VCHEI Science Club

Vigillance on Contemporary Health and Environment Issues

END OF YEAR 2022

COMPILATION OF LITERATURE STUDIES

Topic: Cancer

January, 2023

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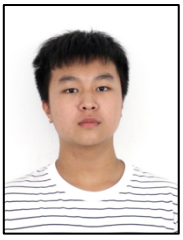

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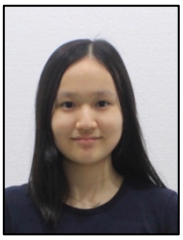

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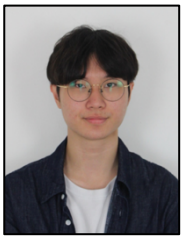

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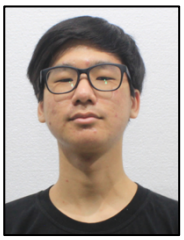

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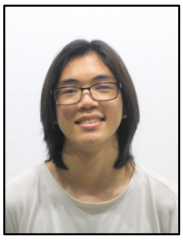

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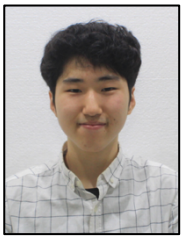

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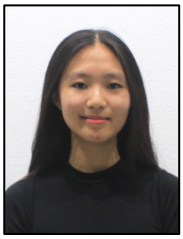

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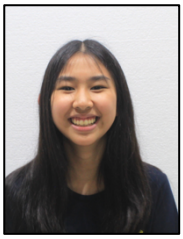

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INTRODUCTION

Introduction to cancer and sub-topics

By: Debora W. Nuhamara

Introduction to Cancer

Cancer is a disease that happens when some cells in the body grow uncontrollably and spread to different parts of the body. In normal condition, cells in our body grow and multiply forming new cells as needed by the body. When they become old or damaged, they'll die and be replaced by new cells. When the orderly process is disrupted, it allows abnormal cells to grow and multiply when they are not supposed to. The growth of these abnormal cells may form a clump of cells called tumor which become cancerous/malignant when they spread into nearby tissues or other parts of the body (National Cancer Institute, 2021).

According to World Health Organization (World Health Organization, 2022), cancer accounts for nearly 10 million deaths in 2020, making it the leading cause of death worldwide (nearly one every six deaths). Figure 1.1. shows the most common cancer in 2020 and Figure 1.2. shows the most common cancer death in 2020. And even though cancer incidence rises as age increases, around 400,000 children already develop cancer each year.

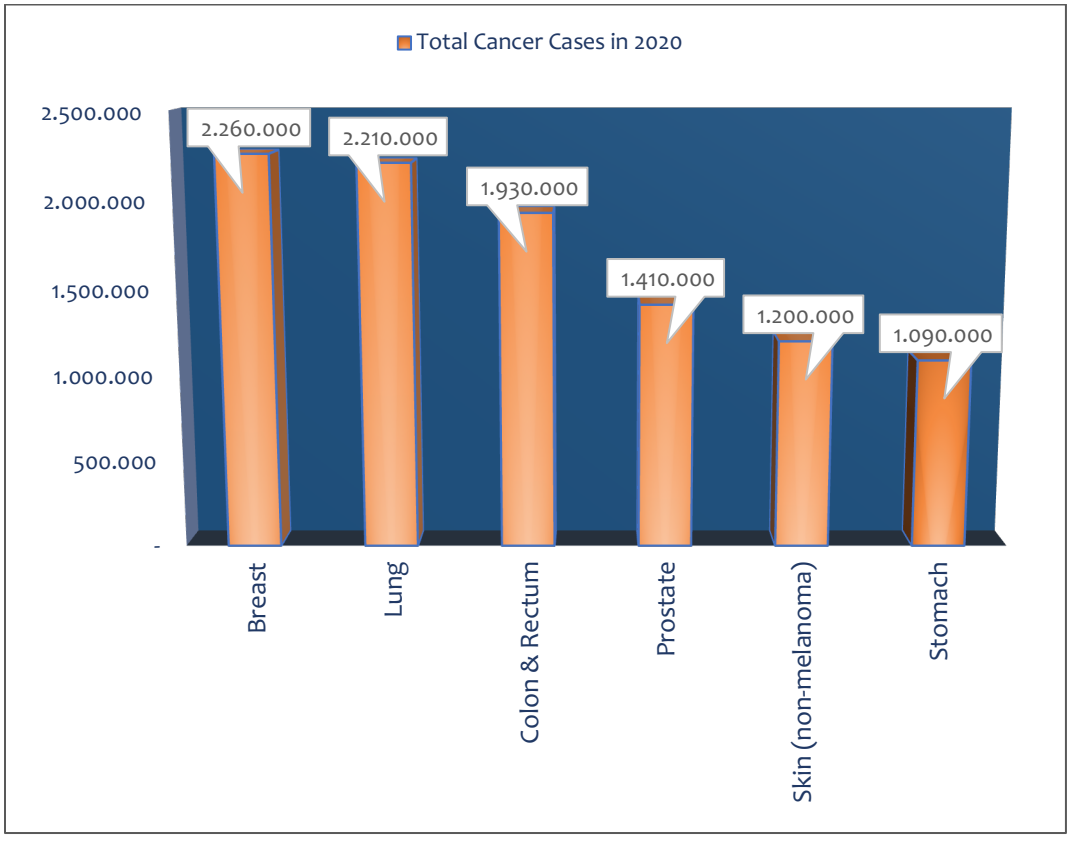

Figure 1.1. The Most Common Cancer Cases in 2020
Source: (WHO, 2020)

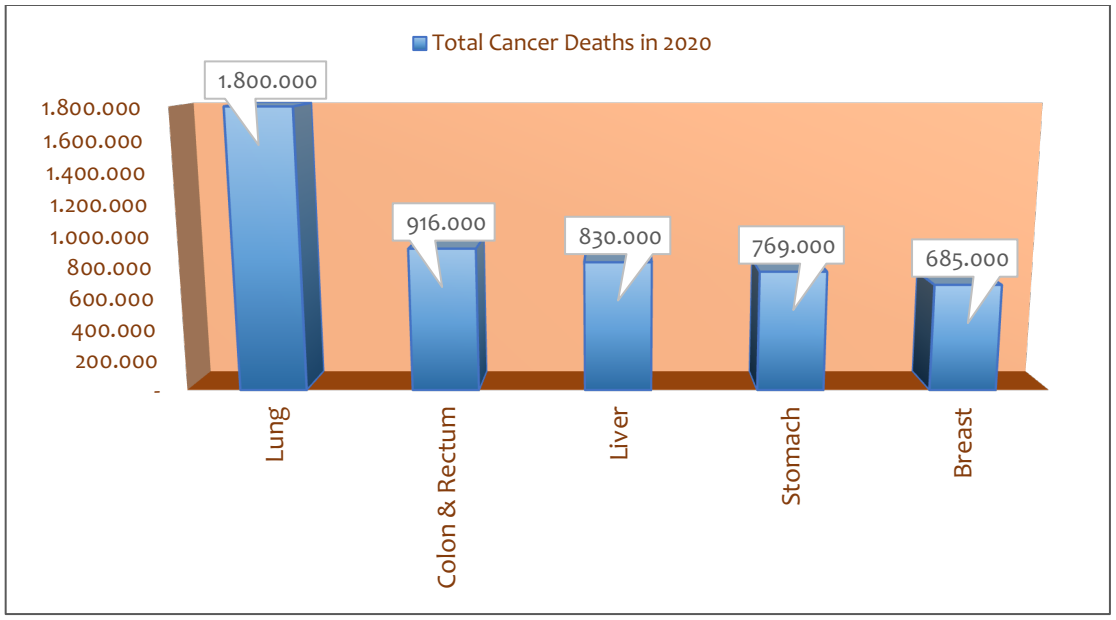

Figure 1.2. The Most Common Cancer Deaths in 2020
Source: (WHO, 2020)

Cancer Characteristics

Cancer cells has unique properties that distinguish them from normal cells. Their growth is rather abnormal and causing them to spread and invade other tissues. This abnormal growth could also vary between different kinds of tumor cells (NCI, 2021).

Cancer cells vs. normal cells

There are many abnormal behaviors that makes cancer differ from normal cells. Generally, cancer cells rely on those abnormality to survive. Researches takes advantage of this by designing therapies to target abnormal behaviors of cancer cells (NCI, 2021). Differences between cancer and normal cells is shown in Table 1.1.

Table 1.1. Differences Between Cancer and Normal Cells

Character	*Normal Cells*	*Cancer Cells*
Growth	Grow only when needed, stops when enough	Grow uncontrollably
Communication	Respond to signals from other cells	Do not respond to signals from other cells
Cell Repair/Death	Repaired/replaced when it's old or damaged	Neither replaced/repaired
Stickiness/Spread	Stay together in assigned area	Can travel solo throughout the body

Appearance	Looks uniform under the microscope	Varies in size, usually larger with darker center under the microscope
Maturation and Function	Reach maturity and perform designated tasks	Do not reach maturity and fail to perform designated tasks
Evasion of Immune System	Can be targeted by our immune system and be eliminated when needed (when damaged/gets old)	Hides/trick our immune system and avoid being eliminated
Blood Supply	Have blood vessel grow towards them to feed normal growth and aid in repairs	Have blood vessel grow towards them more than usual to constantly feed the tumor

(Eldridge, 2022)

Benign Tumor and Cancer

Many cancers form solid tumors, but some cancers of the blood such as leukemia doesn't. Tumor that doesn't spread to other parts of the body are not cancerous and termed benign tumors. Once removed, benign tumors don't usually grow back, while cancerous tumors do sometimes. Even though benign tumors don't spread, it may cause detrimental symptoms and threatens life (e.g., brain tumor) (NCI, 2021). Tumors that invade neighboring tissues and even spreads to other parts of the body are cancerous tumor/malignant tumor (Whelan, 2022).

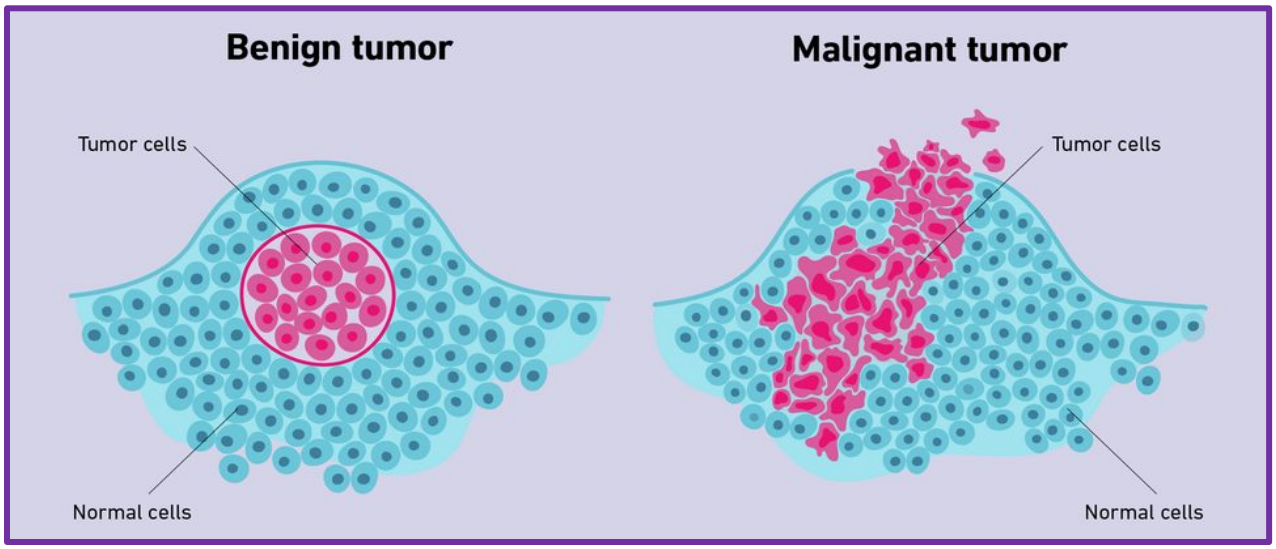

Figure 1.3. Benign tumor and malignant tumor/cancer
Source: (Whelan, 2022)

Basic Cause of Cancer

Cancer is caused by changes in the genes that controls how the cells functions, especially in growing and dividing. The combination of genetic changes in people with cancer is unique and might add up as the cancer continues to grow (NCI, 2021). Genetic changes that lead to cancer might happen because of the following reasons:

- an error occurs during cell division
- DNA is damaged by harmful substance in the environment such as tobacco and UV rays (carcinogens)
- they were inherited (cancer itself is not inherited but there are chances that the genetic changes in cancer will be inherited)

(NCI, 2021)

Normally, the body would eliminate damaged cells containing DNA with errors before they become cancerous. As we age, that ability becomes weaker, making us more risked to have cancer as we grow old. Age is one of cancer risk factor that is unavoidable (NCI, 2021).

Introduction to Cancer Subtopics Studies

To understand more about problems and challenges in cancer as the leading cause of death worldwide, VCHEI Science Club members of Mountainview Secondary Highschool had the chance to do literature studies and discussion about the disease during the first semester of 2022/2023 school year. Sub-topics are studied individually/in small groups followed by whole club discussions. In this book, we compile 12 papers covering 12 subtopics of our literature studies about cancer. These sub-topics includes:

1. **What are the genetic changes in cancer?**
   By: Jayden Nugroho, Alexander T. Salim, and Se Young Oh
2. **What are the behavioral risk factors of cancer that are modifiable?**
   By: Ferrell Herlambang and Min Woo Son
3. **What are the classifications of cancer and how is cancer being classified?**
   By: Benjamin Kegg, Woon Joo Yun, and Hans J. Tan
4. **What are the treatments for cancer and how is it being decided?**
   By: Ji Hye Kim and Marsha Sujanto
5. **What are the different roles of surgery in cancer treatment?**
   By: Chris Thomas Menassery
6. **How does chemoimmunotherapy work in cancer treatment?**
   By: Daniel Hong and Si Rae Yun
7. **What are the side effects of cancer treatments?**
   By: Ju Won Park
8. **What are the roles of physiotherapy in oncology?**
   By: David Park
9. **How does brain cancer/tumor influence the way our brain controls the body?**
   By: Yoon Jin Kim, Cherish Andreea, and Rishit Gautam

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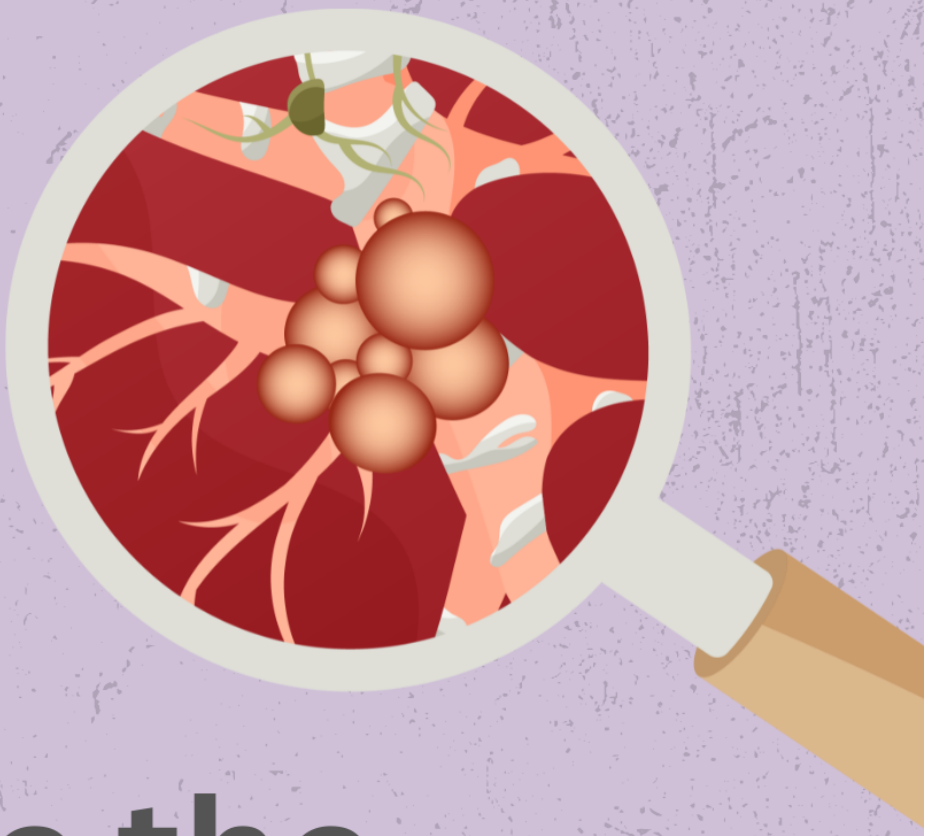


What are the genetic changes in cancer?

What are the genetic changes in cancer?

By: Jayden Nugroho, Alexander T. Salim, and Se Young Oh

Background

Cancer is a genetic disease which is caused by genetic changes in your DNA. These changes happen to the genes that control cell growth and multiplication causing DNA to be damaged/altered. DNA alteration that causes cancer could occur by inherited faulty genes, carcinogen exposure throughout a person's life, or an error in cell division (NCI, 2022).

Inheritance of cancer itself is almost unlikely, but rather the increased risk of cancer might be inherited (Luzzato, 2011). Inherited genetic changes play less role in the development of cancer compared to environmental factors which have a major role. Presence of mutated genes that are inherited at the time of fertilization does not mean that cancer development is inevitable in a person's life, but it does give a greater risk of developing the disease (Yale Medicine, n.d.).

Advances in modern technology enable scientists to understand the mechanism that underlies cancer development. Sequencing nowadays can more accurately map the human genome, enabling physicians to locate mutations in the genome that lead to cancer and providing details on how cancer develops. This would enable scientists to better understand the genetic issue in cancer in hope to develop better therapies to cure the disease with genetic approaches (Stratton, Campbell, and Futreal, 2009; Luzzatto, 2011).

It is known that there are two classes of genes that have roles in the development of cancer: the oncogene and the tumor suppressor gene. The oncogene is the positive growth regulator which promotes cell growth. Activation of these genes by mutation causes abnormal cell growth. On the other hand, tumor suppressor genes act as negative growth regulators. Tumor suppressor genes stop abnormal cells from growing too fast. Inactivation of these genes through mutation will leave the body with dysfunctional tumor suppressor genes, so there will be nothing to stop cancerous growth (Vogt, 1993). In this paper, we are going to talk about the genetic changes that happen on these genes that are known to cause cancer.

Cancer Genes and their Mutations

Oncogene

Oncogene are genes that when activated through mutation can lead to malignancy. (Osborne et al. 2004). These genes send growth signals to the cell's nuclei to promote cell growth (Vogt, 1993). It encodes growth factors, growth factor receptors, and signaling proteins that not only promote cell proliferation but may also prevent apoptosis/programmed cell death (Cooper, 2000).

Before an oncogene is mutated, it is called a proto-oncogene. Proto-Oncogenes are involved in normal, stable cell growth and division. Mutations in an proto-oncogene will lead it to becoming an oncogene which causes cancerous growth in cells (Liu, 2022). There are 3 mutation mechanism known to play role in the activation of oncogene or the changing of a proto-oncogene to an oncogene explained below. The examples of these oncogenes are listed in Table 2.2.

1. **Gene Amplification**

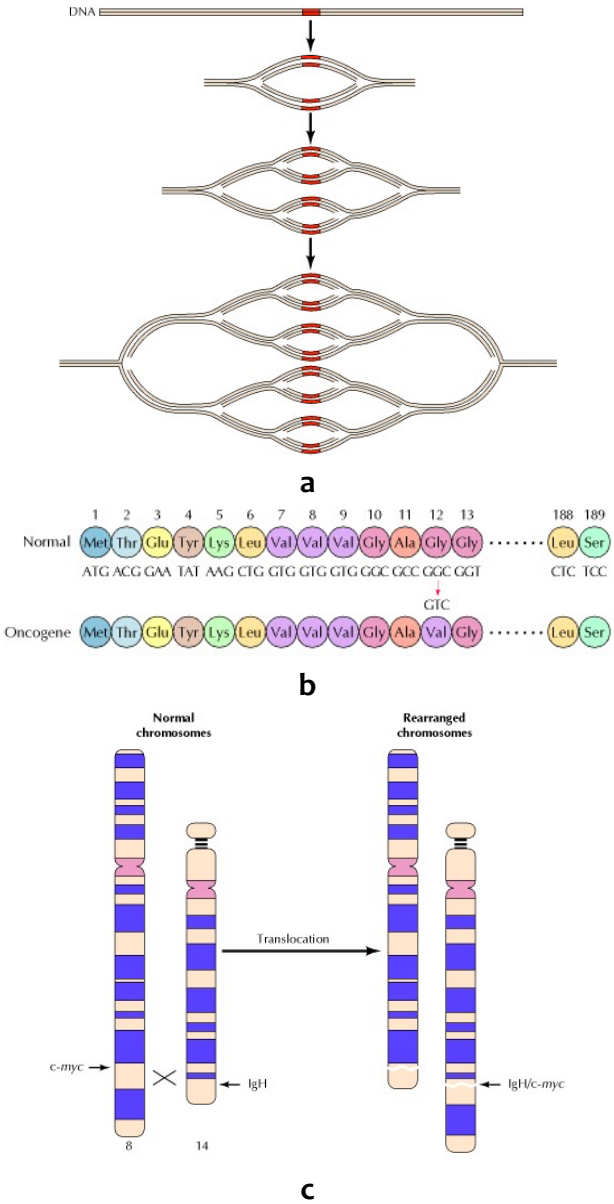
Gene amplification happens when a certain gene is amplified resulting in elevated gene expression, the production of too much encoded protein which in turn also enhances its function (Osborne et al. 2004). Gene amplification is most common in tumor cells. It occurs > 1,000 times more than it does in a healthy cell. Amplification of an oncogene can result in an increased rapidness of tumor growth and malignancy (Cooper, 2000).

