A Review of Breast Cancer Risk Factor Assessment on Women in Developing Countries, Cancer Drug Resistance, and Breast Cancer Treatment in Bangladesh

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A thesis is submitted to The Department of Mathematics and Natural sciences in partial fulfillment of the requirements for the degree of Masters in Biotechnology (MS BIO)

Department of Mathematics and Natural Sciences
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Declaration of Authenticity

It is hereby declared that

1.The thesis submitted is my/our own original work while completing degree at Brac University.

2.The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.

3.The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.

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Approval

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Ethics Statement

I hereby declare, I have not performed any immoral or unethical action for the fulfillment of my thesis. I have completed my work remaining whole heartedly sincere, with my utmost dedication and honesty.

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Abstract

Cancer stands among the most serious causes of mortality internationally. These therapies are one of the most tough in today's globe. As a result, it has a unique complexity, risk factors, and changes in the modern person's life cycle. It is quite difficult to identify early. Other difficulties include that the cost of diagnosis and treatment is kept to a minimum. It will progress to a more serious stage of metastasis. This research attempts to find out risk factors for breast cancer in a developing nation by reviewing previously published studies from 2000 to 2017 in various publications. This research is categorized into three areas. Subtypes, lifestyle-related risk factors, and BRAC mutation are the three. Majority of the risk factors for breast cancer are unknown, which is why this country lacks sufficient articles or study on breast cancer epidemiology, and their research is limited to a specific region. The majority of lawsuits are only concerned with economic and societal consequences. This study covers the most closely connected risk factor, therapy, diagnosis, and cost in Bangladesh, as well as future solutions.

Key words: Cancer; Breast Cancer; Metastasis; Risk factor; Drug resistance; chemotherapy; Diagnosis; Treatment; Future prediction; Life cycle, Bangladesh; Underdeveloped country; Cost

Dedication

I would like to dedicate my work to my parents. They have been my source of inspiration, support, and guidance. They have taught me to be unique, determined, to believe in myself, and to always persevere. They always give me support to my hard of time, that’s the reason I can do this properly. I am ever so thankful for them.

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I would also want to thank my fellow classmate and research assistant of MNS department Shabnoor Binte Dayem for the continuous assistance and advice. I want to also give a thanks to Lecturer of BRAC university MNS department Mahmuda Kabir. She gives me idea about risk factors, types of breast cancer and also suggested me to write literature on different contents.

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CHAPTER-1 INTRODUCTION

Background:

Healthy human tissue is required for survival in the world. **[1**]. This healthy tissue is regulated in all regions of the human body, such as metabolism and optimal organ function. **[2].** If a cell's function is hampered, the cell will be unable to meet the body's needs. This time, look at many diseases in the human body **[3]**. Caner is a kind of illness that causes cell overgrowth and causes a variety of problems in the human body **[4]**. When cancer begins to form, it produces a variety of symptoms. Fatigue is one of the symptoms. Something that feels bulkier or lumpy above the skin, Adjustments in weight, such as accidental loss or gain, alterations to the skin, such as yellowing, darkening, or redness; unhealed sores; revisions to moles already present; changes in bowel or bladder habits; Continual coughing or breathing difficulties, Having trouble swallowing sibilant voice, stomach ache or indigestion that persists after eating Persistent and mysterious chronic fevers or nocturnal sweats, unusual bleeding, or bruising are examples of muscle or cartilage pain **[5-7].**

Overview idea of Cancer Biology:

A medical condition whereby abnormal cells proliferate indiscriminately and have a tendency to infect tissue in the vicinity **[8].** Cancer is a hereditary illness caused by a mutation in the DNA **[9].** Most harmful mutations are either produced by mutagen exposure or occur naturally as part of aging. Some cancers are characterized by epigenetic alterations such as localized increases in DNA methylation and changes in histone modifications. These epigenetic modifications may regulate functions like as growth, survival, and aging **[10].** Heritable genetic alterations in cancer cells are passed down to daughter cells during cell division. As a result, individuals that have these mutations are vulnerable to Darwinian selection (survival of the

fittest, possibly the most significant scientific principle in Biology). Cells with survival mutations alter to benefit from nutrients in another cell. Darwinian selection continues to impact cancer evolution, and it is becoming more aggressive. As a result, the host is malnourished. The term "NEOPLASIA" refers to a kind of cancer **[11]** The term neoplastic refers to new growth. Cancer biology, on the other hand, refers to uncontrolled cell growth and division. Neoplasia is frequently associated with tumors. When cells grow or divide more than they should or do not die, an abnormal bulk of tissue emerges **[12].**

