



# The Applications of Artificial Intelligence in Cancer Biology

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## ABSTRACT

*Having heard that artificial intelligence is going to be used everywhere, the application of artificial intelligence in cancer is one such example. Through deep learning, it is possible to make a model that can particularly predict an individual's response to a specific treatment. It is also said that artificial intelligence can be used to detect the different stages of cancer.*

**Keywords:** Artificial Intelligence, Cancer Biology

## 1. INTRODUCTION

When we hear that someone has cancer in today's society, it is a big deal! Why is that so? Although it does have treatment, every person reacts to the treatment in a different way. For some this treatment works well, while for the rest it fails. But how can we assure that the treatment that is given to each patient will result in a good reaction and a good response? Before we dwell in the specifics of cancer treatment, let us first talk about what cancer actually is.

Cancer, or the uncontrolled growth and abnormal division of cells in a part of the body is one of the leading causes of death in the world. It is caused by the detrimental variation in the human genome through sufficient genetic mutations. There are two primary genes that can influence the formation of cancer : oncogenes and tumor suppressor genes. Proto-oncogenes are genes that enable cell growth. When mutated, they become permanently activated, forming oncogenes that promote cancer. Tumor suppressor genes are genes that slow down cell division or repair DNA damage, and they have the opposite effect of that of proto-oncogenes. These genes when mutated are inactivated and become tumorigenic.

Apoptosis, or the programmed cell death usually occurs when a cell undergoes cellular stresses or abundant DNA damage. However, in a cancer cell, the mutations cause the cell to continue dividing due to reduced sensitivity to the same factors. Tumors, or swellings in a part of the body that are caused by uncontrolled growth of tissues, can be cancerous when malignant. Malignant tumors have the capability to spread to other parts of the body and metastasize. When tumors are benign, they are not cancerous due to the lack of ability to invade neighbouring tissues.

Metastasis is the process by which tumor cells move from the primary tumor to a different organ or region in the body through the lymph or blood. This is the property of malignant tumors that enables cancer. Metastasis occurs through various processes that are supported by the ten cellular hallmarks of cancer, which will be explored in detail later in this paper.

Imaging is used in oncology as a guide through the entire process of cancer screening, diagnosis, staging, treatment response and monitoring. Depending on the individual patient requirements and type of cancer, certain types of imaging like CT scans, MRI scans, ultrasounds, plain films and nuclear medicine are used. Even the various types of treatment used, like surgery, radiation, chemotherapy, immunotherapy, targeted therapy and hormonal therapy vary between patients since each case is unique and requires individual assessment. Some of the most common types of cancer in the world are that of the lung, breast, prostate, colon, liver and stomach.

As we have all heard that artificial intelligence is going to be used everywhere, application of artificial intelligence in cancer is one such example. Through deep learning, it is possible to make a model that can particularly predict an individual's response to a specific treatment. It is also said that artificial intelligence can be used to detect the different stages of cancer. Before we go into detail of where artificial intelligence is being used in terms of cancer and how it can be improvised, it is important to understand artificial intelligence and its components and the usage of it in the medical field is of utmost importance for understanding.

Artificial intelligence is defined to be a wide branch of study of computer science that works towards creating machines whose objectives are to complete complicated tasks that are said to be done only with the use of human intelligence. It is also referred to

as an interdisciplinary between multiple sciences and has multiple approaches from various technical sectors. Two of the main of ideas of artificial intelligence are:

- Deep Learning
- Machine Learning

### Body

It is said that with the mere advancements in deep learning and machine learning, the world is approaching towards creating a paradigm shift in almost every possible sector of the tech industry and eventually every field of study present in the world.

## 2. DEEP ROOTING BACK TO ARTIFICIAL INTELLIGENCE'S EMERGENCE

Not too old, but less than a decade after cracking the Nazi Encryption Machine Enigma, Alan Turing questioned "Can machines think?". Eventually Alan Turing wrote his paper, *Computing Machinery and Intelligence* in 1950, through which the fundamental goal and vision of artificial intelligence was established.