2. **Point Mutation**

Point mutation is a mutation of a single amino acid at a vital place in the DNA (base substitution). The mutation activates the gene to amplify the mechanism of oncoprotein which activates the cell cycle. This single change in the gene leads to an enhanced function of cell cycle activation, causing the cell to grow rapidly. (Osborne et al., 2004).

3. **Chromosomal Translocation**

Chromosomal translocation is described when a part from one chromosome is reattached to a different chromosome (Roukos & Misteli, 2014). Chromosomal translocation may activate oncogene when a fusion gene is coded into a protein that is enhanced in its functions. The functions that lead to oncogenic behavior may include alteration of the cell signaling system that encompasses cell proliferation, drug sensitivity, DNA repair, angiogenesis, apoptosis, protease activity and cell motility (Osborne et al., 2004).



Note:
(a) gene amplification (b) point mutation
(c) chromosomal translocation

Figure 2.1. Oncogene activation mechanisms
Source: Cooper, 2000.

Table 2.1. Examples of Oncogenes

Oncogenes activation mechanism	Proto-oncogenes affected	Cancer Type
Gene Amplification	c-*myc*	Breast & ovarian cancer, squamous cell carcinomas
	N-*myc*	Neuroblastoma
	L-*myc*	Small-cell carcinoma of the lung, neuroendocrine-derived tumor
	erbB	Glioblastoma, squamous carcinoma of the head & neck
	erbB-2 (*HER*-2/*neu*)	Advanced stage breast cancer
Point Mutation	K-*ras*	Carcinomas (lung, colon, pancreas etc.)
	N-*ras*	Hematologic cancers (myeloid leukemias)
	K-*ras*, N-*ras*, H-*ras*	Thyroid Carcinomas
	ret	Endocrine cancer (MEN2A)
Chromosomal translocation	c-*myc* translocation	Burkitt lymphoma & T-cell acute lymphoblastic lymphoma (T-ALL)
	bcl-2, *bcl*-1, *tcl*-1 activation	Lymphoma & leukemia
	bcr/*abl* fusion	Neoplastic myeloid
	NPM/*ALK* fusion	Chronic myelomonocytic leukemia

Source: Pierotti et al, 2003

Tumor Suppressor Genes

Tumor suppressor genes (TSG) are the opposite of an oncogene, the loss of function of these genes will cause malignancy. Tumor suppressor genes act as negative growth regulators or other functions that keep the cell cycle in check and make sure that it doesn't grow abnormally (Osborne et al, 2004). They function to restrain abnormal cell growth and division, but also stimulate cell deaths to keep our cells balanced properly (Chial, 2008). For example,

these genes play a role in cell adhesion and regulation of protease activity (Osborne et al, 2004).

Tumor suppressor genes may lose their function due to genetic changes and non-genetic changes. The "two-hit" hypothesis assumes that the tumor suppressor gene changes that cause tumorous growth happen when a mutation occurs in one allele and deletion in the remaining allele. However, sometimes it isn't just mutation of the tumor suppressor genes that causes the malignancy, instead another mechanism that interferes with the expression of the gene's function ("multi-hit" factors) (Osborne et al, 2004).

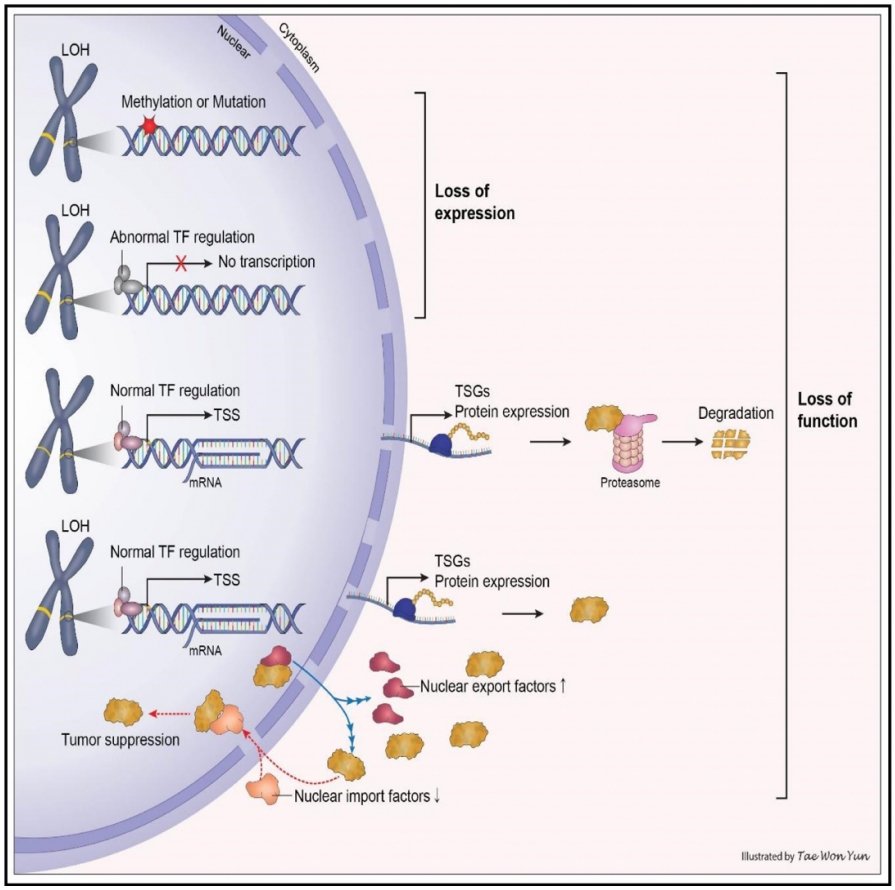


Figure 2.2. "Multiple-Hit" Factors of Tumor Suppressor Gene Function Loss

Source: Wang et al., 2018.

There are some mechanisms that may interfere with tumor suppressor gene expression. For example, methylation of the gene promoter. A promoter in the gene is supposed to initiate gene transcription. Methylation of the promoter may suppress gene transcription instead. Another mechanism is the increasing protein degradation by proteasome. Abnormalities in other proteins may also interfere with tumor suppressor gene products and suppress its function (Osborne et al, 2004). Some interaction abnormalities with other proteins may cause misvocalization of tumor suppressor gene products which prevent them to function normally

in the cell cytoplasm (Wang et al., 2018). Figure 2.2 summarized the different ways tumor suppressor genes are inactivated/loss it's function in our body.

The p53 gene is the most studied tumor suppressor gene and its mutation is estimated to be responsible for more than half of all human cancer including breast cancer, leukemia, sarcomas, and brain tumors. A fully functional P53 gene will regulate both cell cycle process and apoptosis (programmed cell death). When a DNA is damaged during cell replication, p53 gene induce cell cycle arrest to allow for DNA repair. When the damage is unrepaired, p53 gene is required to induce apoptosis. Both are important to eliminate the damaged DNA and prevent it from being multiplied even further (Cooper, 2000).

However, when a DNA damage is rapidly inducing the function p53 gene, it will cause the loss of the P53 ability to stop the cell cycle or induce apoptosis. This will, preventing the repair of damaged genes/DNA, resulting in further genetic instability and the accumulation of DNA damages via the multiplication of the cells. Such genetic instability will most commonly result in cancer. They contribute to further changes in oncogenes and tumor suppressor genes (Cooper, 2000). More examples of TSG, their function, and the types of cancer they are attributed to are shown in Table 1.2 below.

Table 1.2. Examples of Tumor Suppressor Genes

Tumor Suppressor Genes (TSG)	TSG Function	Cancer types
Rb	Cell Division, DNA replication, cell death	Retinoblastoma, sarcomas, bladder, breast, and lung carcinomas
P53	Cell division, DNA repair, cell death	Brain tumors, breast, colon/rectum, esophageal, liver & lung carcinoma, sarcomas, leukemia & lymphoma
APC	Cell division, DNA damage, cell migration, cell adhesion, cell death	Colon/rectum carcinoma
BRCA1	Repair of double stranded DNA breaks, cell division, cell death	Breast and ovarian carcinoma
BRCA2	Repair of double stranded DNA breaks, cell division, cell death	Breast carcinoma

Source: Chial, 2008; Cooper, 2000.

Common Carcinogens and Risk Factor of Aging

UV Damage

Our DNA is made up of chemical bases which are: adenine (a), cytosine (c), guanine (g), and thymine (t). Prolonged exposure to UV radiation can harm/damage the chemical bases that make up our DNA which can then lead to a genetic change. The chemical base in specific is thymine, the thymine dimer can easily be fixed by removing and replacing the dimer with new nucleotides. The longer the cells are exposed to the sun the more thymine dimers is formed, increasing the chance for a mistake in the process of reparation or other dimers formation to be missed. Then when the damaged (skin) cells divide, the new cells are also damaged. The DNA damage will cause the cells to multiply at an abnormal rate which then can lead to cancer. The accumulation of genetic damage can lead to cell death, but if the damage isn't too severe the cells can easily be fixed or recovered (Rammelsberg, 1998).

Tobacco Damage

Smoke has poison that can weaken the white blood cells and damage the cell's DNA which will lead to abnormal cell growth or tumor growth. Tobacco products contain a lot of tar and nicotine that hurt the immune system and leading to lung cancer. When someone smokes, their cell signaling will be affected, where the cell might send incorrect signals that causes abnormal cell growth. The chemicals present in the smoke can also weaken the tumor suppressor gene which increase the risk of getting cancer dramatically. Repeated exposure over many years will cause new field mutations on the pulmonary epithelial cells of the lungs (Yamaguchi 1964).

Chemicals

Cells are exposed to chemicals that enter the body through the respiratory system, digestive tract, or contact on your skin. The DNA structure gets damaged due to covalent binding of chemical carcinogens and the DNA. This binding of the chemicals to the DNA will alter the protein structure and can lead to getting cancer. PAHs or polycyclic aromatic hydrocarbons is one of the most common carcinogens that are naturally found in coals, natural gas, and oil. When burned, coal, oil, natural gas, tobacco, wood, and garbage all release the PAHs into the air. When this poisonous air is inhaled, the chemicals enter the lungs and into the cells, and could damage it (Poirier, 2004).

Age

Cancer percentages and rates increases as age groups increase. As stated before, environmental exposure that contributes to DNA damage can come from everywhere such as UV rays, cigarette smoke, mutagens in food, and virus. As we age, the accumulation of DNA damage gets greater and greater. Avoiding harmful exposure might reduce acquired DNA

mutations but won't eliminate it because sometimes, mutation occurs as our cell/DNA replicates. This mutation will also accumulate over time. Other than that, the body's functioning, which supposed to eliminate any potential cell malfunctioning that could develop cancer, also declines over time, increasing the higher chance for cancer to develop in the body (Gudkov, 2020).

Gene Therapy Treatment

Gene therapy is a new revolutionary kind of therapy where, with the use of genetic mapping, doctors can locate any faulty and/or potentially harmful genes or mutations, then replace the it with a functional healthy copy of it, which in turn will hopefully improve the chances of the body fighting off the disease or completely cure it all together. Compared to chemotherapy, which cause a lot of side effects due to how it attacks both healthy and cancerous cells, the specific targeting of gene therapy is potentially a more beneficial approach for cancer treatment. Various innovative genetic approaches are currently being developed to make the treatment effective and applicable for cancer treatment (Das et al., 2015).

Conclusion

Cancer is a genetic disease in a sense that it is caused by changes/alterations in the genes, especially genes that control cell growth and multiplication: oncogenes and tumor suppressor genes. Oncogenes are genes that when activated will cause malignancy/cancer. Oncogenes could be activated either by being copied more than it should (gene amplification), mutation/changes in the DNA, or when it is mislocated in the chromosome during cell replication. On the other hand, tumor suppressor genes are genes that will cause malignancy/cancer when it lost its function. It could lose its function either by mutation in the DNA, disruption in protein expression process, or when the protein function is interrupted by other substance. Understanding how genetic changes can cause/promote cancer is very crucial to help finding a way in treating cancer. In the future, gene therapy could be used to find a more effective, efficient, and a safer way to cure cancer or to detect cancer potentials as early as possible and prevent the development of cancer in the first place.

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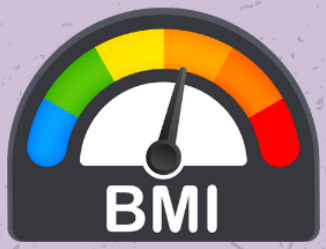
What are the behavioral risk factor of cancer that are modifiable?



What are the behavioral risk factors of cancer that are modifiable?

By: Ferrell Herlambang and Min Woo Son

Background

Cancer is right now the second leading cause of death worldwide. The problem is that today many people do not understand many things about cancer including the cause and the risks factors of it, which is why cancer keeps occurring and causing deaths across the world. Even though many people may be ignorant of these risk factors, studies show that different factors may contribute to the development of different types of cancers in various ways (Sloan, 2007).

In epidemiology studies, cancer risk factors are identified and studied by scientists by comparing people who develop cancer with people who don't in large groups. The study shows that people who do develop cancer are more or less likely to behave in a certain way or exposed to certain substances compared to those who don't. This alone doesn't prove that the identified factors are causing cancer, since it could be a result of chance or something else might be the real cause of the cancer. However, when many studies all seem to show a similar association between the potential risk factor with an increased cancer incidence, and supported by a possible mechanism that could explain how the risk factors cause cancer, scientists could be more assured by these risk factors of cancer (NCI, 2015).

It is important for us to learn about the risk factors. If we know things like tobacco, diet, and how long you exercise can affect the risk of getting cancer then people would be able to know what to avoid/how to control things so that they don't get affected by cancer (Sloan, 2007). Knowing these risk factors of cancer like tobacco, diet, and physical activities provides the basic understanding on how to prevent different types of cancer. It is better for us to figure out a way to prevent yourself from getting cancer by understanding the risk factors better. Understanding how to treat cancer might be a more complex task especially when dealing with incurable cancers. When we know that some of the risk factors could be reduced/eliminated, prevention is possible through a change in our behavior, environment, or even through vaccination and treatment (Sloan, 2007).

Cancer risk factors include exposure to chemicals/substances, certain behaviors, aging, and family history. While there are different ways to control chemical/substance exposure and our behavior, we cannot control risk factors like aging and family history (NCI, 2015). Chemical exposure could include occupational (certain hazardous chemicals or radiation), environmental (UV rays and pollution), or even medical (drugs and radiation). Exposure of these chemicals could be reduced when using protection and improvement of facilities (Sloan,

2007). Tobacco (smoking), diet, physical activity, and alcohol use are factors that could be eliminated through changes in behavior (Stein and Colditz, 2004). This is less complicated since it is relying only on an individual's consciousness and determination. Even though it is more manageable, these behavioral risk factors are known to account for one third of cancer cases worldwide (WHO, 2022). In this paper, we discuss further more about cancer risk factors that could be reduced by changes of behavior.

Modifiable Risk Factor of Cancer

As mentioned above, some cancer risk factors are harder to eliminate than others. Reducing risk factors like occupational chemical exposure might require us to use protection at work, but it doesn't eliminate the risk. Reducing UV rays and pollution exposure in our environment might require efforts to change the condition of our environment like reduction of pollution and CO_2 emission, and could also be reduced through the use of masks or UV protection products like sunblock. Infection by viruses like human papilloma virus (HPV), helicobacter pylori, hepatitis C virus and hepatitis B virus (HBV) are also risk factors of cancer that could be avoided by vaccination and treatments (Sloan, 2007).

Table 3.1. Modifiable Risk Factors for Cancer Deaths

Risk Factor	Theoretical Minimum Exposure Distribution	PAF% (All Cancer)	Specific Cancer Type	PAF% for specific Cancer Type
Tobacco use	Zero Exposure Possible	18	Lung Trachea, Bronchus	60
			Stomach	11
			Liver	11
			Esophagus	37
			Mouth Oropharynx	37
			Uterine cervix	2
			Leukemia	6
Low fruit & vegetable intake	600gr/day	6	Lung Trachea, Bronchus	13
			Stomach	19
			Colon and rectum	2
			Esophagus	19
Risk Factor	**Theoretical Minimum Exposure Distribution**	**PAF% (All Cancer)**	**Specific Cancer Type**	**PAF% for specific Cancer Type**

Physical inactivity	2.5 hours/week of moderate intensity activity/equivalent	18	Colon and rectum	15
			Breast	10
Overweight & obesity	BMI (weight/height^2) of 21	18	Colon and rectum	9
			Breast	7
Alcohol use	Zero Exposure Possible	18	Liver	23
			Esophagus	24
			Breast	4
			Mouth	14

Source: Lopez et al, 2006 in Sloan, 2007.

Some other risk factors are modifiable by changes of our behavior. The most common behavioral risk factors are listed in Table 3.1. Population attributable factor (PAF) is the proportional reduction in disease that will occur if exposure of the risk factor in the population is reduced to the theoretical minimum risk level. Each risk factor is explained below.

Tobacco

Tobacco contributes to around 30% of all types of cancers. It is a major risk factor in lung, trachea, bronchus, stomach, larynx, esophagus, mouth, colon, cervix, kidney, bladder and oropharynx cancer. It is also shown to increase the risk of liver cancer, prostate cancer, and leukemia. Tobacco is the largest contributor to cancer deaths. In the year 2000, 4.9 million died from cancer and were exposed to tobacco (Stein and Colditz, 2004).

Tobacco goes through many stages in our body. Not only does it deliver carcinogens to our body, it also causes inflammation and interferes with our natural barriers in our body. To reduce the risk of cancer caused by tobacco we need to implement programs or rules that may reduce people's initiative to smoke and facilitate in cutting short smoking in our community (Stein and Colditz, 2004).

Low Fruit and vegetable intake

Low fruit and vegetable intake can lead to the risks of getting cancer of the pancreas, bladder, lung, colon, mouth, pharynx, larynx, esophagus, and stomach (Stein and Colditz, 2004). Vegetables and fruits in general contain numerous dietary constituents such as vitamins, minerals, phytochemicals, and fiber that have potential to inhibit cancer progression (Rock et al, 2012). For example, tomatoes that have shown to have a 40-50% reduction in cancer risk, at least among men, contain carotenoid lycopene , which is believed to have the anticancer properties. Folate, a kind of vitamin B, is important in DNA synthesis and repair, and may

reduce adverse effects of alcohol. Selenium is a key part of antioxidant enzymes and an important element in the immune system. (Stein and Colditz, 2004).

A large number of other anticarcinogenic agents are found in vegetables and fruits: vitamin C and E, flavonoids, phenols, plant sterols, protease inhibitors, and many more. These agents have complementary and overlapping mechanisms of action including detoxification enzymes, antioxidant effects, diluting and binding carcinogens in our digestive tract, inhibiting nitrosamine formation, alternating hormone metabolism, and others (Steinmetz & Potter, 1991). It seems to be extremely unlikely that any one substance is responsible for the mechanism (Steinmetz & Potter, 1991).

Because it is not known which of the many components in fruits and vegetables may be the most protective from cancer, it is advised to consume a wide variety of colorful fruits and vegetables every day (Rock et al, 2012). In addition to dietary intake, red meat such as beef, pork, lamb, and veal is also associated with an increased risk of colorectal cancer. Even though the mechanism of this is still unclear, it may be caused by carcinogens that are produced when the meat is being cooked at high temperature (Stein & Colditz, 2004).

Overweight and obesity

Obesity is one of the major factors that is related to the risk of cancers, including colorectal, postmenopausal breast, endometrial, renal, and oesophageal cancer. Studies also show that it may influence cancer of the prostate, liver, gallbladder, pancreas, stomach, ovary, cervix, non-Hodgkin lymphoma, and multiple myeloma. Overall, obesity causes 20% of cancer deaths in men and 14% cancer deaths in women (Stein & Colditz, 2004).