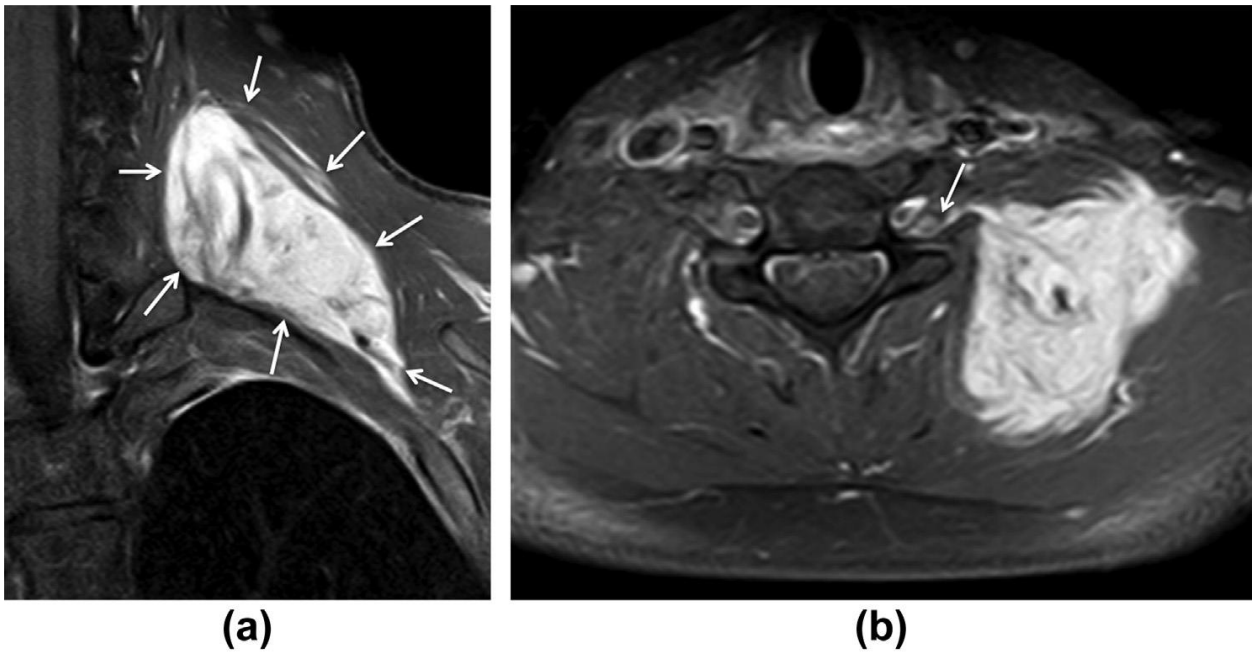

Figure-1: Horizontal neck fibromatosis from the left. Axial STIR MRI (b) and coronal (a) films reveal an infiltrative lesion in the left the brachial plexus area. The lesion is highlighted by arrows. The axial image shows tumor infiltration into the C7 neural exit foramen (arrow) license number 5610100806725 volume 70 **[13]**

Tumors are classified into two types: benign tumors and malignant tumors [14].

Benign Tumor: This form of tumor is not damaging to the body since it cannot absorb nutrients from the host, resulting in no changes in the body **[15].** However, it can cause problems in the

condition of placement, such as in the Intestine or Ovary. Its name is derived from the suffix -oma. It has the appearance of a finger, a glandular structure, and is comparable to polyps. This can sometimes resemble a tiny glandular form. With benign tumor, harmful malignant tumor will emerge. Lipoma, Fibroma, and Osteoma are examples of benign tumors **[16]**

Malignant Tumor: Cancer is a sort of tumor that is extremely destructive to the host. It has the power to spread throughout the body. This is the terminology for -Sarcoma and -Carcinoma. **[17,18]**. It can take over all nutrition from the host, causing the host to lose weight and eventually die. Hepatocellular Carcinoma of the Liver, Malignant Melanoma of the Nervous System, Bronchogenic Carcinoma of the Lung, and others are examples of frequent malignant tumors. **[19]** Leukemia in Hematopoietic stem cell [**20].**

Metastasis: When cancer cells move across the body and seed new cancer cells in new organs, this is a common term in cancer biology. Metastasis is a life-threatening illness for patients and a substantial therapeutic challenge**. [21].** Malignant tumors spread in three ways: (1) by seeding within bodily cavities, (2) through lymphatic spread, and (3) through hematogenous dissemination [**22]**

