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Classification of Prostate Cancer by Gleason Grading in Peshawar, Pakistan

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Abstract

The present study was conducted to explore the performances of Gleason Grading of patients with PC. The purpose of the study was to examine the Gleason Grading to check the status of tumor in the patients The study has an objective to grade the tumor of prostate cancer among the patients. The study was conducted in the Shaukat Khanum Cancer Hospital Peshawar. The study has included 268 random patients were examined in the process of Gradings. The data were collected from the patients from January 2020 to October 10th 2021, 239 were found with Prostate Cancer. Models' performances were evaluated on independent test datasets. Gleason grading model has been adopted with five different pattern. The tumor on the basis of expert opinion categorize in different grades. The majority of high-grade cancers with either Gleason pattern 4 (n = 36, 80% of cases) or Gleason pattern 5 (n = 2, 4% of cases) were found to have glomerulations on the same core. Pattern 4 cases were evenly split between those exhibiting big or irregular cribriform glands and those exhibiting mostly fused poorly formed glands (49 percent and 51 percent, respectively). The highest Gleason score carcinoma in the majority of cases shared a core with the glomeruloid alteration. Only a few of the pattern 4 malignancies developed higher Gleason score carcinoma on further cores (5/36, 14 percent), and none of the cores with only pattern 3 carcinoma and glomeruloid characteristics had higher score carcinoma on other cores (0/7).

Background of the study

The most pertinent uses of artificial intelligence (AI) involve machine learning (ML) techniques that improve cancer diagnosis. These techniques include classifying tissues and subsequently identifying cardiovascular organs. In terms of detecting metastatic breast cancer, the human physician error rate was reduced by 85%. Using computer vision techniques, other prospective applications include the quick diagnosis of radiographic abnormalities, the definition of surgical anatomy, and the categorization of malignant tissues in pathologic specimens (Viscaino et al., 2019). The growth of computer-aided diagnostics in medicine is the result of several reasons.

The medical interview and physical examination of the ear, supplemented by a manual otoscope, are currently used to diagnose these illnesses. To aid in the diagnosis, otolaryngologists also employ additional tools including oto-endoscopes and oto-microscopes. Due to their high cost, clinics only have a few of these tools. As a result, only the most complicated ear disease patients are checked using such tools. Due to a shortage of experts, the situation deteriorates in third-world nations, and general practitioners struggle to provide a precise and trustworthy diagnosis.

Treatment is delayed because manual processing takes a long time. Additionally, manual processing is time- and money-consuming. Deep learning can produce higher Gleason scores while lowering human mistake rates by improving accuracy everywhere. Deep learning methods have already shown encouraging results in the field of medical imaging. Computer-Aided Diagnosis (CAD) has been utilised in several medical sectors since its inception in 1980.

Machine learning techniques are frequently employed to find cancer in CAD applications that leverage medical imagery. Machine learning and deep learning technology have made considerable advancements during the past ten years. Additionally, this advancement benefits CAD applications. High-level characteristics may be extracted from the photos using deep learning. Deep learning techniques may make it feasible to obtain high detection accuracy without the need for manually created features because features may be retrieved during training. Deep learning approaches have also been quite popular in recent years for Gleason grading and prostate cancer diagnosis because to massively parallel computing (GPUs).

- The study has an objective to grade the tumor of prostate cancer among the patients.

Literature Review

Most men with prostate cancer are elderly males. Less than 1% of men with prostate cancer are diagnosed while they are under 50, and more than 80% of men with prostate cancer are over 65. If prostate cancer runs in one's family, one's risk of developing it rises. The precise cause of cancer has not yet been determined, although some diets, including those high in red meat and lipids, have been associated to prostate cancer. The substance created as a result of cooking beef at a high temperature is harmful to the prostate. Depending on what they eat, different nations have different rates of prostate cancer. Compared to nations where the main staples of the diet are vegetables and rice, it is more prevalent in nations with heavy meat and dairy intake.