## 3. MORE ABOUT ARTIFICIAL INTELLIGENCE

To understand the process in more detail we can divide the way it works into 3 different steps:

- **Symbolic Artificial Intelligence:** Early system application and techniques. This involves the initial intuitive processes and capturing them through the fuzzy logic. The fuzzy logic involves variables having truth tables, represented by 0s and 1s along with values accompanying them which further helps in taking control of the system.
- **Data Driven Machine Learning:** Current dominating approaches. This involves all the machine learning and deep learning processes, where a machine is trained based on the data it is fed. After the data is presented for learning, the models analyse them and get exposed to various extremities. It furthers through the graphical representations of results, which indicates specific areas where it estimates the accuracy of the model in terms of human intelligence and accordingly decides whether it has to learn more or not.
- **Future Improvements:** Steps towards artificial superintelligence. This refers to the level of intelligence in machines being calculated to be more than humans. This is when AI becomes as autonomous as to generate further autonomous applications of AI. Self explanatory and contextual AI, Robotic AI, Quantum AI are certain examples that are being looked at which will involve lesser amounts of data for the system learning.

## 4. ARTIFICIAL INTELLIGENCE IN MEDICINE

It is said that the developments in machine learning have indicated great advancements in pharmacology and biotechnology efficiency. The application of artificial intelligence in medicine, in general, is said to work in these 4 specific sectors:

- **Diagnostics:** In particular deep learning algorithms, have worked towards automated diagnosis that makes diagnosing much simpler and cheaper. Machines learn how to diagnose by observing patterns between the different cases presented to them. They require a lot of digitized concrete examples in order to learn how to diagnose. Examples where diagnostics is used in AI are: detecting lung cancer through CT scans, classifying skin lesions in skin images, finding indicators of diabetic retinopathy in eye images. The further advancement in the application of AI in diagnosis can be done by the combination of multiple data sources (CT, MRI, genomics and proteomics, patient data, and even handwritten files) for assessment and progression.
- **Drug Development:** In the pharmaceutical industry, artificial intelligence is already seen in:
- **Identification of targets of intervention:** Assists in rooting the origins of pathways for a particular disease and identifying good target proteins - through automated learning.
- **Discovering effective drugs:** Using the good target proteins, finding compounds that can react with them to form a cure. AI assists in predicting the suitability of a molecule based on the structural fingerprints and descriptors.
- **Speeding up clinical trials:** Machine learning can identify patterns that can segregate good candidates from bad candidates for clinical trials that can make the process much more efficient and faster.
- **Finding biomarkers for diagnostics:** AI automates a huge amount of the work in identifying whether an individual has a disease or not with absolute certainty.
- **Treatment Personalisation:** Considering the fact that patients respond to different drugs in diverse ways, machine learning can automate the process of discovering which characteristics indicate that a patient will have a particular response to a treatment. In other words predicting the exact response for a particular treatment, thereby planning a right treatment plan.
- **Gene Editing:** Machine learning has proved to have the most efficient results in terms of predicting the target position for gene editing and identifying the off-target spots in genetic code.

Before discussing the application of artificial intelligence in cancer, understanding the theoretical aspect of Cancer Biology is important.

## 5. CELLULAR HALLMARKS OF CANCER

The 10 cellular hallmarks of cancer give the cancer cells their characteristics that allow them to grow uncontrollably, invade neighbouring tissues, become aggressive, mobile and endure harsh conditions to metastasize.

### 1. Replicative immortality

Normal cells have a finite ability to undergo mitosis due to shortening of the ends of the chromosomes (telomeres). Once normal cells reach the Hayflick's limit, it undergoes apoptosis. Hayflick's Limit is a concept that explains that cells can divide only a certain number of times after which it undergoes apoptosis. Cancer cells exceed this limit and have the potential for unlimited proliferation or growth because they use an enzyme called telomerase to repeatedly elongate chromosomal ends.