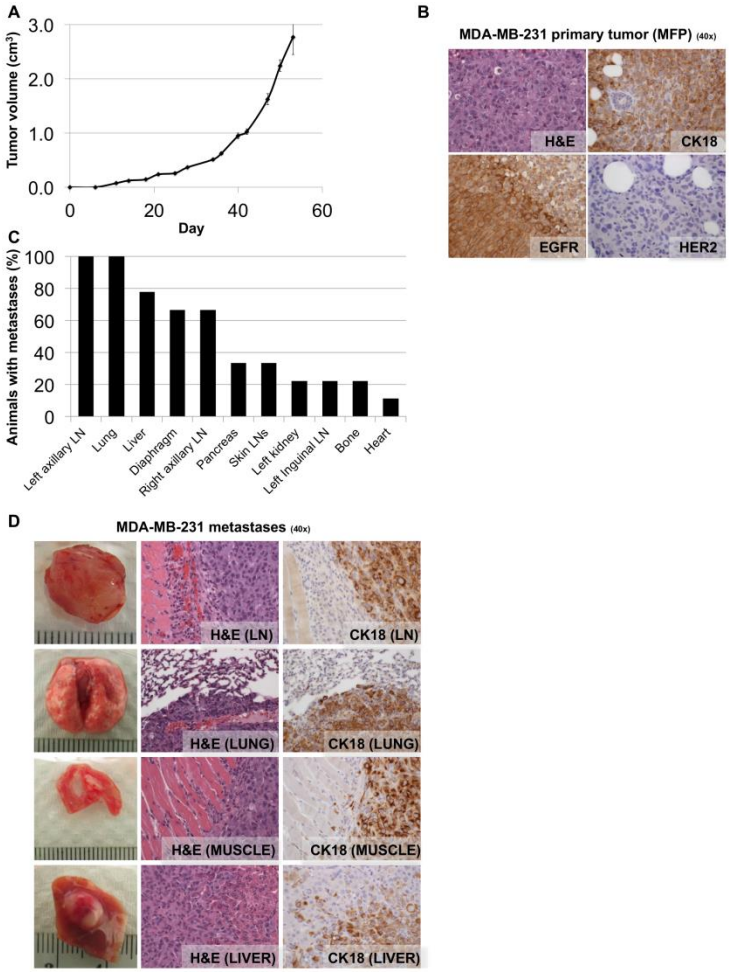

Fig-2: Diagram of metastasis of breast cancer in mouse study [23]

Epidemiology and Cancer:

The scientific field of epidemiology evaluates the occurrence, geographic spread, and probable remedy for disease as well as other issues pertaining to health. Cancer epidemiology is the study of variables impacting cancer in order to identify probable patterns and causes **[24]**. The biggest challenge with today's cancer is late detection and cancer metastasis. Cancer is most

likely caused by a lack of knowledge, tobacco use, alcohol and drug use, and many types of air pollution. Cancer is caused by a constant mutation in DNA caused by a mutagen, while the DNA repair system is unable to function **[25].** Early cancer detection might be improved by developing cancer markers that can be detected using serum **[26].** Plasma, Urine, Stool, Body Fluid, CSF, or Sweat. Cancer can be avoided by the study of cancer immunology, which identifies the specific antibody of cancer cell antigen. Finally, everything is dependent on public understanding of good eating habits and pollution control [**27].**

A big knowledge gap in cancer is what is the specific cause of cancer, particularly a vast gap in study about the mutation, various mutations are detected on cancer cells but cannot identify the real reason mutation in cancer cell **[28**]. The other issue is determining particular risk factor associations on cancer cells, which risk factor is closely associated to cancer cell production. Different parts of the globe spend time doing statistical analyses to ascertain which risk variables are correlated with cancer cells. The other issue is determining a particular marker for detecting cancer cells early on or providing appropriate risk prediction for cancer.**[29].** If this problem is discovered, it may be used to identify cancer cells early on, and particular risk factors can be used to alert people to maintain good health **[30,31].**

So, now discuss about a different kind of Cancer in organ specific Sarcoma or Carcinoma with epidemiological studies with study gap. The top five cancers are given below by the WHO **[32].**

1.Lung Cancer:

The biggest driver of cancer-related morbidity and fatality globally is pulmonary cancer, 1.8 million deaths and 2 million diagnoses have been compensated for. After prostate and breast cancer, lung cancer is the second most common cancer diagnosis in both genders. The

worldwide incidence of lung cancer is rising rapidly as a result of rising tobacco use and industrialization in developing nations **[33]**. Indoor radon, air pollution, arsenic, chromium, asbestos, nickel, cadmium, beryllium, silica, and diesel are among the environmental carcinogens listed by the IARC **[34].** sustained localized swelling **[35,36]** and a limited intake of fresh fruits and vegetables **[37]** are two more risk factors for developing lung cancer **[38].**

2.Breast Cancer:

