015). Virtual microdissection identifies distinct tumor- and stroma-specific subtypes of pancreatic ductal adenocarcinoma. Nature Genetics, 47(10), 1168-1178.

Siegel, R. L., Miller, K. D., & Jemal, A. (2020). Cancer statistics, 2020. CA: A Cancer Journal for Clinicians, 70(1), 7-30.

Karar, M. E., El-Fishawy, N., & Radad, M. (2023, April 17). Automated classification of urine biomarkers to diagnose pancreatic cancer using 1-D convolutional neural networks. Journal of Biological Engineering.
https://doi.org/10.1186/s13036-023-00340-0

Xu Z-H, Wang W-Q, Lou W-H, Liu L. Insight of pancreatic cancer: recommendations for improving its therapeutic efficacy in the next decade. J Pancreatol 2022;5:58-68. doi: 10.1097/JP9.0000000000000093