## 2. Genome instability

In normal cells, if a mutation is detected, DNA synthesis is temporarily stopped by exiting and arresting the cell cycle to repair the mutation. The genes commonly mutated or lost in cancer cells are the tumor suppressor genes (TSG), and the genes that are over-expressed in cancer cells are the oncogenes. This causes the increase in cancer cell proliferation.

## 3. Evasion of growth suppressor signals

Mitosis is controlled in normal cells with pro and anti-proliferation signals, but due to genome instability, the cancer cells avoid these normal signals and continue proliferating. Retinoblastoma (Rb), which is a TSG, inhibits the normal cell's passage through the G1 cell cycle phase's checkpoint. P53, another TSG, is the main regulator of cell death since it arrests the cell cycle if DNA damage is detected. These genes get mutated in cancer cells.

## 4. Resistance to cell death

Apoptosis occurs in normal cells as a result of ample DNA damage and other cellular stresses - like exposure to extreme temperatures, toxins, nutrient deprivation, radiation and other internal damage. However, cancer cells are less sensitive to these factors, and tend to avoid apoptosis.

## 5. Sustained proliferation

As observed in previous hallmarks, growth factors are signalled precisely for proliferation regulation to allow cellular homeostasis. Cancer cells proliferate due to the previous hallmarks and the over-expression of oncogenes. Cancer cells can also induce normal cells in their close vicinity to provide nutrition or growth factors.

## 6. Altered metabolism

Since cancer cells require more energy to undergo continuous proliferation, they find other sources of energy to fuel their metabolism. Normal cells undergo majority of aerobic respiration - they convert glucose into pyruvate to produce ATP, whereas cancer cells undergo anaerobic respiration regardless of the oxygen supply - they convert glucose to lactic acid to produce ATP.

## 7. Avoiding immune destruction:

The body's immune system with cells like T-cells, B-cells, neutrophils and macrophages protect the body against viruses, pathogens, bacteria and other toxins. Cancer cells avoid being killed by the immune system by altering microenvironments to evade immune attack by modulating immune checkpoints.

## 8. Tumor-promoting inflammation:

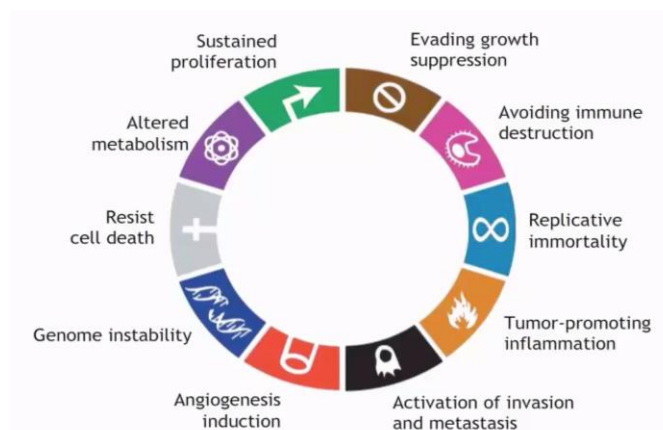
The body's immune cells normally carry out tasks of destroying foreign cells, but when present around tumors, they are often converted into the opposite to benefit the cancer cells. These tumor cells are provided with significant factors like pro-survival, pro-migration and pro-proliferation factors that assist their transition to undergo epithelial-to-mesenchymal transition (EMT) and help them invade blood vessels.

## 9. Induction of angiogenesis:

Cells require sufficient blood supply to grow in size. Since cancer cells typically outgrow their nutrition source, they require greater blood flow. This leads to the cancer cells inducing the formation of new blood vessels to supply more nutrients. These new blood vessels, however, tend to be leaky and allow tumor cells to enter the bloodstream. The process of the formation of new blood vessels from pre-existing ones is called angiogenesis, and pro-angiogenic factors get activated in tumor cells and signal endothelial cells to proliferate.