Globally, breast cancer strikes women with greater frequency than virtually every other cancer; 2.26 million [95% UI, 2.24-2.79 million] new cases are expected to occur in 2020 **[39]**. Women who encounter greater degrees of endocrine stimulation are possibly particularly vulnerable to breast cancer. **[40]**, Breast cancer danger rises in various ways: 1.5% at age 40, 3% at age 50, and above 4% at age 70 **[41]**, One of the primary indicators of risk for breast cancer is an extended family's history of the malady. 13–19% of women with cancer of the breast have relatives who were diagnosed with the same ailment **[42]**, An elevated likelihood of developing breast carcinoma has been tied with certain mutations in the genome. Two key genes with high penetrance are BRCA1 (chromosome 17) and BRCA2 (chromosome 13). Disparities in race and ethnicity are nevertheless common among breast cancer patients, notwithstanding the fact that they are mostly linked to a perched risk of the disease **[43].** The causes of this disparity remain unclear. The overwhelming majority of breast cancer cases remain identified in white, non-Hispanic women **[44, 45].** On the flip side, black women had the lowest survival rates and suffered from significantly greater mortality from this malignancy **[46].** Beyond risk factors include beyond radiation therapy, cigarette and alcohol smoking, breast tissue density, previous experience with breast cancer and benign female breast diseases, physical activity, body mass index, exposure to artificial light, intake of refined foods and dietary regimens, exposure to

chemical substances, and other conditions like calcium channel blocking medications, angiotensin II-converting enzyme inhibitors, and nonsteroidal painkillers (NSAIDs) **[47].**

3.Colon and rectum cancer (CRC):

With 1.9 million new cases forecast in 2020, colorectal cancer—which entails malignancies of the colon and rectum—is the second worst kind of cancer on the planet and the third most common sickness in both genders **[48].** A person's likelihood of developing CRC gets exacerbated by hereditary, environmental, or both causes. Risk factors that contribute to colorectal cancer (CRC) include being over 50, have a low socioeconomic status, being overweight or obese, adopting a life of inactivity, tobacco use, ingesting a lot of alcohol, feeding a low-fiber, high-fat diet, and eating red meat. Long-term deprivation of testosterone treatment, hypertension and insulin resistance, acromegaly, kidney transplantation with protracted immunosuppression, a personal or family history of colorectal adenoma or colon cancer, chronic inflammatory bowel disorder (IBD), and a condition called familial adenomatous polyposis (FAP) **[49].**

4.Prostate Cancer:

Prostate cancer led to 358,989 deaths in 2018 (3.8% of all male cancer casualties), thus being the second fastest-growing malignancy in men around the world after lung cancer **[50,51].** Age is the most prominent risk factor. A man's risk of acquiring prostate cancer climbs with age **[52].**

5.Skin melanoma and non-melanoma:

According to GLOBOCAN, sunburn of the skin constitutes 1.7% of all cancer diagnoses globally, with 325,000 extra cases foreseen in 2020 **[53]**. Extreme sun exposure with UV rays,

Indoor Tanning, Immunosuppression, Moles (Nevi), Family History, and Obesity are risk factors for skin melanoma. However, UV light exposure causes prevalent skin cancer in Caucasian men **[54].**

The present examination of the scientific literature reveals that whilst breast cancer is the principal victim of women, it is the second most prevalent cause of death worldwide **[32].** Worldwide, carcinoma of the lungs is also ubiquitous and has a high mortality rate as well as an elevated likelihood of disseminating **[55].** Nonetheless, tobacco smoking serves as the main driver of lung cancers due to its incredibly specific risk factor, and the public is not properly informed on ways to prevent it. On the flip the same direction, there are a number of other risk factors for breast cancer that varies according on ethnic background, age, and gender. Very few investigations exist in developing countries to identify the risk variables associated with breast cancer. Folks are therefore clueless of the reasons. For this reason, the close-connected risk factor has to be made known to the public. This review study aims to identify hazards that are closely associated with poverty, such as lifestyle-associated risk factors, BRAC1/BRAC2 mutations, and prominent forms of breast cancer in nations that are poor. 'certainties' using this research will help you design plans that will help refrain from breast cancer. It will help drive down the expense of cancer counseling.

CHAPTER-2 PRESENT KNOWLEDGE ABOUT BREAST CANCER

There are distinctions regarding breast cancer into distinct phases in the current study when it begins to rise from normal breast cells, and different subtypes are defined. Different risk factors are studied, but no particular information about risk factors found in a given location is obtained. Different treatments are offered for cancer patients, but no proper understanding of breast cancer prevention is provided. Consider poring through the various sections below to gain insight about contemporary investigations and understanding gaps adjacent to breast cancer.

