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Classification Prediction of SBRCTs Cancers Using Artificial Neural Network

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Abstract: *Small Blue Round Cell Tumors (SBRCTs) are a heterogeneous group of tumors that are difficult to diagnose because of overlapping morphologic, immunehistochemical, and clinical features. About two-thirds of EWSR1-negative SBRCTs are associated with CIC-DUX4-related fusions, whereas another small subset shows BCOR-CCNB3 X-chromosomal par acentric inversion. In this paper, we propose an ANN model to Classify and Predict SBRCTs Cancers. The accuracy of the classification reached 100%.*

Keywords: ANN, DNA, SBRCT.

1. INTRODUCTION

In histopathology, a small-blue-round-cell tumor (abbreviated SBRCT), also known as a small-round-blue-cell tumor (SRBCT) or a small-round-cell tumor (SRCT), is any one of a group of malignant neoplasms that have a characteristic appearance under the microscope, i.e. consisting of small round cells that stain blue on routine H&E stained sections.

These tumors are seen more often in children than in adults. They typically represent undifferentiated cells. The predominance of blue staining is because the cells consist predominantly of nucleus, thus they have scant cytoplasm [1,2].

An Examples of SRBCT are Ewing Sarcoma (EWS), habdomyosarcoma (RMS), Neuoblastoma (NB), Burkitt's lymphoma (BL).

Ewing Sarcoma is a malignant small, round, blue cell tumor. It is a rare disease in which cancer cells are found in the bone or in soft tissue. The most common areas in which it occurs are the pelvis, the femur, the humerus, the ribs, the mandible and clavicle (collar bone) [1].

Since a common genetic locus is responsible for a large percentage of Ewing sarcoma and primitive neuroectodermal tumors, these are sometimes grouped together in a category known as the Ewing family of tumors [2].

Ewing's sarcoma occurs most frequently in teenagers and young adults, with a male/female ratio of 1.6:1[3].

Although usually classified as a bone tumor, Ewing's sarcoma can have characteristics of both mesodermal and ectodermal origin, making it difficult to classify [4].

James Ewing (1866–1943) first described the tumor, establishing that the disease was separate from lymphoma and other types of cancer known at that time [5,6].

habdomyosarcoma, or **RMS**, is an aggressive and highly malignant form of cancer that develops from skeletal (striated) muscle cells that have failed to fully differentiate. It is generally considered to be a disease of childhood, as the vast majority of cases occur in those below the age of 18. It is commonly described as one of the "small, round, blue cell tumours of childhood" due to its appearance on an H&E stain. Despite being a relatively rare cancer, it accounts for approximately 40% of all recorded soft tissue sarcomas [1-3].

RMS can occur in any site on the body, but is primarily found in the head, neck, orbit, genitourinary tract, genitals, and extremities. There are no clear risk factors for RMS, but the disease has been associated with some congenital abnormalities [1,4]. Signs and symptoms vary according to tumor site, and prognosis is closely tied to the location of the primary tumor. Common site of metastasisinclude the lungs, bone marrow, and bones [5,6]. There are many classification systems for RMS and a variety of defined histological types. Embryonal rhabdomyosarcoma is the most common type and comprises about 60% of cases [7].

Patient outcomes vary considerably, with 5 years survival rates between 35% and 95% depending on the type of RMS involved, so clear diagnosis is critical for effective treatment and management [7,8]. Accurate and quick diagnosis is often difficult due to the heterogeneity of RMS tumors and a lack of strong genetic markers of the disease. Treatment usually involves a combination of surgery, chemotherapy, and radiation. Sixty percent to 70% of newly diagnosed patients with nonmetastatic disease can be cured using this combined approach to therapy. Despite aggressive multimodality treatment, less than 20% of patients with metastatic RMS are able to be cured of their disease [9].

Neuroblastoma (NB) is a type of cancer that forms in certain types of nerve tissue. It most frequently starts from one of the adrenal glands, but can also develop in the neck, chest, abdomen, or spine. Symptoms may include bone pain, a lump in the abdomen, neck, or chest, or a painless bluish lump under the skin [1].

Occasionally, neuroblastoma may be due to a mutation inherited from a person's parents. Environmental factors have not been found to be involved. Diagnosis is based on a tissue biopsy. Occasionally it may be found in a baby by ultrasound during pregnancy. At diagnosis, the cancer has usually already spread. The cancer is divided into low-, intermediate-, and high-risk groups based on a child's age, cancer stage, and what the cancer looks like [1,2].