## 10. Activation of Metastasis:

The cuboidal, stationary and strong epithelial cells get converted into stretched, mobile and weak mesenchymal cells. This is called the epithelial-to-mesenchymal transition (EMT). The extracellular matrix (ECM) that provides structure and biochemical support to cells is also altered. All these factors along with a loss of metastasis suppressor genes leads to the activation of metastasis.



## 6. METASTASIS FORMATION

The 10 cellular hallmarks of cancer enable cancer cells to undergo metastasis. The process of metastasis involves a series of steps, explained below.

### 1. Primary tumor growth

A combination of mutations allow the hallmarks of cancer to alter the characteristics of cells. Cells proliferate uncontrollably to form a mass.

### 2. Angiogenesis

Tumor cells outgrow their source of nutrition and induce the formation of new blood vessels for nutrition. The process is controlled by chemical signals like vascular endothelial growth factor (VEGF) which binds to receptors on normal endothelial cells and promotes the growth and survival of new blood vessels.

### 3. Epithelial-to-mesenchymal transition

As previously explained, epithelial cells are stationary, cuboidal cells that have strong interactions with the ECM. These cells get converted to mesenchymal cells, which are mobile, stretched and lack interactions with the ECM. Epithelial cells lose their cell-adhesion property and polarity, while mesenchymal cells are multipotent stem cells that have the ability to differentiate and proliferate continuously, giving tumor cells advantages to metastasize.

### 4. Invasion

Invasion is the process through which tumor cells break through the extracellular matrix and penetrate neighbouring tissues. This allows the tumor cells to approach the bloodstream.

### 5. Intravasation

Intravasation is the process through which tumor cells enter the bloodstream. Cancer cells enter the bloodstream either actively or passively. Actively, tumor cells intravasate into the bloodstream with the help of tumor associated macrophages (TAM) like chemokines that direct the chemotaxis of tumor cells towards the bloodstream and pro-inflammatory factors that increase the permeability of blood vessels. Passively, tumor cells are shed as they enter the bloodstream through leaky vessels formed by angiogenesis or through lymphangiogenesis - the ability to create new lymph vessels - which ultimately reaches the bloodstream.

### 6. Survival in circulation

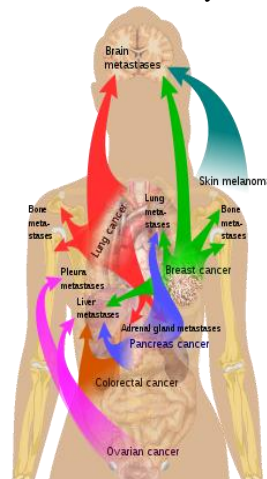
Once the tumor cells enter the bloodstream, they are called circulating tumor cells (CTCs). The CTCs must travel through the venous system, lungs and arterial system. While travelling, the cells must endure extreme conditions and avoid apoptosis through immune system attack and mechanical stresses using the cellular hallmarks of cancer.

### 7. Extravasation

Extravasation is the process through which the surviving circulating tumor cells exit the bloodstream usually through the capillaries and move towards a secondary site. Once they have reached the secondary site, they are called disseminated tumor cells (DTCs).

### 8. Dormancy or secondary tumor growth

Many DTCs may not begin to divide immediately, they might maintain dormancy and regrow into a tumor after a certain period of time. Some DTCs begin growing into metastatic tumors in the secondary site right after extravasation.



## 7. IMAGING IN ONCOLOGY

Medical imaging is the techniques and processes used to create visual images of parts of the body for diagnostic and treatment purposes.