Stages of breast cancer

The study identified five fundamental stages of carcinoma of the breast, spanning from stage 0 up to stage 4, based on a number of studies **[56].**

Stage o

No symptoms associated with breast cancer exist present. Just discovered in an inflammatory condition in the breast skin, such as type 1 hypersensitivity **[57].**

Stage 1

The breast tumor is 20 millimeters (mm) or less in diameter at its widest point. This is a fraction of an inch. This stage is then divided into four substages based on tumor size:

1. A T1mi tumor is one that is one millimeter or less in size.
2. T1a tumors are those that are greater than 1 mm but less than 5 mm in size.
3. T1b tumors are those that are larger than 5 mm but smaller than 10 mm.

4. T1c tumors are those that are larger than 10 mm but smaller than 20 mm **[58].**

Stage 2

Any of the following conditions:

There is no tumor in the breast, but the malignancy has progressed to one to three axillary lymph nodes. It has not spread to other areas of the body **[59].** The tumor is 20 mm or less in diameter and has migrated to one to three axillary lymph nodes **[60].** The tumor is greater than 20 mm but less than 50 mm in size and has not migrated to the axillary lymph nodes **[61].**

Stage 3

Any size tumor has traveled to the intrinsic nipple lymph node network or even 4–9 axillary lymph nodes. The remaining portion of the body has not been harmed. Stage 3 additionally applies to a tumor larger than fifty millimeters in size that has expanded to a few axillary lymph nodes **[62]**. It is sometimes referred to as aggressive breast cancer if the tumor has migrated to the chest cavity and triggered breast fluid retention or ulceration. Up to nine lateral or internal mammary lymph nodes may have been touched by its expansion. The remaining portion of the body hasn't been altered **[63].** any size tumor that has traveled to no fewer than ten interior mammary lymph nodes, underarm lymph the nodes, as well as lymph nodes beneath the collarbone. It does not exist throughout the body **[64].**

Stage 4 (metastatic)

Any size tumor is achievable, and it might have disseminated to other organs such the liver, brain, lungs, bones, outlying lymphatic vessels, or chest wall **[65].** Metastatic breast cancer is found at the time of the initial diagnosis in roughly six percent of cases **[66].** Freshly diagnosed

metastatic breast cancer is a designation for this. In the majority of cases, an earlier diagnosis and course of counseling for the initial stages breast cancer causes a finding of metastatic breast cancer **[67].** This current study of breast cancer stages just represents the condition stages but does not mention the linked risk factors relationship between this condition, therefore it cannot express this study that warns in the start point of cancer.

Common risk factor found in present study

In the current study, the most prevalent risk factors that never change include being above the age of 50, having a BRAC mutation, and having a family history. Not being physically active, being overweight, and taking hormones are all risk factors that can alter **[68].**

Age

The most prominent warning sign for breast cancer in women is age **[68**]. It's partly because our cells are more prone to alter in unexpected ways throughout time. In some circumstances, it may simply be the result of longer time for harmful lifestyle patterns to catch up with us. Smoking, excessive alcohol use, and being sedentary or overweight, particularly after menopause, anything elevates the prospect of breast cancer **[69].**

BRCA mutation

BRCA (Breast Cancer suppressor gene) is one kind of oncogene that help to prevent producing neoplasm from breast cell **[70]**. If this oncogene mutated it cannot prevent to neoplasm, it prevents as like p53 that abnormal cell going to apoptosis and block mRNA for stop the protein synthesis **[71]**. But different kind of study cannot explain how BRCA mutation happens, how to prevent on this. Currently, many groups of researchers are attempting to determine the

specific cause of the BRCA mutation, but they have been unable to obtain the desired results **[72].**

Family history

It has been linked with a higher probability of prostate and breast cancer **[73].** The fact that breast cancer can be triggered by specific inherited factors explains this protective factor **[74]**. However, the latest study uncovers no genetic material connection to breast cancer. If this is discovered, it could potentially pinpoint breast cancer and alert patients about their likelihood of developing the illness in the future **[75].**

Physical activity

Research has shown a relationship between a lower likelihood of breast cancer and between four and seven hours per week of moderate-to-intense exercise. Exercise restricts the circulation of insulin growth factor, a hormone that affects the proliferation and function of cells in the breasts, while also utilizing and managing blood sugar levels. Regular exercisers are more likely than people who do not exercise to maintain an acceptable weight with little to no extra fat. They are also commonly healthier. More estrogen gets generated by overabundance fat cells compared to by fat cells. A prolonged exposure of breast cells to insufficient hormones over time enhances the risk developing breast carcinoma **[76].**