One more element is hormones. Higher fat intake causes testosterone to rise, which promotes the formation of prostate cancer. Prostate cancer is also more common when people don't exercise. There are a few workplace risks that have also been identified as prostate cancer risk factors. For instance, several employment in the rubber and battery industries expose employees to metal cadmium, which increases their risk of developing prostate cancer. Aspirin, finasteride (Proscar), and dutasteride (Avodart) are examples of medications that have been shown to lower the chance of getting prostate cancer. Similar to this, eating vegetables like broccoli, cauliflower, and cabbage regularly has been shown to reduce the risk of developing prostate cancer ["The Basics of Prostate Cancer," 2018].

Artificial neural networks are often the main building block of deep learning models. However, certain kinds, like the nodes in Deep Boltzmann Machines, can include grammatical formulas or latent (unobserved) variables that are organised layer by layer in deep generative models. In deep networks, learning differs from layer to layer in terms of the degree of abstraction and the way that incoming data is transformed. In the case of image processing, the data may consist of a three-dimensional array of pixels. The first representational layer captures the understanding of edges, the second representational layer may capture the order or arrangement of edges, the third representational layer may capture features of a car such as formation of tyres, windscreen, headlights, and wipers, and the fourth representational layer may discern the presence of a car in the image.

Iqbal and others (2021), Due to its inadequate diagnostic infrastructure, prostate cancer (PCa), a serious form of cancer, significantly increases male mortality rates. Cancer patients' photos include intricate and important elements that might be difficult for typical diagnostic methods to easily extract. Long short-term memory (LSTM) and Residual Net (ResNet 101), which are not dependent on manually created features, were used in this study. The outcomes were evaluated against manually created features like texture, morphology, and grey level co-occurrence matrix (GLCM) using support vector machine (SVM), Gaussian Kernel, k-nearest neighbor-Cosine (KNN Cosine), kernel naive Bayes, decision tree (DT), and RUSBoost tree non-deep learning classifiers. This work used machine learning and deep learning techniques to minimise the characteristics of photos of cancer.

Emine and others (2020), One of the hottest subjects in machine learning, a subset of artificial intelligence, at the moment is deep learning. Machine learning is the term used to describe statistical models that enable computers to carry out particular activities without being explicitly trained to do so. In reality, these models look for structural patterns in the data to comprehend novel circumstances and respond as effectively as feasible. Machine learning uses a variety of approaches, including k-NN, SVM, k-means, decision trees, association rules, etc. The idea of combining neural networks to create deep neural networks is what sets deep learning apart from these techniques.

Methodology

The study was conducted for the classification of prostate cancer by using Gleason grading method. The study was conducted at Shaukat Khanum Hospital Peshawar. The study has used needle biopsies for the prostate cancer and then divided into Gleason grading. The study duration was 2 years and the data collection was collected from Feb 2020 to March 2022. The study has included 100 patients of Prostate Cancer in Shaukat Khanum Hospital Peshawar. The biopsies reports were collected for the sample patients from the Laboratories of Shaukat Khanum Hospital. The reports were then reviewed by the Expert Pathologist and then the data has been divided into different grades. Some of the biopsies reports were reviewed by urologist for the best opinion and to collect most accurate data by following Jaudah et al., (2013).

A total of 100 patients were included in the process of data collection. The study has used quota sampling (non probability sampling). The sampling procedure was stopped when the data collected for 100 patients. The data were collected from the reviewed reports of biopsies and then divided the stated information into Gleason grading from 1 to 12. The study excluded vulnerable groups, such as adults with learning disabilities, those who were unconscious or severely ill, adults with dementia or with other psychological disorders.