### 7.1 Types of Imaging used in Oncology

**7.1.1 X-Ray:** An X-ray uses a short wavelength electromagnetic radiation for imaging. The image is generally recorded on plain films called radiographs, with differences in light and dark shades. Light shades are produced by denser objects that absorb the most X-rays, like bones, while dark shades are produced by lighter materials like muscle and fat that absorb less X-rays. Due to technological advancements, X-ray images can now be produced by Computed Tomography(CT), which utilizes a combination of X-ray images in a 3-Dimensional model. Contrast media like barium and iodine are given to patients sometimes to differentiate between structures of similar densities.



**7.1.2 Ultrasound:** Ultrasound transducers produce images called sonograms by transmitting high frequency sound waves into the body that bounce back to the transducer at varying transmissions that get converted to an image. Ultrasounds can tell fluid filled cysts apart from solid tumors due to distinct echo patterns.

**7.1.3 Magnetic Resonance Imaging:** A magnetic field produced by a magnetic resonance imaging magnet is used to produce images. Most tissues in the body have Hydrogen atoms that are randomly aligned, and the magnetic field causes the Hydrogen atoms to become polarised and aligned. After the magnet is turned off, the Hydrogen atoms depolarise differently in different tissues, which creates signals that are converted into an image.

**7.1.4 Nuclear Medicine:** A liquid radionuclide with a lead shield is used to produce images in nuclear medicine. A dose reader detects radioactivity and responds to different tissues differently. A special camera picks up the pattern of radioactivity in tissues as radionuclides decay - releasing energy to create pictures showing hotspots.

## **8. CANCER MANAGEMENT TECHNIQUES**

The Cancer Management Techniques involve the processes to deal with individual situations. It consists of the following steps, of which steps 2-6 require some form of imaging in order to assess.

### **1. Cancer Prevention**

**2. Cancer Screening** - screening tests are done using imaging to identify cancer at an early stage before the occurrence of symptoms, when cancer is easier to treat and possible to cure.

**3. Cancer Diagnosis** - pathology and imaging are used together for diagnosis. One of the common ways cancers are diagnosed are using imaging of biopsies.

**4. Cancer Staging** - used to determine how advanced the cancer is by predicting the course of the disease (prognosis) and then assessing treatment options. The invasiveness of the cancer is determined by the Tumor Lymph-Node Metastasis staging:

- Organ of origin - primary tumor
- Nearby lymph nodes
- Metastasis at any distant tissues

**5. Assess Treatment Response** - used to assess change in tumor burden (tumor shrinkage in response to treatment).

**6. Monitoring** - the imaging that worked best for each individual when the cancer was first diagnosed is used to monitor for recurrent cancer. The hallmarks 6 and 9 of cancer are often used to monitor patients after therapy.

## **9. OLIGOMETASTASES**

The theoretical state of limited metastatic potential, or oligometastases suggests that:

- The conditions in a primary tumor are not too harsh
- Cells that break off from the primary tumor are less aggressive CTCs
- Less sloughed off CTCs survive in through circulation
- The sites of metastasis where these CTCs land are inhospitable

Oligometastasis can be diagnosed by staging with imaging. Oligometastasis diagnosis means treatment intent may be to cure.

## **11. CANCER TREATMENT**

There are various methods of cancer treatment that are employed:

### **1. Surgery and radiation**

Performing a surgery to remove tumors can be effective as they kill the cancer before it spreads. An external beam radiation is used, or radioactive seeds are implanted into the tumor to cause cancer cell death by DNA damage. Radiation is given in several doses over time and can be as curative as surgery. It can also be used to shrink a tumor (palliation).

### **2. Hormones**

Hormones can contribute to the growth of cancer, for example estrogen stimulates breast cancer growth and testosterone promotes prostate cancer growth. Anti-hormone agents like anti-estrogen and anti-testosterone agents are used to treat cancer patients.