Overweight

Overweight Since fat cells discharge estrogen, who may contribute to the development and proliferation of hormone-receptor-positive carcinomas of the breast, maintaining more fat cells in the body boosts the risk associated with these tumors **[77].** Nonetheless, an assortment nation

has established that obesity is not the cause of breast cancer in women who are overweight. Consequently, distinct regional examinations must be done **[78].**

Receiving Hormones

Integrating greater amounts of HRT and a smaller amount of HRT increase the risk of developing breast cancer compared to both of them way around. Combining treatment with hormone replacement therapy additionally boosts the likelihood that breast cancer will be found later. Elevated density of breasts has been related to combination therapy with hormone replacement (HRT), which might decrease the efficacy of mammograms in finding malignancies in the breast **[79].** Nonetheless, notwithstanding having an elevated probability of breast cancer, a number of impoverished nations do not use HRT **[80].**

Subtype of breast cancer

There are several different types of breast cancer. These are triple negative, HER2, luminal A, and luminal B [81]. Knowing which parts of the country have greater numbers of subtypes as well as potential associated risks is crucial.

Luminal A

Cancers categorized as luminal A can be distinguished by the absence of HER2 but the presence of ER and/or PR [81]. About 40% of all breast cancers are attributed to luminal A tumors [82]. Nevertheless, each country's percentage differs. Therefore, precise concepts are needed to determine the precise amount of luminal A that may be utilized to make a diagnosis [83].

Luminal B

In contrast to luminal A tumors, luminal B malignancies are of a higher grading and have a less favorable outcome. They can either be or may not be PR negative in addition to being ER positive **[81].** Luminal B tumors constitute estimated 15–25% of breast cancer instances **[82].** On the other together, it is prevalent throughout **[84].**

HER2

Between ten and fifteen percent of breast cancer patients fall within the HER2-positive team, which is determined by large HER2 expression in a lack of ER and PR **[85].** Since the start of HER2-targeted drugs. They are their prognosis is better and they advance more swiftly than luminal tumors **[81,82].**

Triple Negative breast cancer (TNBC)

Figure 4 shows that Triple-negative breast cancer, which accounts for up around 20% of the overall incidence of breast cancer, is ER-negative, PR-negative, and HER2-negative. Women under the age of 40 are more inclined to get breast cancer that is triple-negative **[81].** TNBC is considered a rare breast cancer, yet other nations have discovered a relatively high incidence **[86].** TNBC is a highly hazardous subtype because it might be difficult to diagnose **[87].** As a result, the number of subtypes is recognized to be particularly relevant in some nations **[88].**

CHAPTER-3 APPROACHES OF RISK FACTOR ASSESMENT

This research attempts to focus regarding the evaluation of several risk factors in 17 nations, one of which is extremely impoverished. There are several breast carcinoma risk factors **[68]** various countries have various risk factors. It is challenging to raise public knowledge about breast cancer prevention in a specific location. That is why it is necessary to discover or ensure that certain risk factors are more prevalent in a specific location. As a result, this is separated into three broad groups. The first is the largest number of subtypes discovered, the second is a lifestyle-related risk factor, and the third is BRCA mutation research discovered in specific nations. These nations are also classified as belonging to the Indian subcontinent, the Oriental region, Africa, and the Sub-Saharan area. This study will determine whether a risk factor number is high or low, the amount of subtype in breast cancer, the amount of BRCA mutation, and any connection between risk factor and subtype and mutation.

This research project tried to ascertain risk factors for breast cancer by getting many papers connected to clinic pathological or demographic studies that have been published in different journals all over the world, such as Google Scholar, PubMed, scientific reports, and Willey. This study examines around 300-400 research papers.

Aim to locate an assessment of risk factor in underdeveloped nations among 300-400 previously published papers since 2000 and 2023 on Google Scholar, PubMed, Willey, and scientific publications. This issue is being researched by HRT on breast cancer, repressor gene associated to breast cancer, clinic pathological or demographic studies on different regions such as Asia, Africa, and so on, elaboration country by country.

CHAPTER-4 RISK FACTOR ASSESMENT

This study describes many regions of breast cancer research via clinic pathological and demographic investigations.