The study has used SPSS v 24 for the data analysis on the data collected from the biopsies reports. The data then entered in MS Excel and Kappa test was used. Kappa test was used to check the significance of the external pathologist and urologic pathologist on the same reviewed reports. The study then following the method of Jaudah et al., (2013) for the Grading the scores:

Kappa < 0.20	=	Poor agreement
Kappa < 0.21 to 0.40	=	Slight agreement
Kappa < 0.41 to 0.60	=	Fair agreement
Kappa < 0.61 to 0.80	=	Good agreement
Kappa < 0.81 to 100	=	Very good

Results & Discussions

Demographics

Gender	Frequency	Percentage
Male	86	36
Female	153	64
Total	239	100

The table shows the findings of gender wise distribution of the patients included for the data collection. In the process of data collection, both male and female patients were included. The PET and CT have been gathered for both genders. The table shows that the male patients were 86 with 36 percent and female patients were 153 with 64 percent. The findings show that the female respondents were in majority.

Age Wise

Age	Frequency	Percentage
Below 30	12	5
31 to 40	51	21
41 to 60	122	51
Above 60	54	23
Total	239	100

The table shows the findings of age wise distribution of the patients included for the data collection. In the process of data collection, both male and female patients were included. The PET and CT have been gathered for both genders with different range of ages. The table shows that the patients with below age 30 years were 12 with 5 percent, 31 to 40 years of age were found 51 patients, 41 to 60 years of age were 122 and above 60 years of age were found 54 patients with 23 percent. The findings show that the patients of age from 41 to 60 years were in majority.

Prostate cancer prognosis might differ from patient to patient. Below grades, with Gleason sums of 6 or lower, may not have any clinical repercussions, but more aggressive tumours, with Gleason sums 8, 9, or 10, might cause mortality in a short period of time (23). A cohort of 767 cancer patients who were untreated was the subject of many investigations by Albertsen et al. Between 6 and 11 percent of men with Gleason total 5 tumours died from cancer before age 20. Few members of the overall cohort survived more than 15 years following diagnosis among patients with tumours that had a higher Gleason sum, with mortality rates from prostate cancer reaching up to 70% (Gleason scores 7 or 8) and 87 percent (Gleason scores 10)..

Pattern 1	The cancerous prostate cells closely resemble normal prostate cells. The glands are small, well-formed, and closely packed
Pattern 2	The glands are larger and have more tissue between them
Pattern 3	The tissue still has recognizable glands, but the cells are darker. Some cells have left the glands and have started to invade the surrounding tissue.
Pattern 4	The tissue has few recognizable glands. Many cells are invading the surrounding tissue
Pattern 5	The tissue does not have recognizable glands. There are often just sheets of cells throughout the surrounding tissue.

No of Patients	66
Mean of Age	44-70
PSA	
< 4	2(4%)
4 – 9.9	20(44%)
> 10	2(4%)
Unknown	21(47%)
Overall Gleason Score	
< 6	7(16%)
7	32(71%)
> 8	6(13%)
No of cores involved in tumor	
< 2	25(55%)
3- 5	13(29%)
> 6	7(16%)
% of cores involved by higher grade (7)	
< 2	33(73%)
3-5	9(20%)
> 6	3(7%)

In our consult material, prostatic carcinoma with glomeruloid characteristics was an uncommon finding, occurring in 0.6% of prostatic adenocarcinoma patients observed over a 9-month period. Table provides an overview of the clinical and pathologic features of the patient group and biopsies. The typical patient was 66 years old (45–86 years). At the time of biopsy, PSA was detectable in 24 instances (53%) and had an average concentration of 7.6 ng/mL (range, 2.9-48 ng/mL). Generally speaking, high-grade and high-volume illness were linked to prostatic adenocarcinoma with glomeruloid characteristics on needle biopsy.

In 84 percent (38/45) of the biopsies in this group, the highest Gleason score was 7 or above (71 percent Gleason score 7, 9 percent Gleason score 8, and 4 percent Gleason score 9). Each instance had an average of 3 cores with tumour (range, 1–10), and tumour made up an average of 30% of each afflicted core (5 percent –95 percent). High-grade carcinoma was detected on average in 2 cores in subjects with high-grade (pattern 4 or 5) illness (range, 1–8). On the needle biopsy, five patients (11%) indicated perineural invasion, although none revealed extraprostatic extension. Typically, glomerulations were only visible on a small percentage of the cores from each instance (1–2 cores).