Changes in the body caused by obesity that may lead to cancer include long-lasting inflammation and high level of insulin, insulin-like growth factors and sex hormones. The risk is said to increase with more excess weight a person gains and the longer the person is overweight (CDC, 2022). Ways to prevent obesity is by balancing energy expenditure by physical activities and caloric intake through diet (Stein & Colditz, 2004, CDC, 2022).

Physical Inactivity

Lack of physical activity can increase the risk of breast, colon, and endometrial cancer. It is shown that people who go through high physical activity can reduce the risk of colon cancer to as much as 50%. It is also shown that the lack of physical activity may increase the risk of lung and prostate cancer (Stein and Colditz, 2004).

There are some proposed mechanisms that explain how physical inactivity may affect cancer risk. Physical activity could reduce the level of insulin, hormones, and other growth factors that circulate in our body. Physical activity can also alter prostaglandin levels as well as improving the immune system. In colon cancer, physical activity is also shown to make

changes in bile acid metabolism, reduced gastrointestinal transit time, and minimization of contact time between potential carcinogens with our colon mucosa, lowering the risk of cancer. It is fortunate that these negative effects of physical inactivity are reversible, and increasing physical activity will reduce the risk of cancer death (Stein and Colditz, 2004).

Alcohol use

Alcohol consumption can primarily increase the risk of esophageal and oral cancer. Moderate use of alcohol could even increase the risk of breast and colorectal cancer. Heavy intake of alcohol can also increase the risk of liver cancer. Alcohol is a carcinogen that raises the risk of cancer by acting as solvent, irritant, and a possible transporter. As a solvent, it allow carcinogens to penetrate the mucosa. As an irritant, it could increase cell turnover. It can also act as a transporter that brings carcinogens into the basal layer of the mucosa.

It is important to limit the amount of alcohol use in every person. People who drink should drink less than one or two drinks per day, and people who do not drink should not be encouraged to (Stein and Colditz, 2004). Increasing taxes, reducing the access of stores selling alcoholic beverages, banning advertisements, random breath tests for vehicle drivers and advising heavy drinkers are cost-effective interventions known to reduce alcohol consumption (Sloan, 2004).

Conclusion

Cancer risk factors include exposure to chemicals/substances, certain behaviors, aging, and family history. While we cannot control risk factors like aging and family history, there are different ways to avoid chemical/substance exposure and control our behavior. Some behaviors that relate to and increased cancer risk are: smoking, unhealthy and unbalanced diet, physical inactivity, and alcohol consumption. Even though it is more manageable, these behavioral risk factors are actually known to account for one third of cancer cases worldwide, so it is really important to know what behaviors could increase the risk of cancer and how to eliminate/reduce those risk.

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What are the classification of cancer and how is cancer being classified?

What is the classification of cancer and how is it being classified?

By: Benjamin Kegg, Woon Joo Yun, and Hans J. Tan

Background

In 2018, approximately 18.1 million new cancer cases were found, and by 2040, 25 million new cancer cases are expected to occur. However, it could not be cured in just any hospitals due to its complexity, and only specialized hospitals could provide cure for this deadly disease. Diagnosis and treatment of cancer are decided by the confirmation of cancer malignancy, origin site, histology, grade and stage (how it spreads throughout the body). World Health Organization (WHO) and Union for International Cancer Control (UICC) describe features to classify cancer to help in decision management in treating people with cancer (Carbone, 2020). In this paper, we are going to explain the classifications of cancer.

Broad Classification of Cancer

Broadly, cancer is classified by the tissue/organ/system where it originates in the body (Carbone, 2020). Classification of cancer by the type of tissue it originates is usually referred to as the histological type classification; while the primary site is the location in the body where the cancer first developed (National Cancer Institute, n.d.a). For example, skin cancer, lung cancer, breast cancer, prostate cancer, and brain cancer are named after their primary site (NCI, n.d.b). Compared with the classification based on histological type, primary site classification may not accurately describe the type of cancer since it did not specify the type of tissue involved (NCI, n.d.b).

Primary Sites of Tumors

WHO classification of tumors is linked to a joint project of the International Academy of Cytology with the International Agency for Research on Cancer (IARC). The project is a report system of cytopathology (cellular diseases) that uses hierarchical systems for diagnosing categories. It classified tumor into 13 groups: hematolymphoid tumors, endocrine tumors, head and neck tumors, urinary and male genitals tumors, pediatric tumors, central nervous system tumors, thoracic tumors, female genital tumors, soft tissue and bone tumors, breast tumors, digestive tumors, skin tumors, and eye tumors (International Agency for Research on Cancer, n.d.).

Cancer Histology Types

Carcinoma is the type of cancer that affects the epithelial tissue, which covers the interior and exterior surfaces of our bodies and skin (NCI, 2021). The majority of cancer diagnoses (80% –

90%), are carcinoma, making it the most common cancer type (Cleveland Clinic, 2022). Carcinoma includes most cancers that affect the skin, breasts, kidney, liver, lungs, pancreas, prostate gland, head and neck. Different types of carcinomas may occur in different types of epithelial tissue (Figure 4.1.): squamous cell carcinoma, adenocarcinoma (in glandular cells), transitional cell carcinoma, and basal cell carcinoma (Cancer Research UK, 2020).

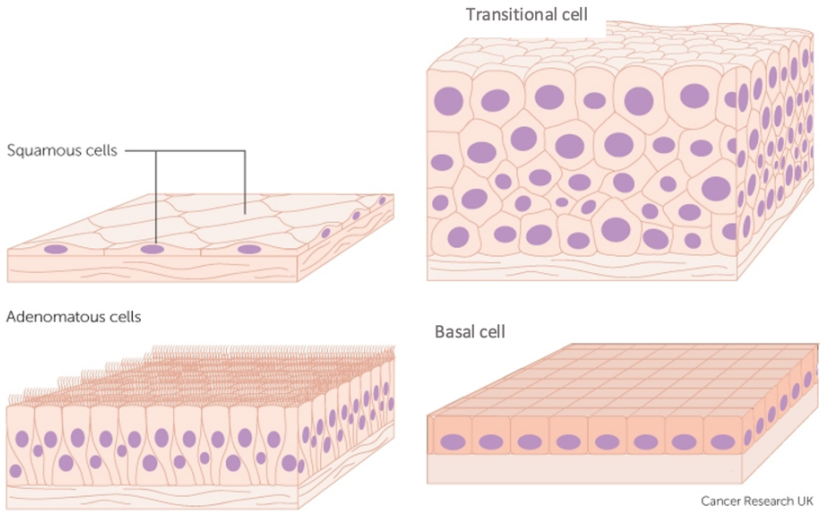

Figure 4.1. Different types of epithelial cell where carcinoma occur
Source: Cancer Research UK, 2020.

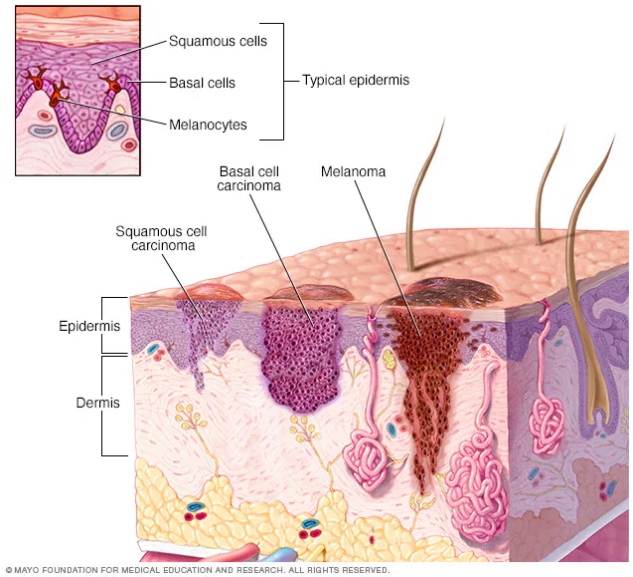

Figure 4.2. Different tissues where skin cancer develops (carcinoma/melanoma)
Source: Balzer, 2020.

Melanoma is the most serious type of skin cancer, and it forms in melanocytes, which are cells that produce melanin/skin pigment in your body. The symptoms are often visible because it creates moles on your skin, but it can also occur in parts that aren't exposed (Mayo Clinic,

n.d.). Skin cancer may be melanoma or carcinoma depending on the type of cell that is affected (Figure 4.2.)

Sarcoma is a type of cancer that starts in the bone or soft tissues like muscle, fat, nerves, fibrous tissues, blood vessels, or deep skin tissues (NCI, 2021). The most typical type of bone cancer is osteosarcoma. Liposarcoma, Kaposi sarcoma, malignant fibrous histiocytoma, liposarcoma, and dermatofibrosarcoma protuberans are the most prevalent varieties of soft tissue sarcoma (NCI, 2021). Figure 4.3. shows different tissues where sarcoma could occur.

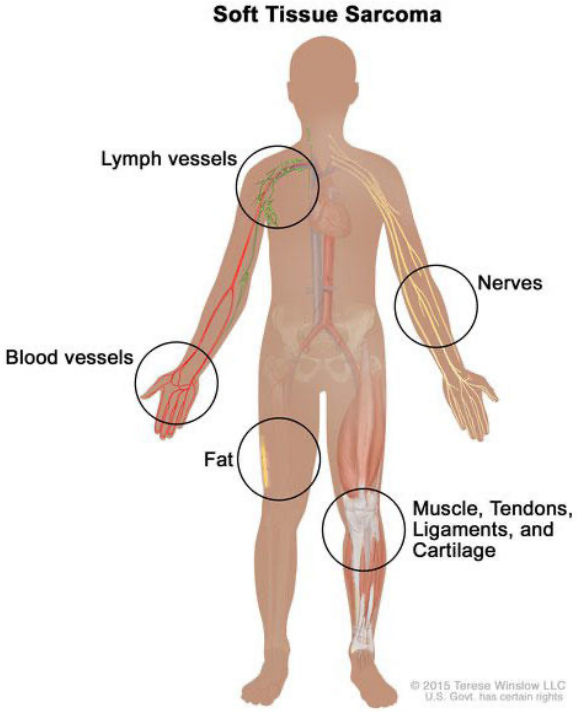

Figure 4.3. Soft tissue sarcoma in the body
Source: NCI, 2021.

Leukemia, Lymphoma and Myeloma are cancers of the body's blood-forming organs. Different kinds of blood cells originate from the hematopoietic stem cell in the bone marrow, which will mature and become specific blood cells with distinct function and role in the body. Some may mature in the bone marrow and some others may travel to other parts of the body to mature. Mutation in the DNA causes immature blood cells to proliferate abnormally instead of maturing. Scientists and physicians classified this blood forming cancer diseases by their location in the body. In Leukemia, cancer cells are discovered to circulate in blood and bone marrow. In Lymphoma, cancer cells tend to aggregate, forming tumor masses in lymphatic tissue. In myeloma, cancer cells are forming tumors in the bone marrow (Klausner, 2001).

> **Leukemia** can arise in two main groups of white blood cells: lymphocytes or myelocytes. Both types could be acute (rapidly progressing and involving very

immature and unstable cells that cannot serve their purpose) or chronic (progress more slowly and involving a more well-differentiated cell that still functions poorly) (Klausner, 2001). As there are various forms of leukemia, some types are more prevalent in children while the others in adults. Depending on the type of leukemia and other variables involved, treatment for leukemia may be difficult. However, there are methods and tools that can aid in the success of the treatment (Mayo Clinic, 2022a).

Lymphoma is a cancer of the lymphatic system, which is part of the body's germ-fighting network. It starts in the lymphocytes (T cells and B cells). The lymph nodes (lymph glands), spleen, thymus gland, and bone marrow are components of the lymphatic system. Each of those regions as well as other organs across the body are all susceptible to lymphoma (Mayo Clinic, 2022b). Two main types of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma (National Cancer Institute, 2021). Hodgkin lymphoma, which is less common than non-Hodgkin lymphoma, is historically characterized by the presence of Hodgkin (large, mononucleated cells) and Reed-Sternberg cells (large, multinucleated cells) (Klausner, 2001; Aggarwal & Limaiem, 2022).

Myeloma is the type of cancer that occurs in bone marrows, which are the inner tissue of some bones that produce blood cells (National Health Service, 2021a). This cancer causes a type of white blood cells that produce antibodies called the plasma cell, to multiply uncontrollably (Cancer Research UK, 2020). This not only causes our bones to be weak and in pain, but it can also outnumber the other cells in the bone marrow that are supposed to produce red blood cells, platelets, and other white blood cells (NHS, 2021a). This may lead to some conditions of low blood cells levels such as anemia (low red blood cells), thrombocytopenia (low platelets), and low normal white blood cells (leukopenia) (American Cancer Society, 2018).

Grades and Stages of Cancer

Once someone is diagnosed with cancer, further tests are needed to determine how far the cancer has progressed. Staging and grading cancer allows doctors to know the size of cancer and whether or not it has spread. It helps the doctor to decide what treatment options are available/is the best. Staging of cancer describes the gross appearance of the tumor: size of tumor, invasion, and its malignancy (spread); while grading of cancer describes the appearance of cancerous cells under the microscope or its cytology features: cell differentiation, morphology and structure. This appearance of cancer cells under the microscope relates to the aggressiveness and prognosis (the forecast of the disease outcome) of cancer (NHS, 2021b; Rosen & Sapra, 2022).

Cancer Grading

The appearance of the cells under a microscope determines the cancer's grade. Typically, higher grade tumors are more aggressive with worse prognosis. Their cells are poorly differentiated, and the highest grade is even described as undifferentiated. On the other hand, low grade tumors relatively appear normal and are well differentiated. In general, a lower grade denotes a cancer that is growing more slowly, whereas a higher grade denotes a cancer that is growing more quickly (NHS, 2021b; Rosen and Sapra, 2022).

Regularly used cancer grading criteria are as follows:

Grade 1 – Cancer cells resemble normal cells and aren't expanding quickly

Grade 2 – cancer cells that don't resemble healthy cells and are developing more quickly than healthy cells

Grade 3 – cancer cells have an irregular appearance and may develop or spread more quickly

(NHS, 2021b)

Cancer Stages

TNM Classification is a cancer classifying for malignancy. Primarily, it is used to classify solid tumors and may assist in cancer prognosis. It helps the anatomic extent of cancer to be established (NHS, 2021b). The system uses letters and numbers to assess the tumor, regional lymph nodes, and distant metastasis as follows:

> **T for tumor** is used to characterize the main tumor's size and the extent of its tissue infiltration. T1-T4 determines the size and extent of the tumor, with enlargement and invasiveness increasing progressively from T1 to T4; whereas T0 indicates the absence of tumor.
>
> **N for nodes** is used to explain how the tumor has affected localized lymph nodes. As fluid from body tissues is absorbed into lymphatic capillaries and travels to the lymph nodes, lymph nodes serve as biological filters. N0 implies that there is no regional nodal spread, whereas N1 to N3 show varying degrees of nodal spread, with a distal spread disseminating gradually from N1 to N3.
>
> **M for Metastasis** is used to identify the presence of distant metastases of the primary tumor. Metastasis is when the tumor spreads beyond regional lymph nodes. A tumor is classified as M0 if no distant metastasis is present and M1 if there is evidence of distant metastasis.
>
> (Rosen & Sapra, 2021b)

Table 3.1. TNM Staging Summary

T	**TX**	Primary tumor cannot be evaluated
	T0	No evidence of primary tumor
	Tis	Carcinoma in situ (early cancer that has not spread to neighboring tissue)
	T1, T2, T3, T4	Size and/or extent of the primary tumor (increasing from T1 to T4)
N	**NX**	Regional lymph nodes cannot be evaluated
	N0	No regional lymph node involvement (no cancer found in the lymph nodes)
	N1, N2, N3	Involvement of regional lymph nodes (number and/or extent of spread)
M	**MX**	Distant metastasis cannot be evaluated
	M0	No distant metastasis (cancer has not spread to other parts of the body)
	M1	Distant metastasis (cancer has spread to distant parts of the body)

Source: Sloan & Gelband, 2007.

The TNM classification system allows a more simplified staging system for cancer, stage 1-IV. Stage 0 which indicates carcinoma in situ is not considered to be cancerous but has the possibility to become cancer in the future. Stage V is used only in Wilms tumor when both kidneys are involved in cancer at initial diagnosis. The simplified version of cancer staging in relation to TNM classification is listed below.

Stage 0 - Indicates no sign of cancer. T0, N0, M0

Stage I - Localized cancer. T1-T2, N0, M0

Stage II - Locally advanced cancer, early stages. T2-T4, N0, M0

Stage III - Locally advanced cancer, late stages. T1-T4, N1-N3, M0

Stage IV - Metastatic cancer. T1-T4, N1-N3, M1.

(Rosen and Sapra, 2022)

Conclusion

Diagnosis and treatment of cancer are decided by the confirmation of cancer malignancy, origin site, histology, grade and stage (how it spreads throughout the body). World Health Organization (WHO) and Union for International Cancer Control (UICC) describe features to classify cancer to help in decision management in treating people with cancer. Cancer is broadly classified by the primary site (tissue/organ/system) location or where it originates in the body. There are 13 classifications of cancer based on its primary site location: hematolymphoid tumors, endocrine tumors, head and neck tumors, urinary and male genitals tumors, pediatric tumors, central nervous system tumors, thoracic tumors, female genital

tumors, soft tissue and bone tumors, breast tumors, digestive tumors, skin tumors, and eye tumors. According to the tissue it affects, cancer could also be classified into: carcinoma (skin/epithelial tissue cancer), melanoma (melanocyte/skin pigment cell cancer), sarcoma (bone and soft tissue cancers), and blood cancers: lymphoma (lymphatic cancer), leukemia (white blood cancer), myeloma (bone marrow cancer).

To identify malignancy, the appearance of cancer under the microscope would also be helpful. In general, grade 1 cancer cells will look pretty similar to normal cell with a slow rate in developing and expanding, while grade 3 cancer that has abnormal shape of cells would usually spread and develop more quickly. The malignancy of cancer cell/tissue can also be classified into different type of staging system. The TNM (tumor, nodes, metastases) system rate had developed in tumor size and infiltrations (T), it's spread into the lymph node (N), and beyond lymph node (M). A simplified version staging related to the TNM staging is stage 0-IV cancer where stage 0 indicates no tumor, stage 1 indicates localized cancer, stage 2 indicates early locally advanced cancer, stage 3 indicates late locally advanced cancer, and stage IV indicates metastasis cancer.

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What are the different treatment of cancer and how is it being decided?

What are the treatments for cancer and how is it being decided?

By: Ji Hye Kim and Marsha Sujanto

Background

Cancer treatment plays an important role in cancer management. When cancer is detected through screening or visible symptoms, a diagnostic service will help to assess the cancer type and stage, so the appropriate treatment for the newly identified cancer can be decided (Sloan & Gelband, 2007). The two main categories of treatments for cancer are curative treatment and palliative care. The main aim behind cancer treatments is to achieve a cure (curative treatment) through surgery, radiotherapy, chemotherapy, or combinations of them (Sloan & Gelband, 2007). This process often requires a team of multidisciplinary medical professionals (Khan, Akhtar, and Seikh, 2005; Sloan & Gelband, 2007). Curative treatments are considered first because the main aim of treatment is curing the cancer (Sloan & Gelband, 2007). However, when the cancer has advanced and becomes beyond curable, palliative treatment is given to prolong the patient's life or relieve their suffering with symptoms (Khan et al., 2005; Sloan, 2007). Palliative treatment aims to give a better quality of life to the patient (Sloan & Gelband, 2007).

Cancer comes in different types and stages, which affects how the treatment is decided. The type, severity, and opinion of the doctor on cancer treatment is decided based on the individual factors of the patients (Markman, 1994). Not all patients have the same strength or health condition, so they won't receive the same treatment even though they have the same cancer type and stage (Markman, 1994). In this paper, we are going to talk about many treatment options for cancer and factors that may influence treatment decisions.

Systemic and Local Therapy

In general, treatments could be grouped into systemic therapy and local therapy. Systemic therapy is a cancer treatment that targets the entire body, and drug treatments are included in systemic therapy (American Cancer Society, n.d.). Systemic therapy moves through the bloodstream and destroys cancer cells (Moffitt Cancer Center, n.d.). In the example of chemotherapy, drugs are administered to circulate throughout the bloodstream, dispersing and destroying cancerous cells in various locations in our body (Moffitt Cancer Center, n.d.). Because of this property, chemotherapy is used to treat cancer that has spread from its original site (Moffitt Cancer Center, n.d.). Other systemic treatments include hormone therapies, immunotherapies, and targeted therapies (Moffitt Cancer Center, n.d.).