Indian subcontinent

This information was gathered from reference no. **[89-96]**

This study explains p value with characteristics such as breast feeding, location urban rural, increased BMI, lifestyle linked behavior, and the important functions of BRCA1/BRCA2

Table-1 for risk factor assessment in South Asia

Country wise study	**Subtypes of breast cancer**	**Lifestyle related risk factors**	**BRCA Mutation**	**Investigators name**
India **1**. Breast cancer investigations in India's most significant cities **[89]**	Giving birth while breastfeeding has an impact on the number of Luminal B breast cancer patients.	Breast cancer is exacerbated by tobacco use and low socioeconomic level.	identified in a patient mutation 2.4% - 2.9%	**[89] Malvia Et al.**
Nepal **1**. Research in students in grades 11 and 12 **[90],** journal of The Nepal Medical Association **[91]**, A new look at Molecular biology of breast cancer **[92]**	Sufficient paper cannot find to determine subtypes	Women in low socioeconomic status were more likely to get breast cancer.	Nearly 60% of cases had a mutation.	[90] **Bandari Et al.** [91] **Singh Et al**. [92] **Ma Et al.**

Pakistan 1.Shaukat Khanum Memorial Cancer Hospital and Research **[93]**, genetic case study in major cities of Pakistan **[94]**	TNBC, Luminal-A less amount found	Not found in any data from previous publications	Amount of mutation is 6.7%	[93] **Bandar Et al.** [94] **Liede Et al.**
Bangladesh 1.This descriptive case-control study [**95],** Identification of Mutation in Exon11 **[96].**	Sufficient study cannot find to determine subtypes	Breast cancer is most closely associated with female abortions.	Sufficient paper cannot find to determine	[95] **Ahmed Et al.** [96] **Nishat Et al**.

Oriental Region

In this area are discussed on reference no **[97-106]**

Table-2 for risk factor assessment in Oriental Region

Country wise study	**Subtypes of breast cancer**	**Life style related risk factors**	**BRCA mutation**	**Investigators name**
Indonesia Clinical and Subtypes of Breast Cancer in Indonesia **[96]** Distribution of BRCA1 and BRCA2 Mutations **[97**].	Luminal A is first, Second Luminal Third HER2 negative, Fourth TNBC	aging is responsible for most of cases	Mutation is 7.8%	[96] **etut Widiana, Hendry Irawan** **[97] Haeyoung Kim, Doo Ho Choi1**

Vietnam Study of largest cancer hospital in Vietnam **[97],** Vietnam National Cancer Hospital study to 4-year period **[98]**.	TNBC is majority, second is Luminal A	Breast cancer is associated with age, body mass index, breastfeeding, and birth control pills, although HRT is not one of these factors.	**Not** found in special study about this.	[97] **J. Nguyenet Et al.** [98] **Thi Hoa Nguyen Et al.**
Philippines Risk factors for breast cancer among Filipino women in Manila [**99**] 2BRCA1 and BRCA2 mutations [**100**] Breast Cancer Subtypes in Asian-Americans **[101-103]**	Luminal -B is high and Luminal-A is lower	The use of birth control pills, alcohol intake, smoking, BMI, and age are risk factors.	Specific mutation rate cannot determine but random study find nearly one of third	[99] **Lorna J. Gibson Et al.** [100] **Maria Lourdes De Leon Matsuda Et al.** [101] **Ellen Chuang Et a**l.
Thailand Tobacco smoke exposure and breast [**104],** Breast Cancer Subtypes Identified [**105]** Characteristics of breast cancer patients tested for germline [**106**]	Luminal -A is first, Luminal B is second, TNBC is third, HER2 is fourth.	Tobacco consuming is major risk factor	Mutation is 18%	[104] **Pimhanam Et al.** [105] **Suebwong Chuthapisith Et.al.** [106] **Songporn Oranratnachai Et al.**

African and sub-Saharan region

This reference pertains to [107-128]