Treatment and outcomes depends on the risk group a person is in [1,4]. Treatments may include observation, surgery, radiation, chemotherapy, or stem cell transplantation [1]. Low-risk disease in babies typically has a good outcome with surgery or simply observation [4]. In high-risk disease, chances of long-term survival, however, are less than 40% despite aggressive treatment [4].

Neuroblastoma is the most common cancer in babies and the third-most common cancer in children after leukemia and brain cancer [4]. About one in every 7,000 children is affected at some time [2]. About 90% of cases occur in children less than 5 years old and it is rare in adults [2,3]. Of cancer deaths in children, about 15% are due to neuroblastoma [3]. The disease was first described in the 1800s [5].

Burkitt's lymphoma (BL) is a cancer of the lymphatic system (in particular, B lymphocytes). It is a highly aggressive lymphoma that is usually found in extranodal sites or presenting as an acute leukemia.

Currently Burkitt's lymphoma can be divided into three main clinical variants: the endemic, the sporadic and the immunodeficiency-associated variants.

- The endemic variant occurs in equatorial Africa. It is the most common malignancy of children in this area. Children affected with the disease often also had chronic malaria which is believed to have reduced resistance to the Epstein-Barr virus and allowed it to take hold. Disease characteristically involves the jaw or other facial bone, distal ileum, cecum, ovaries, kidney or the breast.
- The sporadic type of Burkitt lymphoma (also known as "non-African") is another form of non-Hodgkin lymphoma found outside of Africa. The tumor cells have a similar appearance to the cancer cells of classical African or endemic Burkitt lymphoma. Again it is believed that impaired immunity provides an opening for development of the Epstein-Barr virus. It accounts for 30-50% of childhood lymphoma. Jaw is less commonly involved, comparing with the endemic variant. Ileo-cecal region is the common site of involvement.
- Immunodeficiency-associated Burkitt lymphoma is usually associated with HIV infection or occurs in the setting of post-transplant patients who are taking immunosuppressive drugs. Actually, Burkitt lymphoma can be the initial manifestation of AIDS.

By morphology (i.e. microscopic appearance) or flow immunophenotype, it is almost impossible to differentiate these three clinical variants. Immunodeficiency-associated Burkitt lymphoma may demonstrate more plasmacytic appearance or more pleomorphism, but these features are not specific.[2,3]

Artificial neural network, which simulates the human brain in solving a problem, is a more common approach that can address this type of problem. Thus, attempting to develop an adaptive system such as artificial neural network to predict the tumor condition based on the results of these factors.

2. THE OBJECTIVES OF THIS STUDY ARE:

- To identify some appropriate factors that affect the cell،
- To convert these factors into appropriate models for adaptive system coding, and
- To design an artificial neural network that can be used to class predict based on some predefined data for a given environment.

3. THE ARTIFICIAL NEURAL NETWORKS

In information technology (IT), a neural network is a system of hardware and/or software patterned after the operation of neurons in the human brain. Neural networks -- also called artificial neural networks -- are a variety of deep learning technology, which also falls under the umbrella of artificial intelligence, or AI [8-12].
Commercial applications of these technologies generally focus on solving complex signal processing or pattern recognition problems. Examples of significant commercial applications since 2000 include handwriting recognition for check processing, speech-to-text transcription, oil-exploration data analysis, weather prediction and facial recognition [13-15].

How artificial neural networks work

A neural network usually involves a large number of processors operating in parallel and arranged in tiers. The first tier receives the raw input information -- analogous to optic nerves in human visual processing. Each successive tier receives the output from the tier preceding it, rather than from the raw input -- in the same way neurons further from the optic nerve receive signals from those closer to it. The last tier produces the output of the system[16-18].

Each processing node has its own small sphere of knowledge, including what it has seen and any rules it was originally programmed with or developed for itself. The tiers are highly interconnected, which means each node in tier *n* will be connected to many nodes in tier *n-1*-- its inputs -- and in tier *n+1*, which provides input for those nodes. There may be one or multiple nodes in the output layer, from which the answer it produces can be read.

Neural networks are notable for being adaptive, which means they modify themselves as they learn from initial training and subsequent runs provide more information about the world. The most basic learning model is centered on weighting the input streams, which is how each node weights the importance of input from each of its predecessors. Inputs that contribute to getting right answers are weighted higher [19-22].