On the other hand, local therapy is a cancer treatment that is directed to target specific organs, tumors, or limited areas of the body (NCI, n.d.; American Cancer Society, n.d.). Surgery and radiation are types of local therapy as it targets a specific area rather than the whole body (NCI, n.d.).

Types of Cancer Treatments

There are seven cancer treatments that are currently available for cancer: surgery, radiation therapy, chemotherapy, hormone therapy, targeted therapy, immunotherapy, and stem cell or bone marrow transplant (American Cancer Society, n.d.).

Surgeries remove cancerous cells/tissues from the body (National Cancer Institute, 2015a). They might remove the entire tumor or just a part of a tumor if removing the tumors entirely harms the organ (National Cancer Institute, 2015a). Some surgery may not remove the entire tumor in the body but might shrink the size of the tumor to release pain and symptoms caused by the tumor (National Cancer Institute, 2015a).

Radiation therapy uses the application of ionizing radiation like x-rays, gamma rays, or other radioactive particles to treat cancer (Sloan, 2007; NCI, 2019a). High doses of radiation are used to kill cancer cells and shrink the size of the tumor to treat pain and prevent other problems caused by the tumor (NCI, 2019a). Radiation could kill or slow the growth of the cancer cells by damaging the DNA so that it would stop dividing and die (NCI, 2019a). Radiotherapy could be used by itself or combined with other treatments to cure cancer (curative treatment) or to ease cancer symptoms (palliative treatment) (NCI, 2019a). Also, there is a dose limit to radiation therapy, so the same area can't be treated more than once (NCI, 2019a).

Chemotherapy kills cancer cells through the use of drugs and also slows the growth of the cells (NCI, 2022a). Similar to radiation therapy, chemotherapy could be used to cure cancer or shrink the tumor size to ease cancer symptoms (NCI, 2022a). Chemotherapy can either be used alone or with other treatments; for example, chemotherapy is used to shrink the tumor's size before the treatment or kill the remaining cancer cells after the treatment (NCI, 2022a). In chemotherapy, however, both cancerous and healthy cells might be damaged by chemotherapy, which leads to side effects like hair loss, mouth sores, nausea, and fatigue (NCI, 2022a).

Hormone therapy targets cancers that use hormones to grow (NCI, 2022b). Through the use of drugs it can block hormone production or interfere with how the hormone behaves in the body (NCI, 2022b). Some cancer types that need hormone therapy are prostate and breast cancers (NCI, 2022b). Hormone therapy is mostly used with other cancer treatments; it doesn't only stop the growth of cancerous cells in curative care but also reduces the

possibility of cancer regrowth and may be used to reduce cancer symptoms (palliative) (NCI, 2022b). As hormone therapy stops or interferes with hormone behavior, it leads to side effects like mood changes, weakened bones, nausea, fatigue, and other signs of hormone inactivity (NCI, 2022b).

Targeted therapy uses drugs to control the protein involved in cancer activities: cell growth, cell division, and cancer spreading (NCI, 2022c). The two main types of targeted therapy are small-molecule drugs, which could enter cells easily to target proteins inside of the cells, and monoclonal antibodies, which use lab-grown proteins to target specific proteins on the surface of the cancer cells (NCI, 2022c). These drugs could help to block the cell growth/division process, initiate self-destruction, mark the cancer cell to be easily detected by our immune system, and even starve cancer cells from nutrition (NCI, 2022c). However, the danger of targeted therapy is that cancer cells might develop resistance to the drugs, which leads to other serious problems and may also be toxic to the body and cause side effects like diarrhea and liver problems (NCI, 2022c).

Immunotherapy supports our immune system, which is the system that helps fight diseases, including cancer (NCI, 2019b). Normally, our immune system can detect abnormal cells like cancer and destroy them to prevent cancerous growth (NCI, 2019b). However, cancer cells can change themselves to hide from the immune system to avoid being killed; therefore, immunotherapy is used to help improve the immune system to act against cancer cells by counteracting changes in the cancer cells (NCI, 2019b). As the immune system improves, it might lead to side effects such as damaging the normal cells and tissues (NCI, 2019b). Immunotherapy is still relatively new and not used as widely as surgery, chemotherapy, or radiation (NCI, 2019b).

Bone marrow or stem cell transplant restores bone marrow that is damaged by high doses of treatments, such as chemotherapy or radiation (Pruthi, 2021). Healthy blood-forming stem cells are inserted in the bloodstream where it would travel to the bone marrow that was damaged by treatment (NCI, 2015b). The blood-forming stem cells could come from various sources: the bone marrow, bloodstream, or umbilical cord (NCI, 2015b). It could also come from the patient itself (autologous), other people's stem cells (allogeneic), or from the patient's identical twin (syngeneic) (NCI, 2015b). In an allogeneic transplant, the antigen set from the stem cell donor must match that of the recipient to minimize side effects; close relatives are more likely to have the match (NCI, 2015b; NCI, 2013). Someone who had an allogeneic transplant might develop graft-versus-host disease; it happens when the donor's white blood cells attack the host's cells as if they were foreign cells (NCI, 2015b). In the case of multiple myeloma and leukemia, the donor's white blood cells might attack cancer cells which is advantageous in fighting cancer (NCI, 2015b).

Factors That Influence Decision

There are many aspects to consider when deciding on cancer treatment. In some cases, it may be easier to make the decisions than in other cases. Sometimes, the variety of factors involved in making decisions makes it difficult for doctors to stay firm in one decision, and they might have to change their plans through the process (Markman, 1994). We divided the factors into initial medical factors relating to the cancer type and patient's overall health condition; and extended factors, which include the treatment's effectiveness and toxicity that relates to the patient's quality of life and patient preferences (Markman, 1994; American Cancer Society, 2021).

Initial Medical Factors

Based on the type of cancer alone, treatment options may vary, either limited or many. Cancer care teams will use established treatment guidelines based on research to apply the treatment (American Cancer Society, 2021). However, treatment options that are offered might differ between people with the same type of cancer (American Cancer Society, 2021). This is because the subtype and features of cancer might differ in different people with the same type of cancer (American Cancer Society, 2021). For example, breast cancer might have several molecular subtypes, such as basal, luminal, ERBB2, and Apocrine, and they might have different grades as well (Sims, Howell, Howell & Clarke, 2007).

There are also factors regarding the patients that are considered by the cancer care team (American Cancer Society, 2021). Patients' performance status is evaluated by their ability to carry out essential normal daily activities (Markman, 1994). Besides the patient's performance status, age and comorbidity are also factors considered in evaluating cancer treatment decisions (Markman, 1994). Medically factors that are considered in therapy decisions for cancer patients are listed in Table 5.1.

Table 5.1. Initial Medical Factors in Cancer Treatment Decision

Cancer	Types and subtypes of cancer
	Cancer stage and grade
	Other information about the cancer (for example information from biomarker/hormone receptor test)
Patients	Patient's performance status
	Patient's comorbidity
	Patient's age
	Presence of symptoms
	Other information on patients health and condition (for example blood test, genetic testing, imaging test)

Source: American Cancer Society, 2021; Markman, 1994.

Extended Factors

Besides the cancer characteristics and the patient's health condition, other factors that are considered in cancer treatment decisions relate to the resulting quality of life of the treatment and other non-medical conditions of the patient. Even though doctors'/physicians' evaluation plays a key role in cancer treatment decisions, patient and family preferences will put weight on the final decision (Markman, 1994). Extended factors that are also considered in cancer treatment decisions are listed in Table 5.2. All of the factors combined must be considered in defining general treatment strategies, and all factors have the same level of importance, nothing can be less considered (Markman 1994).

Table 5.2. Extended Factors in Cancer Treatment Decision

Effectiveness and toxicity of the available therapy
Chance of a cure
Potential short and long-term side effects
Likelihood of cancer recurrence
Chance of living longer without treatment
Effects on patient's independency and quality of life
Patients and their family's preference

Source: Cancer.net, 2018; Markman, 1994.

Establishing Realistic Goal for Cancer Treatment

When doctors are treating cancer patients, a realistic treatment goal must be established and proposed to the patients before treatment is started (Markman, 1994). These goals may change frequently during the progression of the disease (Markman, 1994). A realistic assessment needs to be done, otherwise, the chosen treatment might be inappropriate for the patient and cause potential harm (Markman, 1994).

In establishing reasonable goals, for example, if the chance for cure is high and the patient is reasonably fit, short and long-term morbidity could be considered acceptable (Khan et al., 2005). Even when cancer has advanced, when the patient has a good performance status, it could be concluded that the side effects of treatment would be less severe and tolerable in the patients, and the benefit might be higher than the risk (Markman, 1994). However, when dealing with old and frail patients or people with comorbidities, even with the possibility of a cure, the expected side effects, resulting quality of life, and anticipated life span of patients must be considered carefully (Khan et al., 2005; Markman, 1994). In these cases, the anticipated toxicity of treatment might outweigh the limited potential benefit (Khan et al., 2005; Markman, 1994).

In incurable cancer patients whose cancer has advanced, palliative care would be the goal of treatment (Khan et al., 2005; Sloan, 2007). Palliative care given to patients must cause as little morbidity as possible (Khan et al., 2005; Sloan, 2007). The treatment should be effective and completed in a short period, and any resulting acute morbidity should also be tolerable (Khan et al., 2005). In terminal cancer patients, the wise use of analgesics with steroids may be more effective than hi-tech therapies or chemo (Khan et al., 2005). With support from local health facilities, patients may have better symptom control and die comfortably at home (Khan et al., 2005).

Physician Role and Real-Life Cases

It's essential for doctors/physicians to explain with clarity and detail about the illness to the patient. They must constantly weigh the risk and benefit of a particular treatment and give realistic advice in regards to the possible outcome along with the morbidities that may occur (Khan et al, 2005). Although this process cannot be calculated precisely, an objective assessment about treatment risk and expected benefits of the therapy must be informed to the patients (Markman, 1994).

In reality, most of the time it's hard to know whether a cancer is curable or not. While it's important to keep patient hopeful and in good spirits, a physician's responsibility is much more than providing hope. Since the patient's preference of treatment is a critical component in treatment decisions, it is important for physicians to provide the pros and cons for a treatment so patients, along with their families and friends, are able to decide which treatment is the most beneficial (Markman, 1994).

Some desperate families seek alternative and advanced treatments for their cancer because they think that the "alternative treatment program" is more hopeful. However, patients need to think carefully before participating in other new therapies and studies that lack scientific research (Markman, 1994). Therefore, the role of the physician will be to inform the patient about the risk of treatment, also what is known and unknown of the treatment (Markman, 1994). For example, we present you a case in the following table (Table 5.3.) and we'll discuss the rationale on the alternative treatment decision in this case along with the role of the physician in this decision process.

In desperate cases like this, patients and their families might seek hope from treatment trials at cancer research centers (Markman, 1994). These programs are legitimate and could be reasonable to join if patients are eligible for the criteria and are informed carefully about the risk and not yet-known benefits (Markman, 1994). However, if the proposed trial lacks scientific credibility and is promoted based on unrealistic goals and false claims of benefit, physicians must make every effort to inform patients about the scientific nature of the so-called "alternative treatment" (Markman, 1994). Although it is important for the patient to

be hopeful, it is not reasonable to use an approach that involves useless and expensive procedures with inevitable pain and suffering, and physicians need to help patients in informing and to understand this (Markman, 1994).

Table 5.3. Real Life Case of Cancer

Patient's age and sex	47-year-old woman
Cancer type and stage	Metastatic breast cancer
	Evidence of metastatic spread: Cancer has spread to liver, lungs, and bones; 2 new metastatic lesions is recently found in the brain recently;
Notes on treatment	Show no response or effects towards chemotherapy
Patient decision	Continues to seek high-dose chemotherapy from a bone marrow transplant center, despite the advice of her physician.

Source: Markman, 1994.

Advice For Cancer Patient

Cancer patients will have many questions regarding how to decide which cancer treatment. Before we discuss the decision making for the treatment, here are some considerations that we would like to remind cancer patients to take in that process.

1. **Take your time.**
   It may seem that once we are diagnosed with cancer, we need to decide our treatment right away. However, in most situations, you have time to decide your treatment choice. Ask your doctor how much time you have until the decision is needed. Delaying a decision and spending your time worrying about it may drain your energy, so it's wise to not take too long in thinking about your decision.
2. **You can always speak up and ask your doctor for the things you don't understand.**
   You should clarify with your doctor if you have any questions, doubts, or concerns that need to be addressed for your understanding. There is a lot of information that may not be based on clinical trials, and it's wise to ask your physician about what is true or not accurate about the information. You can write down your question before your appointments, take notes, and have a discussion with your doctor, and even ask if there is any alternative way to communicate with them when needed.
3. **You can seek a second opinion.**
   Most doctors understand the need for a second opinion when facing a major decision. It's okay if you need to ask for a second opinion, don't be afraid to offend your doctor. You can ask advice from the people you are close with and even cancer survivors.

4. **You can always change your mind.**
   Once you make your decision, it doesn't mean you are bound to it. Let your doctor know if you have second thoughts. Some side effects may make you want to change your treatment plan and that's OK.
5. **Keep the focus on yourself.**
   Don't let yourself be pressured into choosing a certain treatment. Take your time to choose what treatment you are most comfortable with.
6. **If you prefer, you don't have to be involved with treatment decisions.**
   Sometimes the process of decision making might be too difficult for patients itself. If you really prefer to not be involved in the decision-making process, let your doctor know about that and if possible, you can also designate a person you trusted to make the decision for you. You can always get involved later when you feel more comfortable with the situation.
7. **For patients with advanced cancer, you can choose to not undergo treatments.**
   People with hard to cure cancers may rather treat their pain and side effects rather than treating the cancer itself to make the best of the time they had left. Going untreated doesn't mean you will be left by yourself, there are a lot of ways to control side effects and discomfort.
8. **Ask/accept help and talk with the people you trust**
   Going through cancer might be hard for patients. Your doctors, friends and family that you trust could be a great support system for you in going through your treatment.

Once you are ready to start the decision, these are some helpful pieces of advice that might help the patient or the patient's family through the decision-making process for cancer treatment.

1. The patient should decide how much information about the treatment they want to know because some details might be uncomfortable to hear in the patient's perspective. (don't want to know the survival chances and other specific details)
2. The patient also needs to decide whether the patient, the doctor or even both lead the decision.
3. Always remember to have realistic expectations; the doctor should give the patient estimates from each treatment, such as the side effects, benefits, etc.
4. Set treatment goals considering whether the aim is to cure the cancer, control the disease, or gain comfort (palliating symptoms).
5. Do your own research if you think you need to. Ask the doctor for reliable websites or even books to help you learn each treatment option specifically.

6. Make sure you and your doctor is in the same page about who is going to make the treatment decision, the aim of the treatment and how far you want to be involved in the treatment decision process

(Harish, n.d.; Pruthi, 2022)

Conclusion

Cancer treatment plays a big role in cancer management, which may include: curing cancer, slowing the growth of cancer, shrinking tumor size, easing symptoms, and preventing regrowth. The seven main types of cancer treatment are surgery, radiation therapy, chemotherapy, hormone therapy, targeted therapy, immunotherapy, and stem cell or bone marrow transplant. Treatment is decided by several factors, and it's mainly divided into two: initial medical factors, which depend on the type, stage, or spreading of the cancer cell, and the extended factors, which depends on the effectiveness and toxicity of the treatment. However, the final decision weighs on the patient's preference because the patient should be comfortable with the treatment and need to assure that the treatment is the best for the patient. Therefore, the doctor allows the patient or the patient's family to decide which option they are going to work with.

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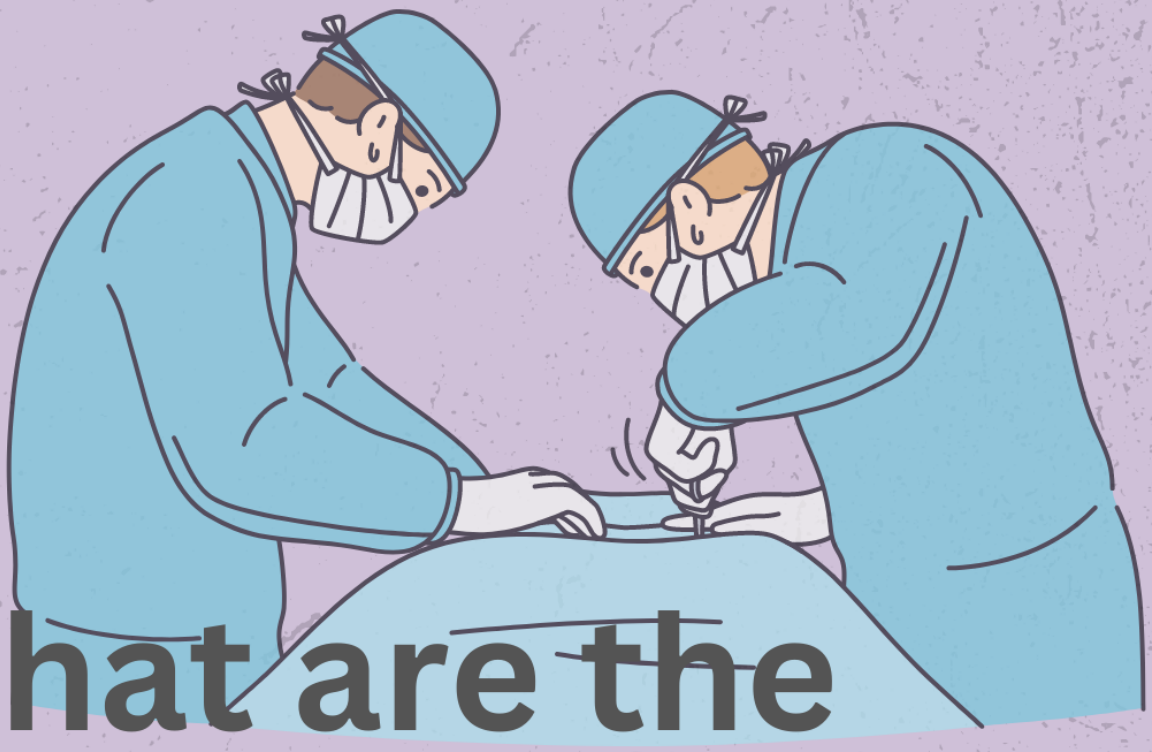


What are the different roles of surgery in cancer treatment?

What are the different roles of surgery in cancer treatment?

By: Chris Thomas Menassery

Background

Surgery is the oldest practice of diagnosing and treating cancer, dating back thousands of years ago (Wyld, Audisio & Poston, 2014). In the past, surgeons used more radical methods of surgery with high mortality rates, as surgical treatment back then was quite under-developed; with many unavoidable issues caused, including blood loss due to a lack of knowledge and technological advancements (American Cancer Society [ACS], 2014). Recently, however, with the constant technological innovation and data gained over the years of advancements in studies, leading to a multitude of therapy and minimal invasive techniques, surgery has evolved to be a process that can be done without the detrimental consequences of previous experiences. These advances in surgery not only increased the cure rate but were also able to focus on preserving the quality of life without compromising survival (Wyld et al., 2014). For example, surgeons developed greater technical expertise in minimizing the amounts of normal tissue removed during cancer operations (Wyld et al., 2014; ACS, 2014).

Together with oncologists, radiologists, scientists, anesthetists, and nurses, highly trained medical professionals nowadays have made cancer surgeries a method that is more routine, safe, and highly effective (Wyld et al., 2014). Today, surgery has become a fundamental method for the curative and palliative treatment of many cancers across the world (Dare et al., 2015). This article will introduce the different roles of surgery in cancer treatment alongside their challenges and risk.

Different roles of Surgeries in Cancer

Surgery is a crucial treatment method for curing and relieving pain for most cancers, in countries of all economic backgrounds (Dare et al., 2015). The application of surgery in oncology may come in many forms, such as the following.

1. **Curative Surgery** removes cancerous tumors or growth from the body. Surgery is primary treatment when the cancerous tumor is localized in any area of the body. It may be used as a single treatment or in combination with other treatments like radiation to completely remove cancerous growth (Stanford Medicine, n.d.).

2. **Preventive Surgery** removes tissue that does not contain cancerous cells, yet may develop into a cancerous tumor. Tissues like polyps are considered precancerous and removing them most likely prevents cancerous growth (Stanford Medicine, n.d.). Preventive surgery could also be done when someone has genetic testing/family there is risk of getting cancer like ovarian cancer (Ovacare, n.d.)

3. **Diagnostic Surgery** takes tumor cells/tissues from the body to determine whether cells are cancerous or not. The evaluation of the tumorous tissue may help to confirm the diagnosis, identify cancer type, or determine the stage of cancer (Stanford Medicine, n.d.).