### **3. Chemotherapy**

Chemotherapy drugs are designed to block cancer cells from division. Chemotherapy drugs not only kill cancer cells, but also normal cells like those of hair follicles and WBCs. This results in hair loss and risk of infection in patients. There are two classes of chemotherapy drugs:

• Agents that interfere with DNA replication:

1. Anti-metabolites: Base pair drugs that are included into the DNA strand and do not allow replication to occur
2. Topoisomerase inhibitors: Inhibit topoisomerase enzyme from unwinding and rewinding DNA strands during replication
3. DNA intercalation: metals, alkylators and antibiotics that prevent DNA strands from replicating

• Agents that interfere with cell division by inhibiting microtubules and blocking mitosis

1. Vinca alkaloids: Prevent microtubule assembly

2. Taxanes: Prevent microtubule disassembly

### **4. Targeted therapy**

Targeted therapy inhibits proteins that have been mutated or overexpressed, and proteins that help cancer proliferation. This treatment is specific to cancer cells, and does not result in many side effects.

### **5. Immunotherapy**

Immunotherapy is the use of medicines to promote the patient's immune system to effectively recognise and destroy cancer cells. The immune system normally prevents attacking itself using checkpoints that are switched on or off to generate an immune response. Checkpoint inhibition that targets PD-1 or CTLA-4 are generally used. PD-1 and CTLA-4 are proteins on the immune system cells (T-cells) that normally help prevent these cells from attacking other body cells. This will promote the response against cancer cells.

## 12. HOW CAN THE ADVANCEMENTS OF ARTIFICIAL INTELLIGENCE IN MEDICINE HELP US IN THE SPECIFIC SECTOR OF CANCER?

Based off of the methods and areas where artificial intelligence has played a role and is developing to play a role in the medical field, some of the aspects where AI can help in terms of cancer using the same methodologies are:

- Determining and diagnosing the different stages of cancer
- Predicting the response of treatment in each individual
- Having a model of a personalised simulation of an individual's body that can help in the future planning for righteous treatment

It is proven that **traditional analysis methods** such as **statistical analysis** and **multivariate analysis** are not as efficient and accurate as artificial intelligence.