How neural networks learn

Typically, a neural network is initially trained or fed large amounts of data. Training consists of providing input and telling the network what the output should be. For example, to build a network to identify the faces of actors, initial training might be a series of pictures of actors, nonactors, masks, statuary, animal faces and so on. Each input is accompanied by the matching identification, such as actors' names, "not actor" or "not human" information. Providing the answers allows the model to adjust its internal weightings to learn how to do its job better. For example, if nodes David, Dianne and Dakota tell node Ernie the current input image is a picture of Brad Pitt, but node Durango says it is Betty White, and the training program confirms it is Pitt, Ernie will decrease the weight it assigns to Durango's input and increase the weight it gives to that of David, Dianne and Dakota.

In defining the rules and making determinations -- that is, each node decides what to send on to the next tier based on its own inputs from the previous tier -- neural networks use several principles. These include gradient-based training, fuzzy logic, genetic algorithms and Bayesian methods. They may be given some basic rules about object relationships in the space being modeled. For example, a facial recognition system might be instructed, "Eyebrows are found above eyes," or, "Moustaches are below a nose. Moustaches are above and/or beside a mouth." Preloading rules can make training faster and make the model more powerful sooner. But it also builds in assumptions about the nature of the problem space, which may prove to be either irrelevant and unhelpful or incorrect and counterproductive, making the decision about what, if any, rules to build in very important.

Further, the assumptions people make when training algorithms causes neural networks to amplify cultural biases. Biased data sets are an ongoing challenge in training systems that find answers on their own by recognizing patterns in data. If the data feeding the algorithm isn't neutral -- and almost no data is -- the machine propagates bias[23-26].

Types of neural networks

Neural networks are sometimes described in terms of their depth, including how many layers they have between input and output, or the model's so-called hidden layers. This is why the term *neural network* is used almost synonymously with deep learning. They can also be described by the number of hidden nodes the model has or in terms of how many inputs and outputs each node has. Variations on the classic neural network design allow various forms of forward and backward propagation of information among tiers [27-30].

The simplest variant is the feed-forward neural network. This type of artificial neural network algorithm passes information straight through from input to processing nodes to outputs. It may or may not have hidden node layers, making their functioning more interpretable.[31-35]

More complex are recurrent neural networks. These deep learning algorithms save the output of processing nodes and feed the result back into the model. This is how the model is said to learn.

Convolutional neural networks are popular today, particularly in the realm of image recognition. This specific type of neural network algorithm has been used in many of the most advanced applications of AI including facial recognition, text digitization and natural language processing[36-37].

Applications of artificial neural networks

Image recognition was one of the first areas to which neural networks were successfully applied, but the technology uses have expanded to many more areas, including:

- Chatbots
- Natural language processing, translation and language generation
- Stock market prediction
- Delivery driver route planning and optimization
- Drug discovery and development

These are just a few specific areas to which neural networks are being applied today. Prime uses involve any process that operates according to strict rules or patterns and has large amounts of data. If the data involved is too large for a human to make sense of in a reasonable amount of time, the process is likely a prime candidate for automation through artificial neural networks[38-40].

History of neural networks

The history of artificial neural networks goes back to the early days of computing. In 1943, mathematicians Warren McCulloch and Walter Pitts built a circuitry system intended to approximate the functioning of the human brain that ran simple algorithms.

In 1957, Cornell University researcher Frank Rosenblatt developed the perceptron, an algorithm designed to perform advanced pattern recognition, ultimately building toward the ability for machines to recognize objects in images. But the

perceptron failed to deliver on its promise, and during the 1960s, artificial neural network research fell off [41-45].
In 1969, MIT researchers Marvin Minsky and Seymour Papert published the book *Perceptrons*, which spelled out several issues with neural networks, including the fact that computers of the day were too limited in their computing power to process the data needed for neural networks to operate as intended. Many feel this book led to a prolonged "AI winter" in which research into neural networks stopped.
It wasn't until around 2010 that research picked up again. The big data trend, where companies amass vast troves of data, and parallel computing gave data scientists the training data and computing resources needed to run complex artificial neural networks. In 2012, a neural network was able to beat human performance at an image recognition task as part of the ImageNet competition. Since then, interest in artificial neural networks as has soared and the technology continues to improve [46-52].