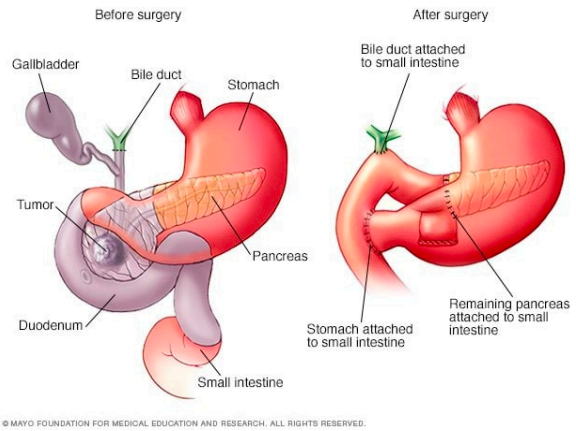


Figure 6.1. Curative Surgery in Pancreatic Cancer
Source: Mayo Clinic, 2022a.

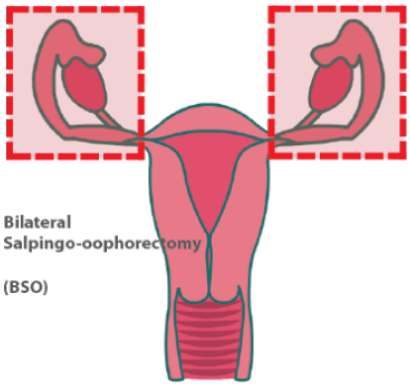
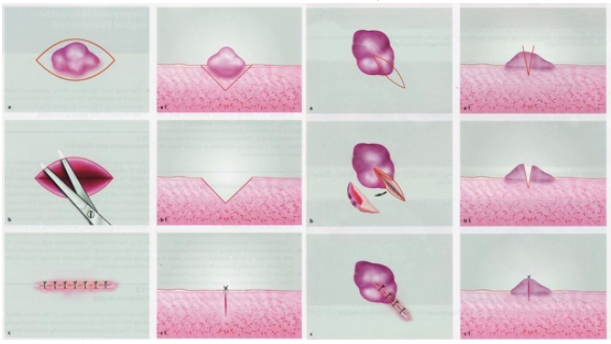


Figure 6.2. Preventive Surgery
Prophylactic salpingo-oophorectomy
Notes: Ovary and fallopian tube is removed when genetic testing/family history indicates a strong risk of ovarian cancer
Source: Ovacare, n.d.



a b.

Figure 6.3. Diagnostic surgery
Notes: (a) whole tumor is removed for diagnostic (b) a part of tumor is removed for diagnostic
Source: Exodontia, n.d.

4. **Staging Surgery** uncovers the stage of cancer or the extent of it in the body. For example, a small incision is made to insert a viewing tube with a small camera to examine or even remove tissues inside our body. This is called laparoscopy (Stanford Medicine, n.d.).

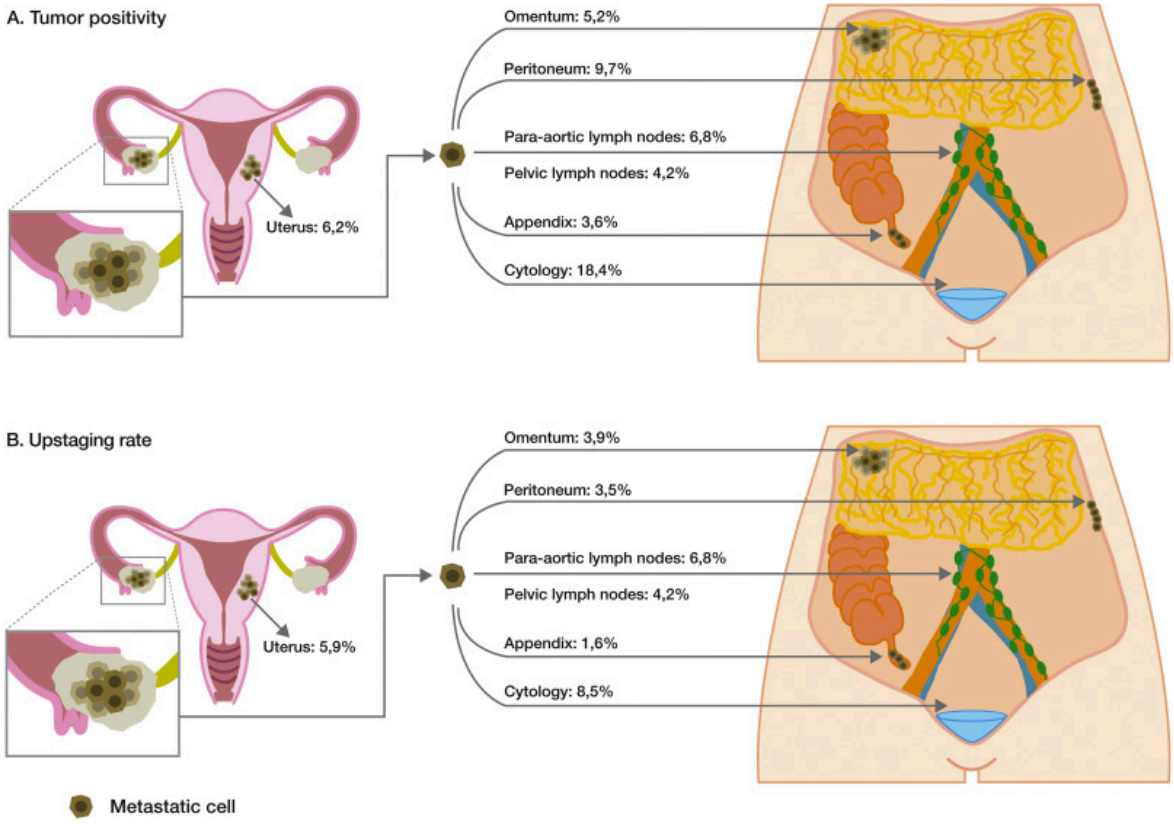


Figure 6.4. Staging surgery for ovarian carcinoma
Source: Van de Vorst et al., 2021.

5. **Debulking Surgery** removes a portion, though not all, of a cancerous tumor, especially if removing the entire tumor will damage organs. It may be used along with other treatments such as chemotherapy and radiation (Stanford Medicine, n.d.).

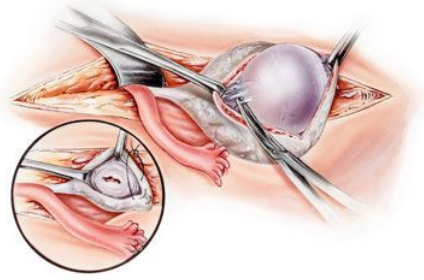


Figure 6.5. Debulking Surgery in Breast Cancer
Source: Lewis, 2015.

6. **Palliative Surgery** treats cancer at advanced stages by relieving discomfort & corrects mistakes in cancer/cancer treatment. For example, removing a painful mass of tumors in solitary spinal metastasis (Stanford Medicine, n.d.; National Cancer Institute [NCI], n.d.a).
7. **Supportive Surgery** helps other cancer treatments work effectively, like making a small opening to place a port for a catheter to help with chemotherapy. Once the

chemotherapy procedure gets more complicated, needing more medicine, blood test, and blood transfusion, or done for patients with small and fragile veins, using a port catheter for chemotherapy could be more effective than peripheral IV, thus small surgery is needed to insert the port (Stanford Medicine, n.d.; MacMillan Cancer Support, 2018).

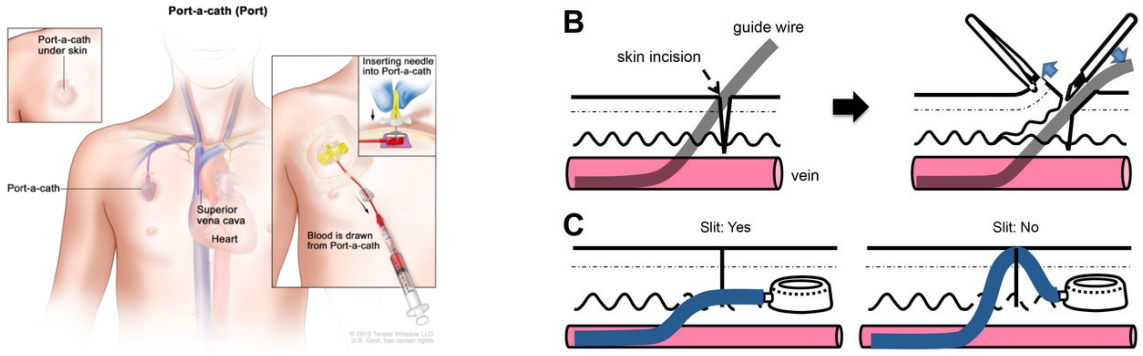


Figure 6.6 Supportive surgery to insert port-a-cath
Source: NCI, n.d.b; Shiono et al., 2014.

8. **Restorative Surgery.** Sometimes, cancer treatment may damage or alter parts of the body, which is where restorative surgery can help reconstruct the body in order to return a sense of normalcy and can help some people move forward with confidence in their life after the treatment. Some examples of restorative surgery that are available are scar revisions, artificial implants, and tissue transfer (Stanford Medicine, n.d.; Regional Cancer Care Associates, 2019).

Figure 6.7. Before and After Restorative Surgery
Source: John Hopkins Medicine, n.d.

Alone, surgery for cancer treatment is mainly functional only in the early stages of cancer, especially when cancer/tumorous growth hasn't spread to other parts of the body. In this case, the cancerous tissue/tumor can be safely and efficiently removed. However, once the cancer has spread; removing a part of the cancer through surgery will not cure the patient, and attempting to remove the whole of the cancer could cause detrimental damage to the body, which would not be optimal. (Dare et al., 2015).

Challenges

The availability, access, and quality of surgery for cancer treatment vary widely, leading to just as wide variations in outcomes among and within other countries (Dare et al., 2015). In many underdeveloped and developing countries, access to safe, optimal surgical services for cancer

is poor, and much of the population cannot access even the most basic surgical care (Dare et al., 2015). Table 6.1 below compares the number of surgeons, anesthesiologists, operating rooms, and operating volume in high-income countries and low-income countries.

Table 6.1. Different Surgery Aspects in High-income Countries and Low-income Countries

Measure	High-income countries	Low-income countries
Number of surgeons	34–97 per 100,000	0.13–1.57 per 100,000
Number of anaesthesiologists	34–97 per 100,000	0–4.9 per 100,000
Number of operating rooms	> 14 per 100,000	< 2 per 100,000
Volume of operations	172.3 million procedures per year (73.6 percent of the global total, for 30.2 percent of the global population)	8.1 million procedures per year (3.5 percent of the global total, for 34.8 percent of the global population)

Source: Dare et al., 2015.

High-volume hospitals are hospitals that have a high count of surgery procedures. These hospitals generally have a better quality of care, and they improve their care by frequently providing complex care and highly advanced treatment (Ubrach & Baxter, 2004). In contrast, low-volume hospitals don't have as much efficient quality of care; with fewer surgeons, and operating rooms, which leads to an overall lower volume of operations (Dare et al., 2015).

In general, cancer surgery procedures in higher-volume hospitals tend to have lower mortality rates than those in lower-volume hospitals. Furthermore, studies show that higher-volume hospitals also have a lower risk of nonfatal complications. Meanwhile, in low-volume hospitals, the risk seems to be higher. This is most likely because there are fewer facilities, surgeons, anesthesiologist in low-volume hospitals compared to the high-volume hospitals (Birkmeye et al., 2007).

Risk

Although surgery can serve as a great way to cure cancer, it also has quite a few risks to be aware of (ACS, 2019). However advancements in technology have allowed doctors/surgeons to limit these risks. Some of those risks includes:

a. **Bleeding** can result from a blood vessel not being sealed off properly (internal bleeding), or a wound opening up as a result of the surgery (external bleeding). Doctors can limit the chances of bleeding during surgery by conducting their work attentively and cautiously whilst dealing with blood vessels so as not to add further damage. If the bleeding has occurred, however, doctors may need to conduct another

operation to find the source of the bleeding and stop it. Blood transfusions may even be needed to restore the lost blood,

b. **Blood clots** form when masses of blood like platelets, proteins, and cells in the bloodstream stick together. It can form in the veins after surgery, especially when the patient remains inactive. The clot can become serious if it breaks loose and travels to another part of the body, such as a lung, where blood clots will block the passage of blood to and from the heart. (ACS, 2019; Mayo Clinic, 2022b; Medline Plus, 2022; Wu, 2018). Due to the risk of the clots spreading whilst inactive, doctors encourage patients to get active and out of bed as soon as possible.
c. **Damage to nearby Tissues and Organs** like Internal organs and blood vessels could happen during the surgery. Doctors will be careful to limit the damage as little as possible. Advanced technology is also developed to help minimize the damage of surrounding tissue and organs. (ACS, 2019). Like bleeding, the only way doctors and operators can prevent such damage is to work carefully near tissues and organs so as to not cause any damage.
d. **Drug Reactions** can occur during surgery when drugs/medicine is needed, in which an accidental reaction in the body can occur with the drugs causing dangerous/lethal effects. During surgery, heart rate, breathing rate, blood pressure, and other signs are monitored closely to prevent bad effects from happening or to correct them. For example, anesthesia treatment may be used in surgery through anesthetics, which are drugs that keep you from feeling pain during medical procedures. However, in rare cases, the anesthetics can lower your blood pressure to dangerous levels (ACS, 2019; Wu, 2018). Doctors will be closely watching the patient's heart rate, breathing rate, and blood pressure to prevent these dangerous side effects, should they occur during surgery. If for example, the person's blood pressure lowers, doctors can give medications through an IV to help bring the blood pressure back to a state of normalcy (ACS, 2019; Wu, 2018).
e. **Infections** can occur as a result of openings made during surgery, that may have been contaminated when the stomach or intestines were opened in an operation. Doctors are cautious not to cause infections, but in case infections do occur; doctors can give antibiotics that are effective for most infections.
f. **Pain** after surgery is quite common among patients, however, it should not slow down the recovery of said patients. For example, this pain could inhibit a person's recovery process; disturbing their rest (sleep), and rehabilitation after surgery, which could lead to further problems, such as blood clots (Corke, 2013; ACS, 2019). Doctors can give medicine for pain that varies; from acetaminophen (Tylenol) to anti-inflammatory medicines or stronger drugs, like morphine.

g. **Low energy level**. some bodily functions may take a longer time to recover, and thus may lead the patient's energy levels to lower. The patients might also have to remain immobilized to recover fully, leading to blood clots and further infections (Wu et al., 2018; ACS 2019). Like Blood Clots, Doctors too will obligate patients to start getting active and moving as soon as possible to prevent these complications. (ACS, 2019).

h. **Metastasis** is the process by which Cancer spreads to a different part of your body than where it originated from, in which case, it has "metastasized" (Cancer.Net, 2022). Although very rare, surgery can also stimulate the spread of cancer, like how it can increase the shedding of cancer cells into the circulatory system, where the cancer cells are then transported through the blood to other tissue, where they grow, and continue to spread (Tohme et al., 2017; ACS, 2019;). If the metastatic growths are diagnosed earlier, the patients will have a higher chance of having themselves free from metastatic cancer, as by that time the growth will still be in its early stages, and thus will be susceptible to early effective treatments (Menezes et al., 2016). Doctors may use neoadjuvant therapy to reduce the size of the cancerous growth which improves the success of the surgery to remove the growth before it spreads. In addition to that, they may then follow this with adjuvant therapy to eradicate any remaining cancer cells, reducing the risk of its recurrence (Thomas, 2022).

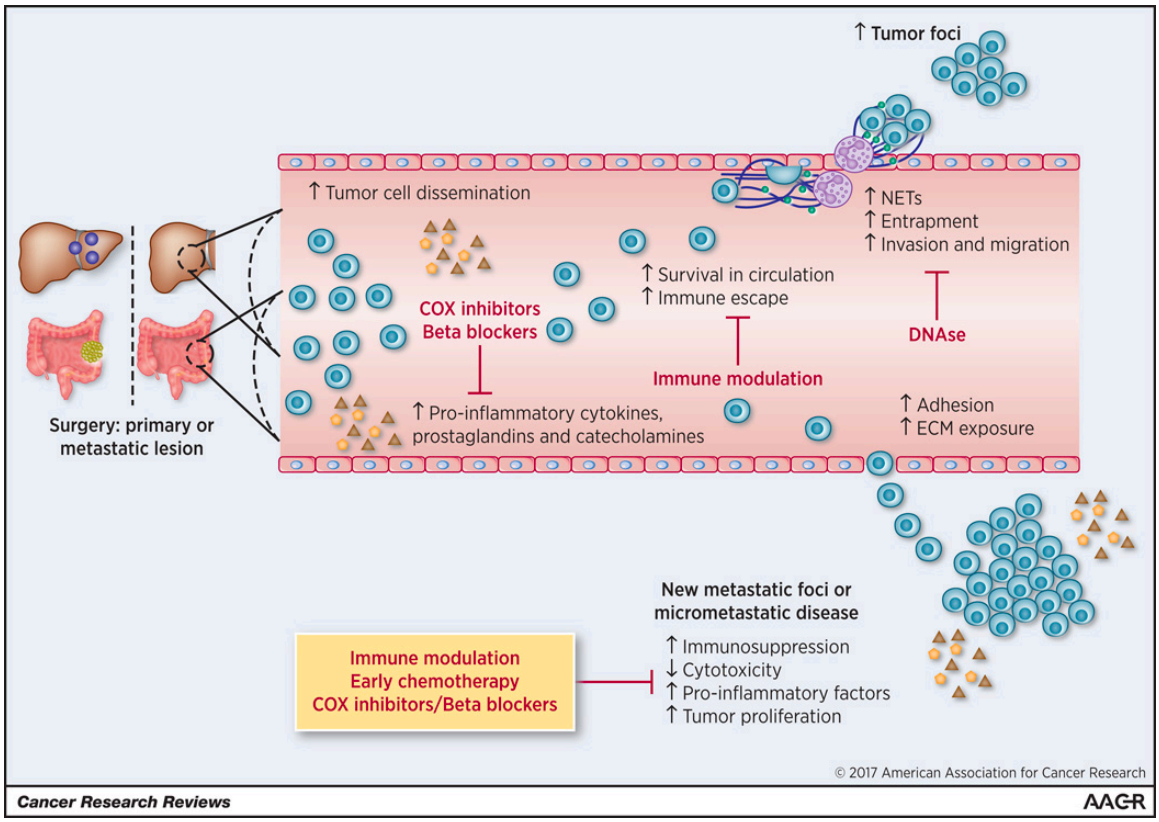


Figure 6.8. Metastases Risk From Surgery.
Source: Tohme et al., 2017.

Conclusion

In the field of oncology (the study of cancer), surgery has many roles including: to cure cancer, to prevent cancer, diagnose cancer and cancer stage, debulk cancer, relieve cancer pain, support treatment, and restore scar. The two main roles of surgery in cancer, diagnostic surgery and curative surgery, are interconnected branches that make up surgical treatment for cancer which each contains its own unique methods and purposes suited for specific conditions, yet at times support each other to increase their own efficiencies. However, like all treatments, surgery has a variety of risks that all have their own corresponding treatments and preventions measured and carried out by doctors. Although surgical services for cancer has their own challenges in different countries, overall they are still an important method for curative and palliative treatment for most cancers in countries around the world, no matter the income level.

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How does chemmoimmuno-therapy works in cancer treatment?

How does chemoimmunotherapy work in cancer treatment?

By: Daniel Hong and Si Rae Yun

Background

Have you ever considered the possibility of combining various cancer treatments? The solution to that query was recently discovered by researchers who created a combined treatment of chemotherapy and immunotherapy. The future of cancer therapies appears more promising than ever thanks to this newly discovered drug approach.

Cancer treatment might include a combination of methods with the goal to achieve the highest rates of disease control. While surgery and radiotherapy are used to control cancer in certain places in the body, systemic therapies like chemotherapy are used to treat cancer that has spread in the body (Emens & Middleton, 2015). While most of the time conventional cytotoxic cancer chemotherapy are associated to be immunosuppressive, some chemotherapy drugs, when used in a certain pattern and dose are known to be able to induce our immune system to activate and work against cancer cells (Wu & Waxman, 2019). This means that the use of certain chemotherapy drugs, instead of just acting to kill (cancer) cells in our body, are actually able to be used to produce immunotherapy effects. In this paper, we will discuss how chemotherapy could be used to enhance the ability of our immune system in fighting cancer.