In the majority of glomerulations, smooth, spherical cribriform structures with only tiny slit-like gaps were seen inside relatively small dilated glands (Figs. 1-3), while in a few unusual instances, bigger cribriform structures with many "punched-out" lumina were present (Fig. 4). The cribriform gland was always attached to the surrounding dilated gland by a slender stalk-like stalk. Rarely, the base of the cellular tuft revealed a fragile fibrovascular core (Fig. 5).

Gleason pattern of carcinoma on same core as glomerulations

The majority of high-grade cancers with either Gleason pattern 4 (n = 36, 80% of cases) or Gleason pattern 5 (n = 2, 4% of cases) were found to have glomerulations on the same core. Only a small percentage of glomerulations (n = 7, 16% of cases) were completely encircled with pattern 3 malignancy. Only a minority of the cases with surrounding pattern 4 cancer (n = 3, 9 percent) were 4 + 4 = 8, whereas the majority of cases with surrounding pattern 4 cancer (n = 24, 66 percent) were rated as 3 + 4 = 7.
Pattern 4 cases were evenly split between those exhibiting big or irregular cribriform glands and those exhibiting mostly fused poorly formed glands (49 percent and 51 percent, respectively) (Figs. 6 and 7). Small glomerulations, massive glomeruloid structures, and cribriform pattern 4 cancer often underwent morphological changes (Figs. 8 and 9).

Gleason pattern of carcinoma on other cores

The highest Gleason score carcinoma in the majority of cases shared a core with the glomeruloid alteration. Only a few of the pattern 4 malignancies developed higher Gleason score carcinoma on further cores (5/36, 14 percent), and none of the cores with only pattern 3 carcinoma and glomeruloid characteristics had higher score carcinoma on other cores (0/7).

Pathologic follow-up on subsequent radical prostatectomy

All 7 patients who had glomerulations evident on needle biopsy but no associated pattern 4 carcinoma or Gleason pattern 3 cancer were followed up. Following the cancer diagnosis, 6 (86%) of these patients had brachy therapy or external beam radiation treatment. We only looked at one patient who had a radical prostatectomy. This specimen, which was partially submitted, exhibited tertiary and intensely focused cribriform Gleason pattern 4 cancer in addition to a predominance of Gleason 3 + 3 = 6 carcinoma.

Conclusion

The Veteran's Affairs Cooperative Research Group (VACURG) research from 1959 to 1964, which involved 270 men with prostate cancer, served as the foundation for the Gleason grading system. A prostate cancer grading system was developed by Dr. Donald Gleason, Chief of Pathology at the Veteran's Hospital in Minnesota, based on the various histologic features of the disease. A score was developed that combined a tumor's two most frequent grade patterns, with values ranging from 2 to 10. This was done since most tumours generally had two histologic patterns. The Gleason grading system continues to be one of the most effective prognostic indicators in prostate cancer despite considerable changes in the clinical and histologic diagnosis of the disease. Although this system has undergone major changes, it still includes flaws that may have an adverse effect on patient care. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma led to recent revisions to the Gleason grading system, which are highlighted in this article's description of the current prostate cancer grading landscape. We also examine the shortcomings of the existing Gleason grading scheme and offer a Gleason score substitute that has been independently verified. The Gleason score continues to be the most accurate predictor of the prognosis for prostate cancer and is important for therapeutic therapy. For a patient's prognosis and treatment choices, a proper prostate cancer diagnosis and grading are essential. The Gleason grading scheme as a whole has been enhanced by the ISUP grading consensus conferences in 2005 and 2014. A new prostate cancer grading system, however, improves upon the drawbacks that this method still has.

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