4. METHODOLOGY

By looking deeply through the literature and soliciting the experience of Small Blue Round Cell Tumors (SBRCTs) Cancer, a number of factors that are considered to have an effect on the performance of a Small Blue Round Cell Tumors (SBRCTs) Cancer were outlined as in table 1. These factors were cautiously studied and synchronized into a convenient number appropriate for computer coding within the environment of the ANN modeling. These factors were classified as input variables. The output variables embody classification of the cancers.

4.1 The Input Variables

Input variable represent gene names were given numeric abbreviations. These variables were converted into a format suitable for neural network analysis in Just Neural Network (JNN) tool environment.

Table 1 : Input variables.

1- Input 1	7- Input 7
2- Input 2	8- Input 8
3- Input 3	9- Input 9
4- Input 4	10- Input 10
5- Input 5	11- Input 11
6- Input 6	12- Input 12

4.2 The Output Variable

The output variable represents the classification of Small Blue Round Cell Tumors (SBRCTs) . The output variable is based on the current DNA SBRCTs Cancer Dataset.

Table 2 : output variable.

S/N	Output Variable		Represent
	Output 1	Output 2	
1	**0**	**0**	EWS
2	**0**	**0**	BL
3	**1**	**0**	**NB**
4	**1**	**1**	**RMS**

4.3 Design of the Neural Networks

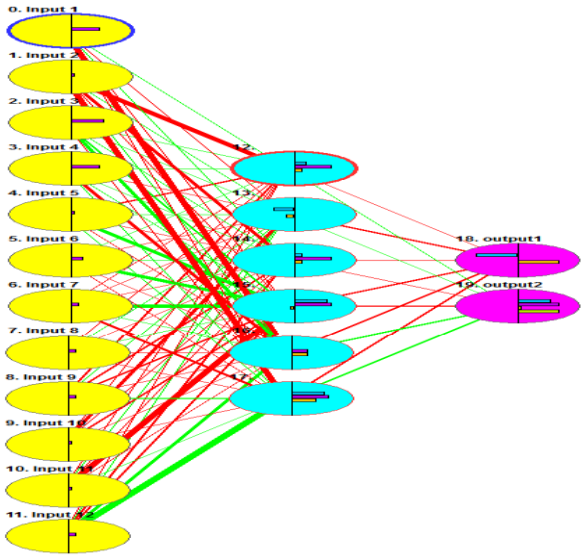

Figure 1: ANN model Architecture

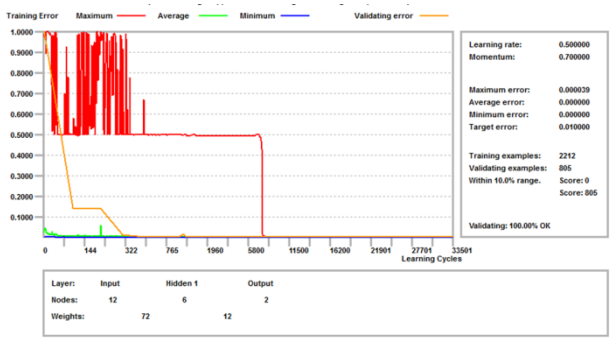

Figure 2: ANN model trained and validated

4.4 Evaluation

Each instance of the dataset represents a patient afflicted with small round blue cell tumors (SBRCT) found during childhood. The dataset consists of 3017 samples. The tumor types include: Ewing Sarcoma (EWS), habdomyosarcoma (RMS), Neuoblastoma (NB), Burkitt's lymphoma (BL).

The dataset contains 4 Classes: 17 BL, 30 EWS, 17 NB and 24 RMS Tumor samples. The training samples consist of 2212 training and 805 test samples. The original data contains 59 attributes. 12 of the most significant are given in the current dataset. Numeric abbreviations are given for gene names.

The final ANN architecture used form training the DNA SBRCTs Cancer is shown in figure 1. The most important factors affecting the DNA SBRCTs Cancer were outlined as shown in table1. JNN tool read the data set and was trained and validated and tested. The accuracy reached 100% as seen in Figure 2.

5. CONCLUSIONS:

DNA SBRCTs Cancer is a very dangerous disease worldwide in the course of revealing the cancer this disease plays a very significant role to evade grave phases and to decrease its development in the world. Artificial Neural network model is a diagnostic system that achieves at an accuracy level is Built. The prediction of DNA SBRCTs Cancer diseases can aid doctor to plan for an improved medication and offer the patient with timely diagnosis. In this paper, ANN model was trained, validated, tested, and the accuracy was 100%. Just Neural Network (JNN) was used for the training and valuation and testing.

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