Chemotherapy

Chemotherapy is the most widely and commonly used cancer treatment in the present day. It is basically applying powerful drugs in our body to deteriorate the cancer cells, preventing it from growing and spreading (National Health Service [NHS], 2020). Chemotherapy is applied as a systemic medication, where drugs are introduced into the bloodstream (through IV injection or tablets), allowing it to reach all parts of the body through blood flow (Cancer.Net, 2022). Because its nature in disrupting cell growth and multiplication, these drugs also kills healthy cell where it reached, causing side effects like hair loss, nausea, making the body weak, sore mouth, sore and itchy skin, diarrhoea, and low immunity, which can be treated and can pass as the treatment is stopped (NHS, 2020; Cancer.Net, 2022).

Although chemotherapy is effective in terms of killing the cancer cells, it also kills some of the important cells of our body. Due to this, patients may suffer with long term damage to the heart, lung, kidneys, or reproductive organs. Sometimes, patients prefer to rest in peace than to take chemotherapy because the process and the aftermath of chemotherapy is extremely painful, such as causing intense sore throughout the body.

Immunotherapy

Immunotherapy is another type of cancer treatment that utilizes the immune system to kill cancer cells. Normally, our immune system have the ability to detect and destroy abnormal cells which prevents the growth of many cancer. Specific cells called tumor-infiltrating lymphocytes (TILs) could usually be found around tumor cells, indicating that the immune system is still responding to tumor, giving patient a better chance in their treatment. However, cancer cells also develop to avoid being destroyed by the immune system (National Cancer institute [NCI], 2019).

Immunotherapy uses various methods to enhance the immune cells in order to help them detect and act against cancer cells. They can use drugs containing chemicals that enhance immune function, immune cells (T-cell) therapy, antibodies marker, vaccines, and other specific or general modulators to enhance the immunes system (NCI, 2019). This treatment might seem applicable and convenient, but it is a newly found cancer treatment so there are still challenges in the development of this area. Further improvement needs to be studied and developed to make immunotherapy more efficient in treating cancer (Smith, 2020).

Chemoimmunotherapy

Chemotherapy was thought to be immunosuppressive (works against the immune system) since the drugs used in chemotherapy killed not only cancer cells, but the healthy immune cells as well. However, certain drugs are known to be able to kill cancer cells in a way that activate the immune system to act against cancer cells or what could be called an immunogenic cell death pathway. These drugs, for example, includes doxorubicin, mitoxantrone, and cyclophosphamide (Wu & Waxman, 2018). Studies show that as these drugs are used in chemotherapy, the work of the immune system to act against cancer cell could be enhanced, showing effects of immunotherapy. Chemotherapy that is used to enhance immune system could also be paired with other forms of immunotherapy in the settings of combination therapy.

Chemoimmunotherapy Mechanism – Standard Dose

A large body data shows that some chemotherapy drugs induce immunogenic cell death by the natural releases of tumor antigens and other chemical "alarm" signals called "danger associated molecular patters" (DAMPs), which occurs after the deaths of cancer cells. In Figure 7.1. it is shown that when cancer cells die because of chemotherapy drugs, they release certain compounds such as tumor antigens, HMGB1, ATP, CRT, and type 1 IFNs that will bind with their receptor on the surface of an certain immune system cell called the Dendritic cell (DC) which is still immature (Emens & Middleton, 2015).

When these DAMPs compounds are bind to the receptors in the immature dendritic cells, it activates a series of events that enables the immune system obtain the ability to track down other similar cancer cells. This includes, the evolution of tumor-specific T cells and the maturation of DC cells for inflammation development by the activation of NRLP3 inflammasome and secretion of IL1β. These inflammation events are responsible for the work of the innate immunity to fight the surrounding cancer cells. Meanwhile, the maturation DC cells and evolution of T cells are part of the adaptive immunity development to detect specific cancer antigens that are attached on the surface of other cancer cells so they can fight/disable those cancer cells. Other immunogenic chemotherapy-induced cell death may also come in the form of autophagy, necroptosis, and T cell-mediated lysis (Emens & Middleton, 2015).

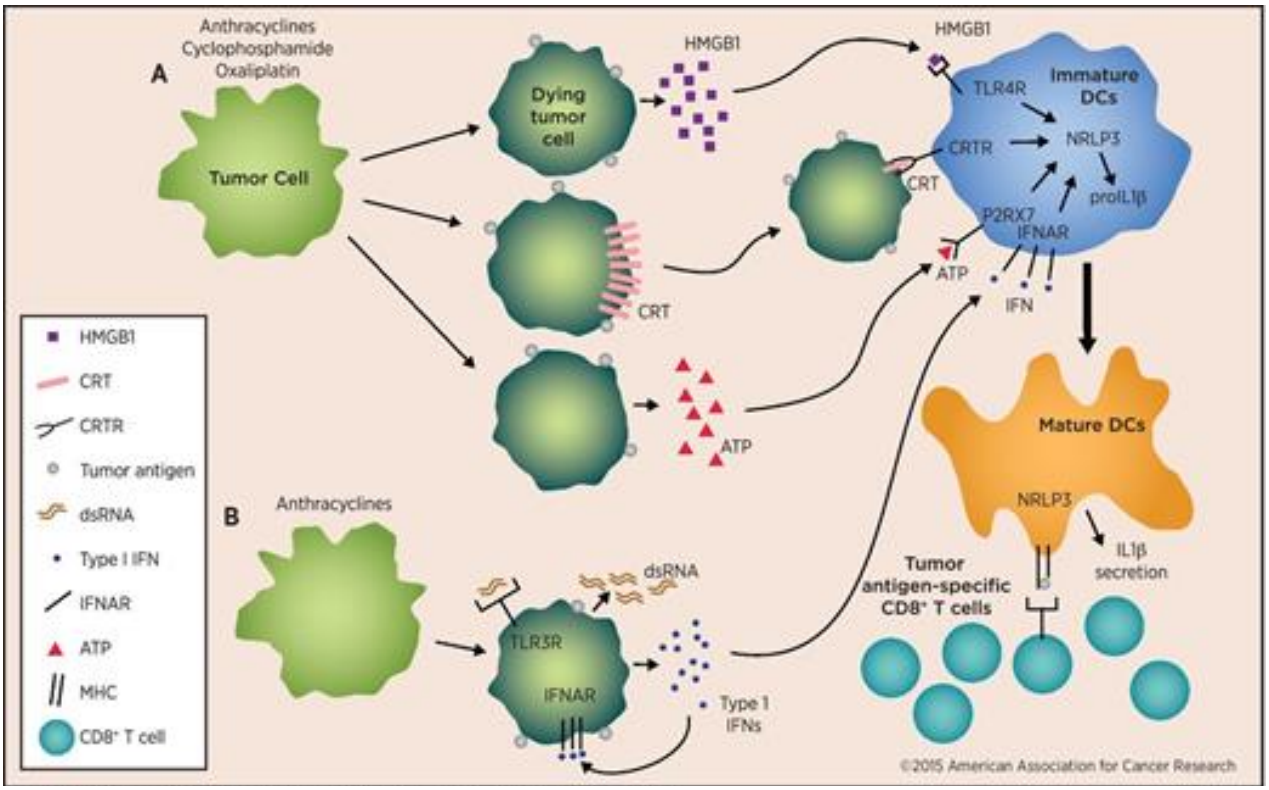

Figure 7.1. Chemoimmunotherapy mechanism
Source: Emens & Middleton, 2015.

Dose and Schedule of Chemoimmunotherapy

Drug dosing needs to be done with great precision. Since cancer cells can develop resistance to the drug used in chemotherapy, it is important to schedule drug injections thoroughly. If the drug effects are too weak, the cancer cells will slowly develop resistance to the drugs, and it will be harder for doctors to treat the cancer (Wu & Waxman, 2018).

To achieve a strong anti-tumor response, it is important to select a chemotherapeutic drug that induce immunogenic cell death and administer it at a dose that can eradicate a large

fraction of tumor cells without causing suppressive effect on the immune system. For chemo-immunotherapy to be effective, the chemotherapy dose needs to be lower than the threshold dose that induces severe myeloablation (decrease in bone marrow activity or in other words, decrease immune system activity) and causing host toxicity; but not too low that it doesn't reduce tumor volume significantly and do not induce anti-tumor response (Wu & Waxman, 2018).

The break between drugs needs to also be properly timed to achieve the right balance between cytotoxicity to tumor cells and a sustained immune response. Using a high dose of chemotherapy will cause the need for a long drug-free break. This will allow the development of immune suppression, weaken the anti-tumor immune response, and enabling drug-resistant tumor cells to emerge. On the other hand, a drug-free break that is too short will cause responding anti-tumor response of the immune cells. It is thus proposed to employ an intermediate-length drug-free break. Multiple cycles of combination treatment is necessary to abolish sufficient numbers of tumor cells and to achieve strong, sustained anti-tumor immune responses, while preventing the development of immune suppression and the emergence of drug resistant tumor cell populations (Wu & Waxman, 2018).

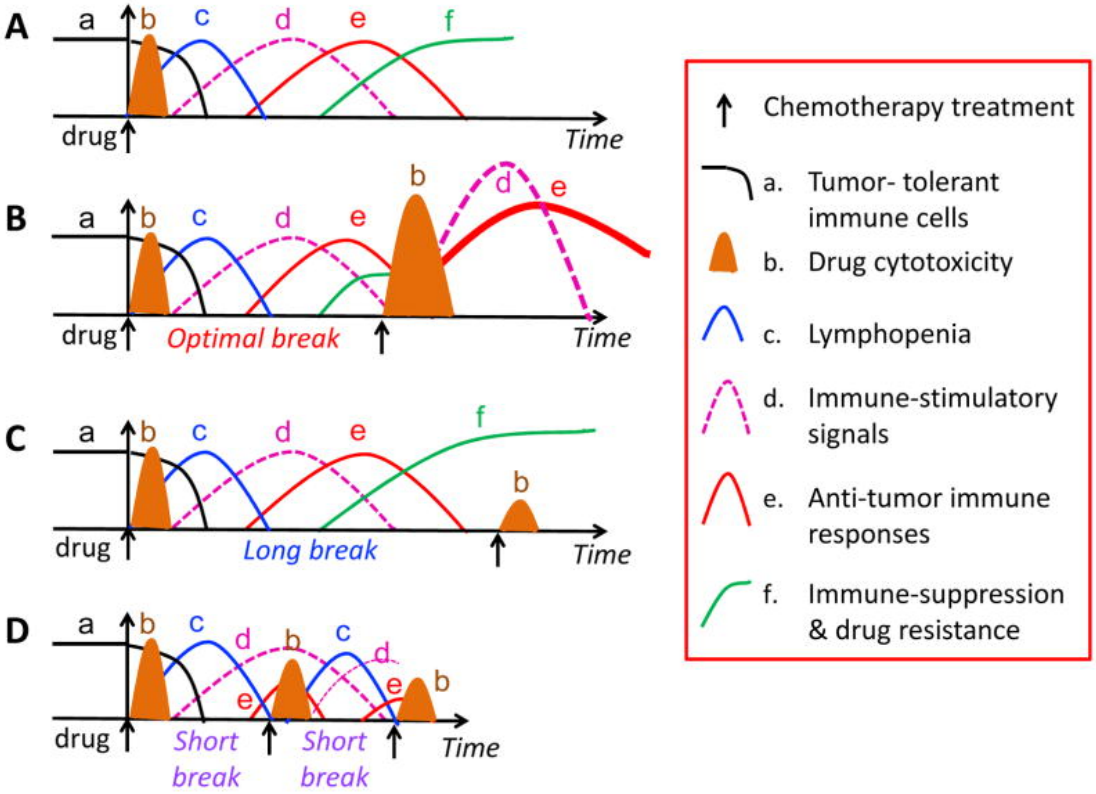

Figure 7. 2.
Source: Wu & Waxman, 2018.

Conclusion

The whole purpose of the combination therapy is so that doctors can help treat patients the most efficient and safest way possible by combining different therapies and utilizing each other's strength to cover the drawbacks of each other. For example, chemotherapy is very effective in terms of treating the patient but at the same time, very risky. However, by combining immunotherapy with it, it would minimize the damage caused by chemotherapy by enhancing the patient's immune system. Although this method is yet to be fully functional, doctors can perceive a great potential of it. Once this method becomes available and fully developed, the number of cancer patients surviving and recovering would hopefully increase drastically.

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What are the side effects of cancer treatment?

What are the side effects of cancer treatment?

By: Ju Won Park

Background

As technology continues developing and medical discoveries are being made, cancer survival rates have also been increasing. Some reports have even shown that about 50% of the people who were diagnosed with cancer during the year 2010-2011 have survived for 10 or more years (Cancer Research UK, 2020). However, even to this day, almost every kind of cancer treatment brings a certain amount of side effects, and those side effects may arouse doubts to the effectiveness of the treatment. This paper aims to go through the various types of cancer treatments which are mainly used today and also study their major side effects in hopes for relieving unnecessary worries and knowing what to be expected when going through treatments.

Cancer Treatments and Their Side Effects

Surgery

Cancer surgery, as the name suggests, is a treatment method of using surgery to find out about the existence and locations of tumors, prevent cancer, remove them, or help recovering. It is the oldest type of treatment still in use today, and so, various techniques exist within the criteria of cancer surgery, such as open surgery, Laparoscopic surgery, Laser surgery, Cryosurgery, and Mohs surgery (Cancer.Net, 2021).

Side Effects

Surgery includes the physical opening of the body, and therefore certain side effects are inevitable for this kind of treatment. Some side effects include pain and bleeding from the cut that has been made, blood clots that may form due to laying down for a long time, and a slow recovery of body functions due to the nature of the treated organ. Also, depending on the patient and surgeon, surgery may cause unintended infections or reactions. So, prior to a surgery, it is important to study the state of the patient and identify any threats that may happen (American Cancer Society [ACS], 2019a).

Radiation Therapy

Radiation therapy is a method of treating cancer using high doses of radiation, which is emitted either by an external machine, or a source that is put inside the body. It works because accumulated high levels of radiation are able to damage the DNA of cancer cells enough so that they die over a period of time (National Cancer Institute [NCI], 2019).

Side Effects

Radiation therapy causes side effects that may vary depending on the situation of the patient. Physical, mental, and emotional fatigue is just one of them. Skin and hair problems also frequently occur, including changes in skin color and texture, hair loss and weaker hair strands. Other than that, radiation therapy may also affect the circulatory system in ways such as low blood counts of white, red blood cells and platelets that reduce immunity; and also the accumulation of lymph fluids that cause swellings (ACS, 2020a).

Chemotherapy

Chemotherapy is a type of cancer treatment in which drugs are used to kill any fast-growing cells in the body. Although it is very effective in growing the cancer cells that duplicate without restraint, it also carries a major risk as the chemicals may attack normal cells too. Chemotherapeutic drugs are meant to travel through the whole body, and therefore the number of side effects are much more diverse (Mayo Clinic, 2022).

Side Effects

Side effects of chemotherapy are very diverse and they occur throughout the whole body because the drugs used in this treatment would essentially kill every fast-growing cell regardless of whether thay are cancerous. Just like radiotherapy, chemotherapy may also cause fatigue, problems with skin and hair, and low blood counts. In addition to that, chemotherapy is able to cause problems in the digestive system such as vomiting, diarrhea, pain when consuming food or drink, and constipation (less movement of the bowels). Finally, chemotherapy may cause problems with the nervous system such as the chemo brain which reduces focus, limits on muscle motion ranges, problems with reproduction, weight changes, and mood changes (ACS, 2020b).

Targeted Therapy

Targeted therapy aims to target certain proteins which help the growth and spreading of cancer. These treatments use various ways such as interfering with signals that make cancer cells duplicate, deliver cell killing substances, or starving cancer cells of the hormones required in order to stop the spreading of or cure cancer (NCI, 2022).

Side Effects

The side effects of targeted therapy may be similar to the other previous treatments, but it also has a few unique complications. Targeted therapy may cause problems on the skin, such as feelings as if a sunburn occurred, rashes, itchiness, dryness, color changes, and the hand foot syndrome, a disease where symptoms such as skin sensitivity, tingling, and numbness develops into swelling and pain. Other than that, Targeted therapy may bring about changes in hair, high blood pressure, bleeding blood clots, slow wound healing, and heart damage (ACS, 2020c).

Immunotherapy

Immunotherapy is a type of cancer treatment which utilizes the patient's immune system to fight against cancer. Against the hidden cancer cells, immunotherapy helps the immune system prepare for, recognize, and fight against cancer cells (NCI, 2019).

Side Effects

The side effects of immunotherapy differ according to the medication that is being applied. Thalidomide, lenalidomide, and pomalidomide, also called the immunomodulating drugs, may cause drowsiness, fatigue, constipation, low blood cell counts, neuropathy (painful nerve damage), and even serious blood clots that start in the leg and can travel to the lungs. Another treatment which uses germs called Bacillus Calmette-Guérin (BCG) has side effects of fever, chills, fatigue, and pain with the urinary system. Finally, a treatment that is called by the name Imiquimod, may have reactions with the skin when it is applied as a cream (ACS, 2019b).

Hormone Therapy

Hormone therapy, also known as endocrine therapy, is a type of cancer treatment which interferes with the hormones that are used for cancer growth. This treatment can be divided into two main branches, one which prevents the hormones from producing, and and the other which changes the hormone's behavior (NCI, 2022b).

Side Effects

Since hormones regulate various body functions, the symptoms of the treatment are also seen in various places. Hot flashes, bone loss and a higher risk for fractures, fatigue, nausea, weight gain (especially around the belly) with decreased muscle mass, memory problems, and an increased risk of other health problems are some of the possible side effects of hormone therapy (ACS, 2020d).

Conclusion

Patients that go through Cancer treatments will experience certain side effects. Problems such as fatigue, pain, problems that arouse on the skin and in the intestines; these side effects may occur throughout the whole body, even in parts which may be unrelated to the cancer. Because of this, when unknown, these side effects would naturally worry the patients and arouse doubts on the process of curing. However, by knowing what side effects would be expected, patients will be able to prepare themselves for the treatment that is incoming and rather accept it, as it is a sign that the treatment is having effect, and work with doctors and health care providers in trying their best to manage these side effects.

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What are the roles of Physiotherapy in Cancer Treatment?

What are the roles of physiotherapy in oncology?

By: David Park

Background

Physiotherapy, also known as Physical Therapy is a type of supportive treatment mainly used to improve locomotion systems in patients that experience physical defects from varying causes such as injuries and side effects from medical treatments (Zyzniewska-Banaszak, Kucharska-Mazur & Mazur, 2021). There are two main functions of physiotherapy in oncology: rehabilitation of the musculoskeletal system and the care for the mental and social well-being of patients (Zyzniewska-Banaszak et al., 2021). These factors not only contribute to the patient's quality of life but also to the course of treatment itself (Zyzniewska-Banaszak et al., 2021).

Physiotherapy Roles/Functions in Oncology

Rehabilitative Function

Rehabilitation of the musculoskeletal system aims to restore patients from physical deficiencies derived from various cancer treatments and cancer itself. The common side effects due to oncology that are associated with the physical spectrum include limited tissue mobility, contractures (tightening and hardening of muscles, tendons, or other tissues), swelling, muscle weakness, and joint disorders (Zyzniewska-Banaszak et al., 2021). Other common complications that cancer patients generally experience include lymphedema, myofascial pain syndrome, general pain from cancer itself, and Cancer Related Fatigue. (Zyzniewska-Banaszak et al., 2020)

Cancer Related Fatigue (CRF) is a major complication that is brought about by cancer treatment and cancer itself. In advanced cancer patients, it usually comes along with symptoms of weakness and exhaustion (Hofman et al., 2007). CRF is not the usual tiredness that could be healed by simply resting (Hofman et al., 2007). This fatigue is a major issue in oncology as it reduces a patient's quality of life (QoL)and worsens as treatment is continued (Piraux et al., 2020). Continuous fatigue that is not managed through physiotherapy later leads to further issues such as muscle weakness and deconditioning (Piraux et al., 2020). CRF along with other issues related to the musculoskeletal system makes it difficult for patients to even perform activities of daily living that are necessary for independence. The vicious cycle of CRF is shown in Figure 9.1.