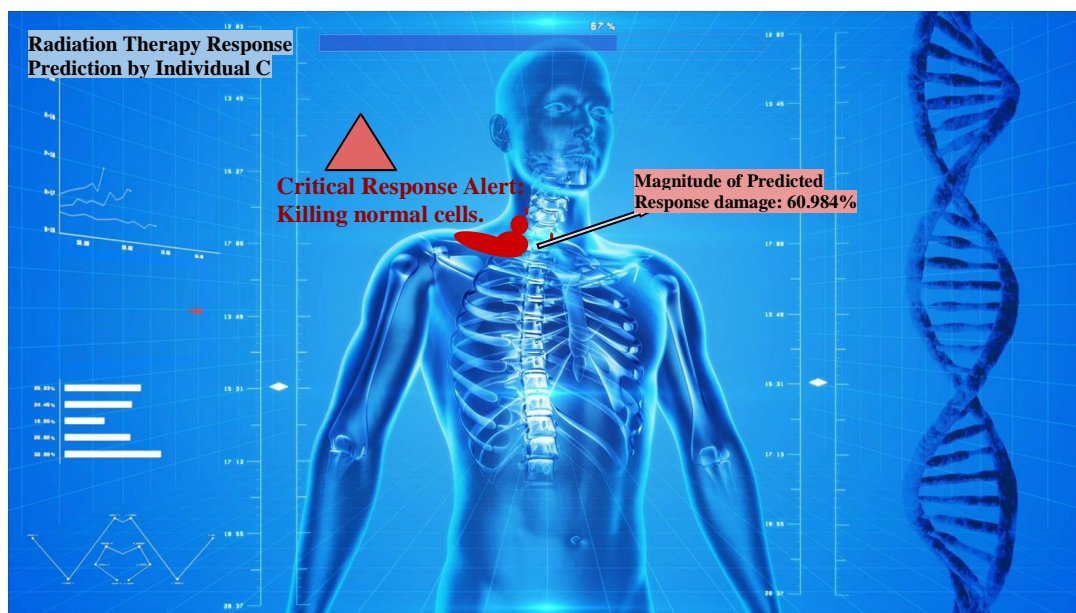
## 13. CLINICAL CANCER PROGNOSIS PREDICTION AND ARTIFICIAL INTELLIGENCE

Knowing that the statistical analysis is not very accurate in determining the progress of cancer, doctors today are alarmed by the patient's risk of contracting the disease, tumour recurrence and scenarios of death after treatment. With the possibility of having prognoses of different patients being predicted at a much higher accuracy rate, more precise treatments can be provided. This can also lead to individualised and customised treatment for each patient, but as of now it is extremely hard to implement. But when AI steps into the court, it can be used to process and analyze multi-factor data from multiple patient examination data to predict cancer prognosis as well as the survival time and the disease progress of patients more accurately.

In more detail, this can be done by applying the **Artificial Neural Networks (ANNs)** which will assist in considering all the variable interactions and thereby creating a non-linear prediction model. This model would offer more accurate predictions of survival time than traditional methods. As AI recognizes patterns amongst large volumes of data by extracting relationships between complex features in the data and identifying characteristics in data - these features of AI could possibly assist in modelling the patterns in each individual for certain treatments and medications. How these individuals progress in different stages, how they respond to ongoing treatment and what specific symptoms are shown due to specific triggers can be predicted. All these together added up, can further help doctors in predicting the right treatment that must be used for this individual. If this is given a closer thought, making a model for each and every individual in order to accomplish the above mentioned tasks will become tedious. A solution for having this personalised treatment would be to create a standard model of a human body with specific parameters that would differ from individual to individual. This would be an efficient way as this would not only be easier and much more simpler to use but also time efficient and yet accurate. In other terms just like an *Individual Cancer Treatment Predicting Model*.

According to the visual appearance of this model, AI can be further used to help in the righteous procedure planning. This can be done through the implementation of automated visual evaluation. **Automated Visual Evaluation** is a deep-learning, AI approach that is used to evaluate digitized images, predicting the responses like seen in the figure below or in other scenarios the probability of precancer or cancer.

## 14. VISUAL



## 15. ARTIFICIAL INTELLIGENCE IN ONCOLOGY & DIAGNOSIS

Prior research by the NCI suggests that there are multiple capabilities of AI to improve cancer screening. Basics of artificial intelligence in oncology can be seen in an algorithm running on a trained computer to analyze images of MRI scans. This method can come into function by using AI in capturing the diagnostic expertise and making this tool accessible. This tool can be used to help with the diagnosis and clinical decision making of cancer.

## 16. ARTIFICIAL INTELLIGENCE IN CANCER TREATMENT

While speaking about the different ways AI assisted in the medical field, drug discovery and development was mentioned to be one of the main components. In the same sense, AI can be used in the specific drug development and drug discovery of medications for cancer. Through the use of machine learning and ANNs (Artificial Neural Networks) algorithms, the match for the specific proteins that can treat the cancer can be accelerated. Once these medications have been developed, to make the most efficient use of it, it can be yet again plugged in as a compound in one of the parameters of the human body simulation of an individual to make accurate predictions of the effects of that medication and the progress of that medication on that individual.

## 17. CONCLUSION

To conclude, knowing the risk associated with cancer, it can be termed to be a deadly disease. However, with the advancement in technology, there can be a method found to personalize treatment mechanisms to suit each individual's body type. Artificial intelligence is much more effective than the already existing traditional analysis methods. With specialized medical professionals and artificial intelligence researchers, the creation of a model or simulation that can diagnose and predict the responses to treatment through pattern observation would offer personalized treatment which would be specific to each individual. As discussed above, this can be done by creating a standard simulation of the human body and having certain parameters that could be manipulated in order to make the simulation similar in terms of the characteristics and responsive natures of each individual. This personalized treatment could lead to more accurate treatment than already existing generalized treatment. This could reduce or even potentially eliminate the side effects and failuristic responses to cancer treatment.

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