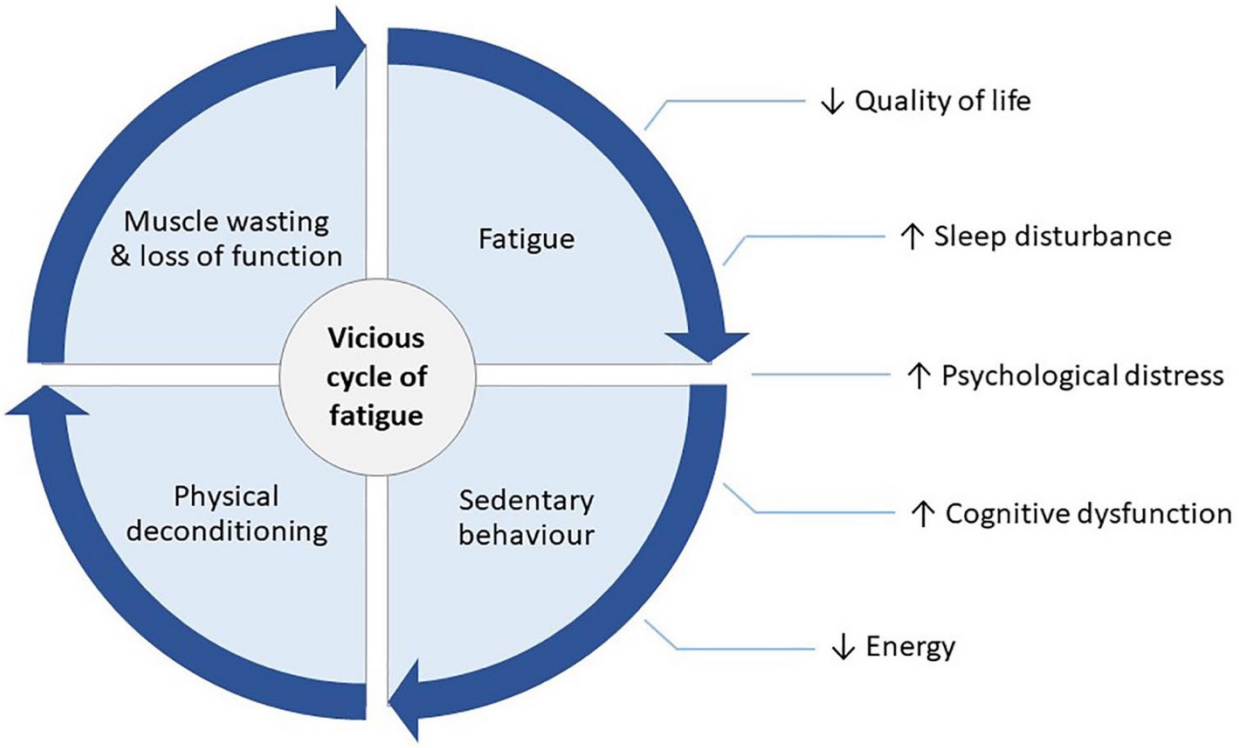

Figure 9.1. The cycle of fatigue shown in many patients after Radiotherapy treatment
Source: (Piraux et al., 2020)

Psychological Function

The psychological function of physiotherapy revolves around helping in the social and mental health of cancer patients. Firstly, patients experience a lack of social interaction as they begin their treatment. The social interaction is usually limited to their family, friends, and healthcare professionals that are in charge of them. And usually, most of these people just visit them once in a while, and the patients usually spend most of their time alone. This is where physiotherapists come in. Physiotherapists spend long periods of time with their patients through exercise and rehabilitation every day. This social interaction between the therapist and patients allows them to talk while engaging in activities together which could benefit the patient's mental health.

Physiotherapy also benefits patients' mental health directly through the exercises and activities that it provides. Many patients start to develop psychological problems such as depression, anger, inferiority, grief, and anxiety (Zyzniewska-Banaszak et al., 2021). These kinds of problems could be derived from factors such as change of appearance and course of treatment, and they can negatively affect the patient's course of treatment significantly (Zyzniewska-Banaszak et al., 2021).

Physiotherapy Treatments in Oncology

Lymphatic Drainage Massage is a type of massage used to treat patients experiencing lymphedema, a common complication experienced throughout oncology. Lymphedema is a condition where the lymph fluids in our body are crowded into certain parts of the body; this leads to inflammation in the area, resulting in uncomfortably (Centre for Disease Control and Prevention [CDC], 2022). In oncology, this side effect often comes from radiotherapy, surgery, and tumor enlargement (CDC, 2022). Radiotherapy could disrupt lymph nodes causing overproduction of lymph fluids, surgery could remove lymph vessels that help carry these fluids around, and tumor enlargement could get in the way of the lymphatic system causing a blockage (CDC, 2022). Lymphatic drainage massage helps spread out the fluid that has gathered on a specific spot and caused swelling.

Transcutaneous Electrical Nerve Stimulation (TENS) is a physiotherapy treatment given to patients to reduce the amount of pain experienced due to cancer (NHS, 2022). This chronic pain is a common side effect of cancer itself and cancer treatments such as radiotherapy and chemotherapy (Hurlow, Bennet, A Robb, Johnson, Simpson & Oxberry, 2012). TENS is a machine attached to a part of the patient's body part (NHS, 2022). The attached parts aim to interfere with the nerves that go through the body to stop the pain signal from reaching a person's brain (NHS, 2022). This means that the pain is still there; however, the machine just helps the patient from feeling the pain (NHS, 2022).

Myofascial Release Therapy is a type of therapy used in physiotherapy that aims to cure one of oncology's side effects: myofascial pain syndrome (MPS) (WebMD, 2021). This is a type of syndrome that occurs with the tightening of the fascia which is a type of connective tissue found all across the body, and the main problem it causes is general pain (WebMD, 2021). This syndrome is usually caused as a result of treatments that cause trauma to the bone or soft tissue. Some of these are surgery, chemotherapy, and radiotherapy (WebMD, 2021). Myofascial release therapy is carried out with the therapist massaging certain pressure points called trigger points in order to reduce the tightness around it to alleviate pain (WebMD, 2021).

Proprioceptive Neuromuscular Facilitation (PNF) Exercises are stretching techniques utilized in physiotherapy to treat patients with a limited range of motion post-treatment (Hindle, Whitcomb, Briggs & Hong, 2012) This side effect (limited ROM) is usually experienced in patients after taking treatments such as surgery, radiotherapy, and chemotherapy, and it can significantly reduce their activities in daily living (Hindle et al., 2012). There are mainly two methods that this exercise is carried out with and it is the Contract-Relax (CA) method and Contract-Relax-Anatogonist-Contract (CRAC) method. The CR method starts with passive stretching into isometric contraction (Hindle et al., 2012). Then, the position is held for a

certain period of time before letting go. Finally, these steps are repeated; however, this time, you go into a deeper stretch than the previous time (Hindle et al., 2012). The Contract-Relax-Anatgonist-Contract (CRAC) method starts similarly to the CR method (Hindle et al., 2012). The exercise begins with stretching into isometric contraction (Hindle et al., 2012). However, this time, it is followed by a force exerted towards the antagonist muscle for further stretching (the opposite muscle to the one that is stretched, biceps - triceps, quads - hamstrings, etc). The steps are repeated into deeper stretches each time it repeats. (Hindle et al., 2012).

There are also other exercises that physiotherapists commonly use in oncology in order to relieve and treat symptoms of cancer and side effects from its treatment. These include **resisted exercises**, **balance exercises**, **manual stretching**, i**sometric exercises**, **patient education,** and **behavioural training**. These exercises help patients face side effects, treat possible psychological issues derived from these side effects, and allow them to gain independence post-oncology.

Palliative Treatment

Palliative treatment is a special type of treatment usually reserved for patients with life-threatening or serious levels of cancer. In this treatment, physiotherapy is mainly used to alleviate symptoms and pain that patients experience. Physiotherapy in palliative care helps patients improve their quality of life throughout a very rough period of their life. In turn, the social part of physiotherapy also helps patients with their mental health (Morishita & Tsubaki, 2017).

Conclusion

Physiotherapy certainly plays an important role in oncology. It not only helps rehabilitate physical deterioration through exercise in patients, but it also supports patients' mental health through social interactions. These two roles of physiotherapy in cancer treatment is important to support the patient' physical strength and well-being who is going through treatments. Without this strength and well-being, treatment might also be challenging for patient, and even hiders treatment from being successful, whether it's for curative or palliative treatment. Although physiotherapy is not the main character in the show in oncology, it certainly plays a vital role that sways the course of oncology.

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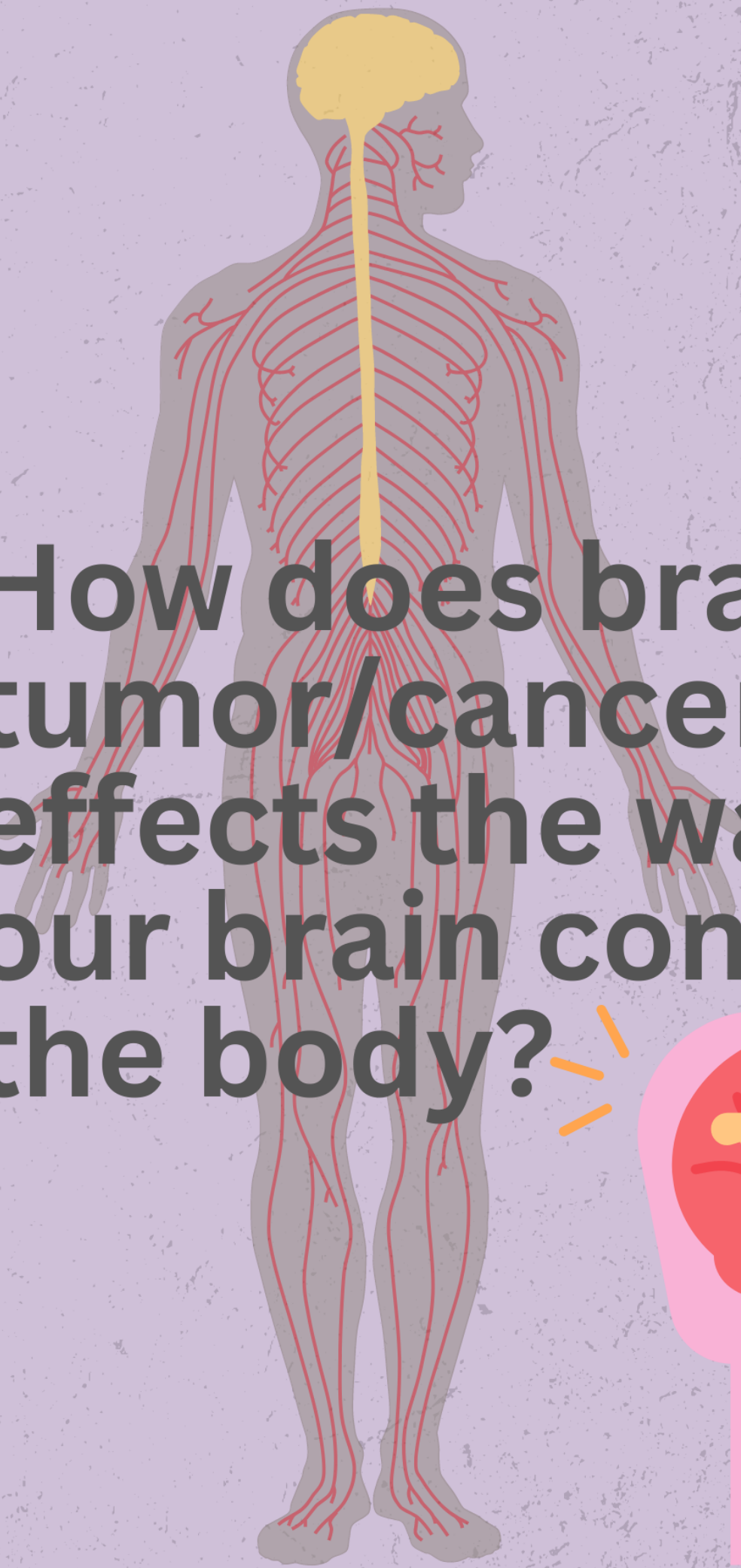


How does brain tumor/cancer effects the way our brain control the body?

How does brain cancer/tumor influence the way brain controls the body?

By: Yoon Jin Kim, Cherish Andreea, and Rishit Gautam

Background

Brain cancer is a disease of the brain that results from the abnormal growth of cells in the brain due to the development of mutations in the DNA of normal cells. When these cells in the brain are overproduced, their mass forms either cancerous or benign brain tumors (Mayo Clinic, 2022a). There are more than 100 different types of brain tumors/cancer which each of them having their own spectrum of symptoms, treatments, and outcomes. Compared to other tumors, brain tumors can have a lasting and life changing physical, cognitive, and psychological impacts on the patient's life. Despite medical and research development, brain cancer survival rates remained unchanged in recent years, even when the survival rater of other cancers has significantly increase (National Brain Tumor Society, n.d.). Additionally, it is estimated that 251,329 patients throughout the world died from brain cancer in 2020 (Cancer.Net, 2022).

Table 10.1. Deaths and Mortality Rates of Brain Cancer Patients in the US (1986-1955)

Category	Number of Deaths	Annual Mortality Rate/100,000
Male adults (⩾ 20 years old)	58,060	6.9
Female adults (⩾ 20 years old)	48,650	5.3
Male children (< 20 years old)	2,808	0.85
Female children (<20 years old)	2,254	0.75

Source: Fang, Kulldroff & Gregorio, 2004.

As the it progresses, brain tumor can bring more pressure on the brain and cause behavioural, cognitive, and psychiatric problems. Neurobehavioral issues often show up in patients and affect a patient's social relationships with family members, friends, and more. These issues potentially lead to stress and massive mood changes such as anger, lack of emotional control, and depression (Boele, Rooney, Grant, and Klein, 2015). Scientists have also noticed that brain cancer can cause massive neurocognitive issues that affect the ability of a person to think and process information. Approximately 90% of the patients diagnosed with brain cancer are known to suffer from neurocognitive impairments (Abu-Hegazy and El-Hadaad, 2016).

The brain is a part of the Central Nervous System (CNS) that controls important functions in the body, including emotions, vision, thoughts, speech, and movement. Since different parts of the brain have their own specific roles in controlling how the body functions, specific changes vary among patients diagnosed with brain cancer; the location of brain tumor determines the symptoms a patient experiences. It is important to know where the tumor is located in the brain to understand the symptoms and how it could influence the way our body functions (National Cancer Institute [NCI], 2018).

The purpose of this paper is to discover and analyse how brain cancer and its location influence how the body functions. Bringing awareness about this information can help the public learn the deadly effects of brain cancer on an individual. As more knowledge about brain cancer spreads, faster access to the solutions to brain cancer can be gained. In other words, more research is needed to help and treat future patients to increase the survival of lives.

Anatomy Of The Brain

The brain consists of six main areas that have different functions — the frontal lobe, parietal lobe, occipital lobe, temporal lobe, brainstem, and cerebellum. Figure 10.1 shows the anatomy of the brain with different colours that represent a certain area, and Table 10.2 shows the functions of each area.

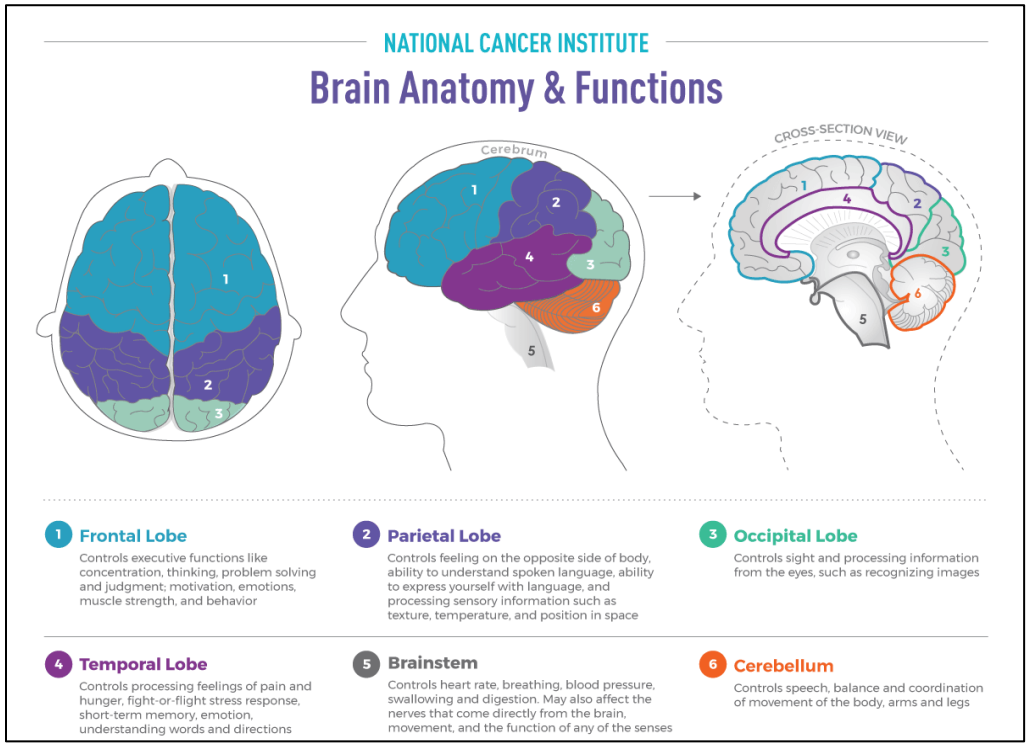


Figure 10.1. Anatomy of the Brain
Source: National Cancer Institute, 2018

Table 10.2. The Areas of the Brains and Their Functions

Label	Area of the Brain	Function
1	**Frontal Lobe**	Helps with concentration, thinking, problem-solving, and judgment; controls muscle strength, emotions, and behaviour
2	**Parietal Lobe**	Important for processing sensory information like temperature. Also helps with understanding language and controlling feelings.
3	**Occipital Lobe**	Responsible for controlling sight and processing information from the eye.
4	**Temporal Lobe**	Helps with concentration, thinking, problem-solving, and judgment.
5	**Brainstem**	Controls the heart rate, breathing, swallowing, movement, blood pressure, digestion, and function of the five senses, which are sight, hearing, smell, touch, and taste.
6	**Cerebellum**	Controls our speech, balance, and coordination of movement of the body.

Source: NCI, 2018

The effects of the tumor, which appear as signs or symptoms, occur differently, as they depend on the brain's location. For example, patients with tumors that develop in the frontal lobe may have behavioural changes, while patients with tumors in the temporal lobe may show signs of speech problems. Tumor irritations in the cerebral cortex could also cause focal or generalized seizures (Mesfin & Al-Dhahir, 2022).

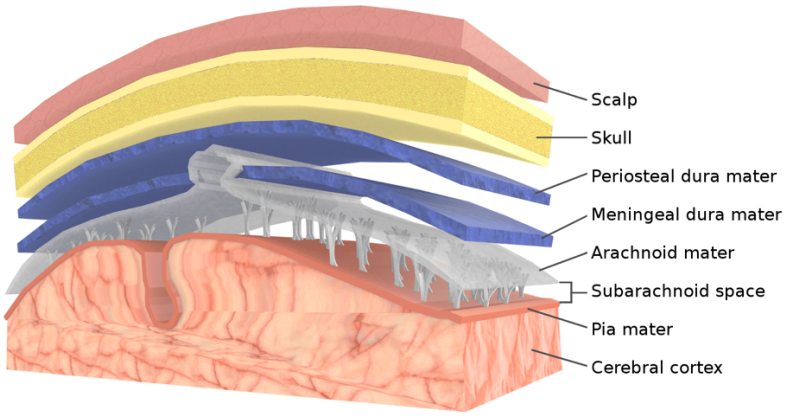


Figure 10.2. Meninges Layer of the Brain
Source: Bailey, 2019

Figure 10.2 shows the meninges layer of the brain. Meninges tissues are the outer three layers of tissue that cover and protect the brain under the skull. These tissues are significant to know, as they are common areas of the brain where tumors occur. Structure and function of each layer of the meninges is shown in Table 10.3. (Bailey, 2019).

Table 10.3. The Meninges Layers

Meninges Layer	Structure	Function
Dura Mater	Consists of two layers: the periosteal layer (outer layer) and the meningeal layer (inner layer). In between the two layers are veins called the dural venous sinuses.	The components of the Dura Mater have their own specific roles. The periosteal layer connects the meninges to the skull, the dural venous sinuses transport blood from the brain to the heart, and the meningeal layer creates dural sections for the subdivisions of the brain.
Arachnoid Mater	Has fibrous extensions that connect to the pia mater, subarachnoid space which is a pathway, membrane projections that connect to the dura mater, and arachnoid granulations.	Connects the dura mater and the pia mater, protects the brain and spinal cord, and provides a pathway for blood vessels and nerves that gather cerebrospinal fluid that gets sent to the dural venous sinuses (where absorption of the fluid to the venous system takes place).
Pia Mater	Consists of two layers: a collagen fiber-consisting outer layer and an inner layer. Also contains blood vessels and the choroid plexus (a network of capillaries and specialized tissues called ependyma).	Protects the cerebral cortex and spinal cord, supplies nutrients to nervous tissue, and produces cerebrospinal fluid.

Source: Bailey, 2019

Types Of Brain Tumors

Brain tumor that forms from the abnormal growth of cells that occur in the brain, causes a lesion in the brain, resulting in an area of damaged tissue. It can develop in any part of the brain and the skull. With the complexity of the function our brain has, brain tumors can cause different issues depending on where it is located (John Hopkins Medicine, n.d.). A tumor's location, size, and grade level are extremely important for doctors to determine what kind of brain tumor a patient has (NHS, 2021). Over 120 different types of brain tumors are classified by the tissue they arise from (John Hopkins Medicine, n.d.). Brain cancers are characterized by their grade levels, which define the severity of the tumor. Tumor grade levels 1 and 2 are benign and tend to grow slowly, while grade levels 3 and 4 are malignant, tend to grow quickly, and are more difficult to treat (NHS, 2021).

Benign and malignant brain tumors

Not all brain tumors are cancerous; non-cancerous tumors are called benign tumors. Even though benign brain tumors grow slower compared to cancerous tumors, they could be life-threatening if they are located in vital areas of the brain. Some benign tumors include meningioma and pituitary adenoma (John Hopkins Medicine, n.d.). Cancerous tumors, or malignant tumors, grow more rapidly and invade the surrounding healthy tissues. They may also be life-threatening, as they cause changes to the vital structures of the brain that are in charge of certain functions that our bodies perform. Some examples of malignant tumors are chondrosarcoma and medulloblastoma (John Hopkins Medicine, n.d.).

Primary and Metastatic Brain tumor

Brain tumors are also categorized as either primary or secondary tumors. In primary tumors, the abnormal growth of cells begins in the brain. In secondary tumors, which are also known as metastatic brain tumors, the growth of cells forms from a different location of the body and spreads into the brain (Mayo Clinic, 2021). Primary tumors could spread to other parts of the brain or the spinal cord, but this case is very rare. More commonly, metastatic brain tumors happen when cancer cells spread from other parts of the body. Some common cancers that spread into the brain are breast cancer, colon cancer, kidney cancer, lung cancer, and skin cancer (John Hopkins Medicine, n.d.).

Different Types of Brain Tumors

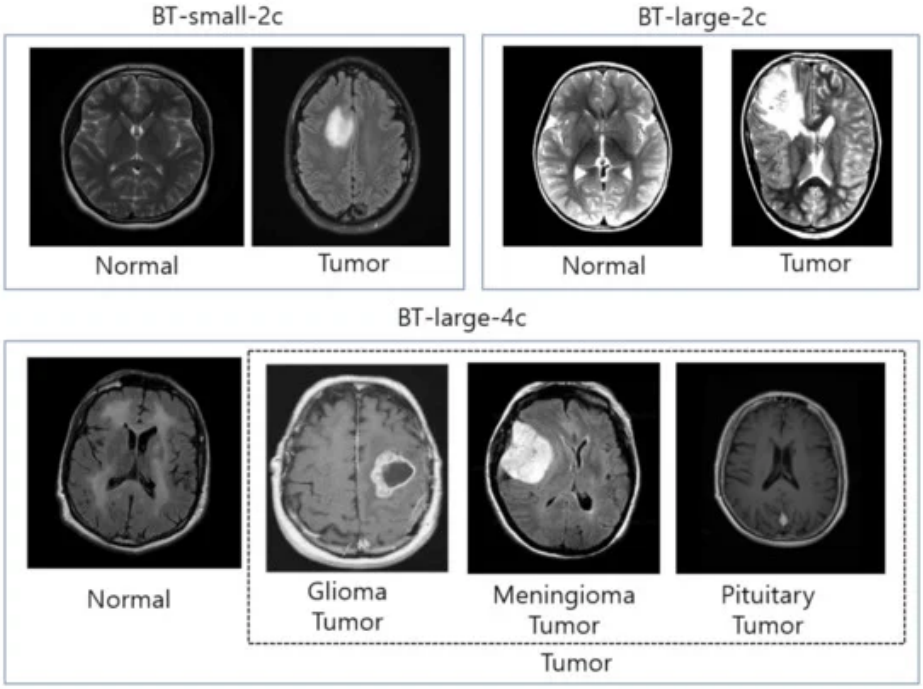
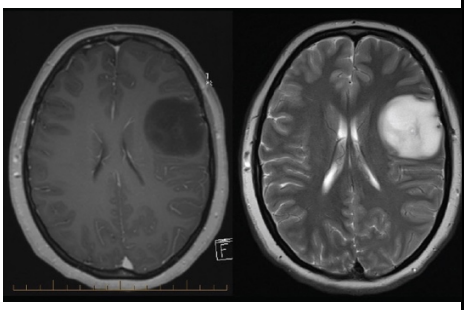
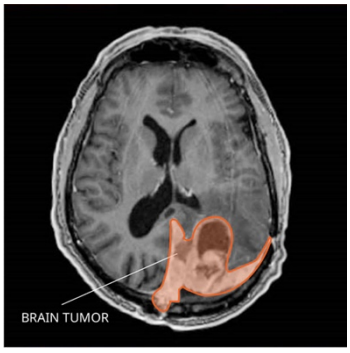
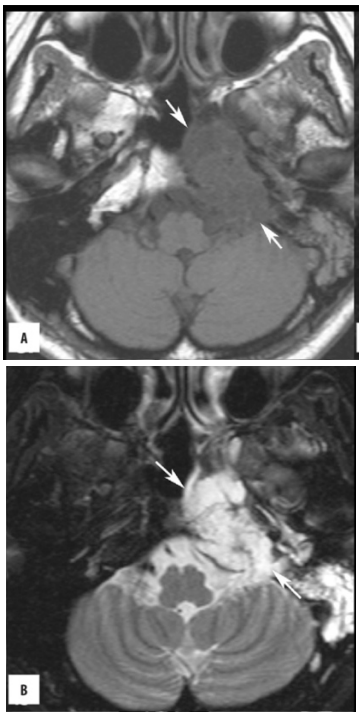
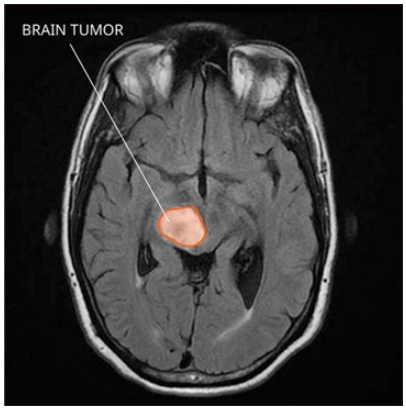


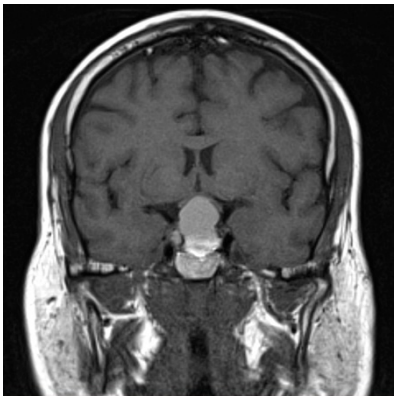
Figure 10.3. Tumor location in different types of brain tumors
Source: Kang, Ullah, & Gwak, 2021

Figure 10.3. shows the comparison between normal brains, in healthy conditions, and brains with a tumor. Specifically, different types of brain tumors are shown to affect different locations of the brain. Further explanation about the different types of some of the most common brain cancers is shown in Table 10.4.

Table 10.4. Different Types of Brain Tumors

Name	Information	Image
Glioma[1,2]	Glioma is an umbrella term for cancer of the glial cells that surround nerve endings in the brain. Glial, are cells that supports the neurons. Neurons are cells responsible for a lot of things: for walking, talking, thinking, seeing, and more. Slower growing gliomas are also called "low grade", which includes grade 1 and 2. High grade gliomas are Grades 3 and 4, which are more aggressive with a rapid multiplication of cancer cells. Low grade gliomas that occur most commonly in younger patients. While higher grade glioma that are more likely to occur in older patients. Symptoms of glioma usually relates to where the tumor is developing in the brain. Common ones are headaches, nausea, and vomiting because of the pressure of the mass to the bones; seizures in early astrocytoma; and in more advance glioma may include decline in brain function, weakness or moving problem, and vision problems.	 **Figure 10.4 Typical low-grade glioma with minimal mass effect** Source: Jeffree, 2020.
Meningioma[3,4]	Meningiomas are the most common type of primary tumor that occurs in the brain or spinal cord in meninges tissues (Figure 10.5), which are the outer three layers of tissue that protect the brain right under the skull. Around 85% of the cases are benign and grow slowly, but meningiomas can come back to the patient after treatment. Patients diagnosed with meningiomas experience vision changes, loss of smell, seizures, language difficulties, and severe headaches depending on where the tumor	 **Figure 10.5. MRI of a Meningioma** Source: Courtesy of NCI Connect from NCI, 2021a.

	is specifically located. For example, when the tumor grows in the parietal lobes, which are one of the essential cognitive areas, it can interrupt the process of verbal delivery because it is damaging the area responsible for language.	
Chondroma (Skull Base Tumor)[5,6,7]	Skull base chondroma is a very rare skull base benign tumor made up of cartilage. This particular type of tumor remains in only one area, and bone overgrowth or and destruction may occur in the area where the tumor is located. Chondromas in the skull base, where they are commonly found, affects the nervous system showing symptoms like headaches, double vision, facial numbness, hearing changes, or dizziness. In some cases, it can also turn into cancer, which is then called chondrosarcomas. Some of the common symptoms experienced by patients with chondrosarcomas are headaches and vision changes. Hearing problems may also occur.	 **Figure 10.6. Skull base chondrosarcoma** Source: Kunimatsu & Kunimatsu, 2017
Diffuse Midline Glioma[8]	Similar to meningiomas, diffuse midline gliomas are primary tumors that start in the brain or the spinal cord. All diffuse midline gliomas are Grade 4 tumors, meaning that they are malignant and grow fast. Diffuse midline gliomas spread into other areas of the CNS and can even go beyond what the MRI can show. A patient with diffuse midline glioma may experience double vision, loss of balance, and difficulty in swallowing. Due to the uncontrollable growth of cells, it can increase the pressure within the skull, causing a problem known	 **Figure 10.7. MRI of a diffuse midline glioma in the brain** Source: NCI, 2021b.

	as hydrocephalus. In hydrocephalus, a patient may experience nausea, headaches, seizures, and vomiting[7].	
Pituitary Tumors[9]	Pituitary tumors grow in the pituitary gland, which is the gland located at the base of the brain behind the nose. This type of tumor can lead to the excessive production of important hormones that help the body function. Pituitary tumors are benign and generally do not spread to other areas of the. The possible symptoms of a patient diagnosed with a pituitary tumor are headache, vision problems, drooping eyelids, nausea, and seizures.	 **Figure 10.8. Coronal MRI of a pituitary adenoma** Source: Yan et al., 2022

Source: [1]Rose, 2022; [2] Memorila Sloan Kettering Cancer Center,n.d. [3]NCI, 2021a; [4]John Hopkins Medicine, n.d.; [5]UMPC, 2022; [6]American Brain tumor Association, n.d.; [7]Aurora Health Care, n.d.; [8]NCI, 2021b; [9]Mayo clinic, 2022b.

Brain Tumor Signs And Symptoms

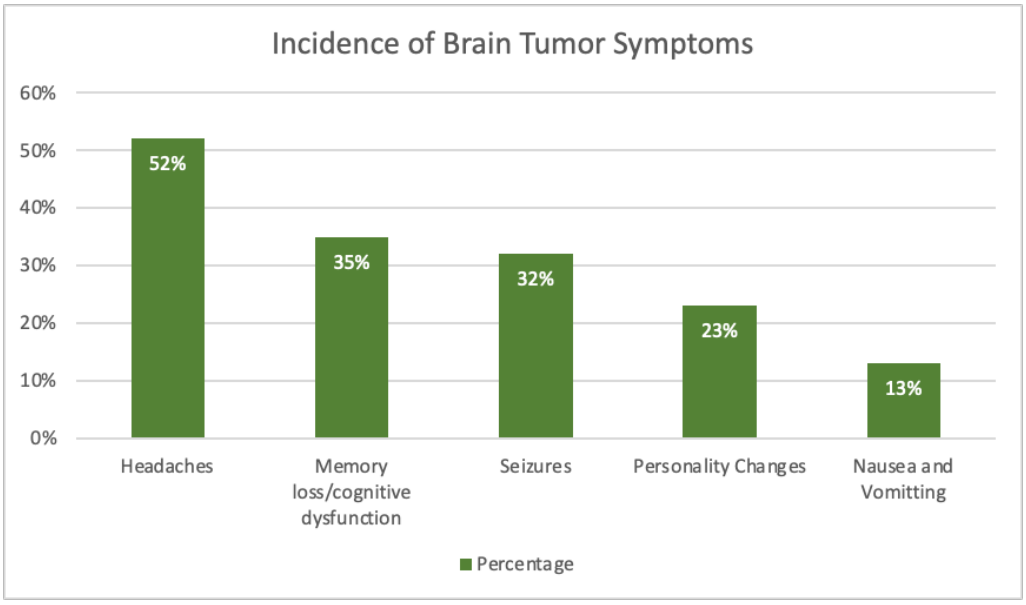


Figure 10.9. Incidence of Brain Tumor Symptoms

Source: (Adam et al., 2015)

Some common symptoms that appear in brain tumor patients are headaches, memory loss, seizures, personality changes, focal weakness, nausea, and vomiting. Figure 10.9. shows the

incidence of these symptoms in patients (Adam, Sullivan & Vitas, 2015). As we can see from here, headaches are by far the most common symptoms followed by memory loss/cognitive dysfunction and seizures.

Other studies show different percentages in the incidence of each symptom, as different areas have patients with different symptoms. For example, a study in an emergency department in Italy showed that focal signs were the highest symptoms among the other symptoms (Comelli et al., 2017). Another study on brain metastasis tumors showed that headache was the most common symptom followed by focal weakness (DeAngelis & Posner, 2009). It also included speech, visual, and sensory disturbances as common symptoms (DeAngelis & Posner, 2009). A study in Semarang, Indonesia, also showed that, in primary brain tumor patients, headaches were the most common symptom followed by focal weaknesses, which are signs of hemiparesis (Ardhini & Tugasworo, 2019).

Headaches

Headaches, in the beginning, happen mildly, but over time they can increase as pressure also increases; along with other signs of increased pressure are nausea and vomiting. Even though the inside of our brain does not have pain receptors, headaches occur due to intracranial pressure, which is the pressure inside the skull. Intracranial pressure happens when the mass lesion causes tractions in an area with pain-sensitive structures inside the skull such as the dura, cranial nerves, and large venous sinuses (DeAngelis & Posner, 2009).

Older patients with atrophic brains, which are brains that have lost some cells or neurons, often suffer less from headaches. This is because, despite them having a tumor, they are still able to accommodate the tumor, allowing it to cause minimal pressure on the brain. All headaches are not caused by intracranial pressure, though; there are some headaches that occur within small tumors. The cause of this kind of headache is yet to be understood (DeAngelis & Posner, 2009).

Seizures

Another common symptom expressed by brain cancer patients includes seizures/epilepsy. Even though epilepsies and seizures are found in many patients with brain tumors, scientists are not aware of how epilepsy exactly occurs in relation to brain tumors. However, it is believed that factors such as tumor burden, type, location, growth rate, and the microenvironment of the blood-brain barrier play a role in the occurrence of seizure/epilepsy in brain cancer patients (Adhikari, Walker & Mittal, 2021).

Seizures may occur due to irritation of the cerebral cortex, which can either be caused by the tumor itself or edema (fluidal swelling) to the surrounding area of the tumor (Adhikari, et al., 2021; Adam et al., 2015). This particular symptom is most likely experienced by patients that

have tumors located in the frontal, temporal, and parietal lobes of the cerebral cortex (Adhikari, et al., 2021; Adam et al., 2015). Seizures occur more often in patients with low-grade gliomas since slow-growing tumors provide more time for vascular changes and mechanical disruption to take place, stimulating seizures (Adhikari, et al., 2021; Adam et al., 2015). It is also hypothesized that dysregulation of neurotransmitters such as GABA, glutamate, and ADK, which result from tumor growth, is capable of provoking seizures (Adhikari, et al., 2021; Adam et al., 2015). In short, changes in the brain created by the development of a brain tumor can lead to abnormal depolarization in the brain, which can cause seizures to occur (Adhikari, et al., 2021; Adam et al., 2015).

When a huge portion of the brain is affected by depolarization, generalized seizure happens in the form of unresponsiveness and loss of consciousness, followed by a period of confusion (Adhikari et al., 2021). This loss of consciousness in a generalized seizure may occur with or without following rhythmic movements (Adhikari et al., 2021). In rare cases, a brief staring spell (blank out) without motor movements may occur as a form of the generalized seizure (Adhikari et al., 2021). On the other hand, when only a small area of the brain is affected by depolarization, a focal seizure may take place; usually, uncontrolled motor movements and twitching or sensory discomfort occur in focal seizures (Adhikari et al., 2021).

Neurocognitive dysfunction

Neurocognitive dysfunction encompasses memory problems, personality or behavioural changes, and mental disturbances like mood. In brain tumor patients, it is a symptom that tends to stay even after treatments, which may affect the overall quality of life of the patient. In some cases, the changes might be too severe that they may alarm the family or close people and lead to tumor diagnosis. However, the changes may also occur slowly and be overlooked or assumed to be related to aging or stress instead before the diagnosis step is considered (Adam et al., 2015; DeAngelis & Posner, 2009).

The frontal lobe controls the majority of cognitive processes, such as planning, motivation, personality, judgment, abstraction, communication, emotion, and memory. However, a lot of these processes also require input from other parts of the brain, such as the temporal and parietal lobes. It is not a surprise that tumors found in the frontal lobe or in multiple parts of the brain have a wide range of effects affecting social functioning, executive or professional skills, and emotional expressions. This may lead to declining quality of life; patients may also experience a hard time being independent. Furthermore, it may even affect the tumor treatment process. Although interest and studies in neurocognitive dysfunction due to brain tumors have risen, experts still do not have a full understanding of how to prevent neurocognitive dysfunction in the early stages of brain cancer (Adam et al., 2015; Borde et al., 2021).

Focal Weakness

Focal weakness (neurological deficit) signs vary in brain tumor patients depending on the location of the tumor. These appear as a result of the growth or edema pressure of the tumor in the brain parenchyma or cranial nerves. Focal weakness is found to cause motor deficits more often than sensory deficits. It also causes language deficits, visual deficits, dizziness, and balance problems (Adam et al., 2015).

Based on the known brain structure and function, focal weakness signs localize the tumor's location (Adam et al., 2015). For example, tumors in the cerebral hemisphere produce weakness on the opposite side of the tumor (which is a sign of contralateral weakness), sensory loss, language disorder (dysphasia), coordination disorder (dyspraxia), and visual field loss. Moreover, tumor in the posterior fossa (cerebrum) causes poor muscle control (ataxia) and paralysis (cranial nerve palsy). Patients with tumors in the midbrain could also experience a different sign of focal weakness; they would have difficulty controlling the movement of their eyes (Parinaud's syndrome), and a tumor in the cerebellopontine angle of the brain causes progressive deafness in one ear, facial sensory loss, and ataxia (Rees, 2011).

Conclusion

With its many roles in regulating the body function as part of the central nervous system, tumor/cancer growth in the brain have the potential to impair the functioning of many parts of the body. This depends so much on the size, location, and grade of the tumor. In general, headaches grows as the tumor growth increases the pressure inside the skull. This could be accompanied with nausea, vomiting, and visual impairment. Tumor in the frontal, temporal, and parietal lobe, or lower grade tumor are more associated with seizure. This seizure could cause unresponsiveness/unconsciousness, or uncontrolled movement and sensory discomfort in parts of the body. Neurocognitive dysfunction which affects memory, mental awareness, and thought process and social functioning is associated with tumors in the frontal lobe of the brain. While focal weakness which may cause body paralysis, sensory loss, language disorder, coordination disorder, poor muscle control, sight loss, dizziness and balance problems is the result of tumor growth in the brain parenchyma or cranial nerves.

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POSTFACE

We want to thank God for allowing us to use our passion in science and interest in cancer to complete our literature studies and assemble this book. Science Club has been a platform for students in Mountainview Christian School to express their passion in science, to grow in scientific experiences, and to share the grace of science to a bigger community. This semester we take the opportunity to do literature studies and discuss on a topic which we feel is widely related in many ways to the community of Mountainview Christian School. This community includes students, staff, and their close relatives/families. Cancer is a general topic and it has a wide range variety of types and severities. We believe that almost every member of our community might have known, is related to, or become the person that the lives has been affected by cancer. Yet, cancer remain as the hardest disease to control. This is why, as a club, we wanted to understand more about this disease and share those understanding by doing a literature study, club discussion, and publish our club findings about cancer. We want to study how far science has developed the understanding about what used to be unknown about cancer. We also want to show how these scientific discoveries and advancement has positively helped in the effort of controlling the disease. This shows that science is one of the grace of God that is gifted to us, one of our values that we hold in Science Club of Mountainview Christian School.

January, 2023

Editor