Table-3 for risk factor assessment in African and sub-Saharan Regio

Country wise study	Subtypes of breast cancer	Life style related risk factors	BRCA mutation	Investigators Name
Morocco TNBC study on Moroccan women **[107],** Risk Factors for Breast Cancer of Different Age **[108],** Contribution of BRCA1 and BRCA2 germline mutations **[109]**	TNBC found in 19.5%, others have no study	BMI and birth control pill is major risk factor.	Mutation of BRAC1 9%, BRAC2 6%.	[107] **Ghizlane Et al** [108] **Laamir Et al**. [109] **Bakkach Et al**.
Egypt Breast cancer in women aging 35 years old **[110],** Assessment of Human Papillomavirus Infection and Risk factor **[111],** BRCA1 and BRCA2 truncating mutations and variants [**112**].	Luminal-B 28.8%, HER2 above 30% and overexpressed than another subtype	Birth control pill, family history, Menopause is major risk factors	Percentage of mutation cannot find but classified mutation in 8 variants.	[110] **A.D. Darwish, A.M. Helal, N.H. Aly El-din, L.L. Solaiman, A. Amin** [111] El-**Sheikh Et al**. [112] **Sherihan G. Abdelhamid, Abdel-Rahman N. Zekri, Hany M. AbdelAziz, Hala O. El-Mesallamy**
Mauritius	Not found in any special study about this	Not found in any special study about this	Not found in any special study about this.	
Kenya **1.** Breast cancer risk factors in relation to molecular subtypes **[113**], 2 The Kenyan BRCA1/2 Testing [**114].**	TNBC is uncommon, but Luminal-A, Luminal-B, and Her2 are enriched.	High BMI and menopause women are major risk factor	Mutation is 62% found	[113] **Sayed Et al.** [114] **Torrorey-Sawe, Rispah, Nicole van der Merwe, Simeon Kipkoech Mining, and Maritha J. Kotze.**
Tunisia Breast Cancer in Tunisia **[115],** Breastfeeding reduces breast cancer risk **[116],** Contribution of BRCA1 **[117]**	HER2, Luminal-B is common, TNBC is rare case	Breast feeding is a factor of breast cancer	Mutation is 8.7%	[115] **Bouguerra Et al.** [116] **Awatef.Et al**.. [117] **Mahfoudh Et al.**
Algeria Epidemiological profile and distribution **[118]**, A Case-Control Study in	Majority of cases are Luminal-A, luminal-B,	Low educational level, Birth control pill, High BMI is major risk factor.	Mutation is 25%.	[118] **Elbasyouni, Amel, Leila Saadi, and AbdelKarim Baha** [119] **Hamdi-Cherif Et al.**

the Northern Algeria **[119**], BRCA1 and BRCA2 Germline Mutation **[120]**	HER2.TNBC is rare.			[120] **Mehemmai Et al.**
Nigeria Pitutary and gland hormone ratio studies [**121**], Distribution of Breast Cancer Subtypes Nigerian women [**122]**, Inherited Breast Cancer in Nigerian women **[123]**.	Luminal-A and Luminal-B is high number	obesity, physical inactivity, alcohol consumption is main risk factor	7.0% in BRCA1, 4.1% in BRCA2 mutation.	[121] **Ajayi Et al.** [122**] Adeniji Et al.** [123] **Zheng Et al.**
Tanzania The distribution of reproductive risk factors **[124],** Breast cancer in East Africa [**125**]	Most of cases is HER2	Breast feeding is major risk factor of breast cancer	Overall percentage of, mutation cannot find but six mutated variants found	[124] **Rweyemamu Et al.** [125] **Rweyemamu, Linus P., Büşra K Et al**.
Uganda Immunohistochemical Typing in Women with Breast Cancer in Kampala, Uganda **[126],** Breast Cancer Risk Factors among Ugandan Women at a Tertiary Hospital **[127**] 3. Prevalence of Inherited Mutations in Breast Cancer **[128]**.	First is Luminal-A, second is Luminal-B, third is TNBC, fourth is HER2	Rural urban area, birth control pill, Parity, high BMI is major risk factor	. In mutation of 5.6% in BRCA1, 5.6% in BRCA2	[126] **Mlole Et al**. **[**127] **Galukande Et al.** [128] **Adedokun Et al.**

Chapter-5 BREAST CANCER DIAGNOSIS AND TREATMENT IN BANGLADESH

Abortion is a crucial breast cancer risk factor in Bangladeshi women, as indicated by earlier research in the risk factor evaluation for Bangladesh **[95, 96]**. However, this study is unable to identify prevalent subtypes or provide more details on BRAC mutation. Bangladesh is therefore unable to do breast cancer research, and what research is done there is extremely restricted **[129].** Due to research limitations, Bangladeshi women's understanding of certain lifestyle-related risk factors cannot be improved **[130].** Sufficient research on risk factors using a questionnaire for patients with breast cancer, sample analysis to determine the number of mutations, and development of chemotherapy may all aid in raising awareness of the disease **[131, 132].** Consequently, breast cancer becomes a life-threatening condition for women extremely quickly. This chapter describes the types of diagnoses and treatments that Bangladeshi hospitals provide for women.

Diagnosis of breast cancer in Bangladesh

In Bangladesh, both public and private hospitals frequently diagnose breast cancer. This kind of service is also offered by several corporate diagnostic centers. A list of breast cancer diagnoses is shown below **[133].**

1.Breast Exam [**134]**

2.Mammogram **[135**]

3.Breast ultrasound **[136]**

4.Removing cancer cells from breast(biopsy**) [137]**

5.Breast Magnetic resonance imaging (MRI) **[138**]

6.Blood test such as Complete Blood Count (CBC**) [139]**

7. Mammogram of the other breast to look for signs of cancer **[140**].

8. Breast MRI **[141**].

9.Bone scan **[142].**

10.Cancer antigen test **[143].**

11. Computerized tomography (CT) scan **[144]**.

12.Positron emission tomography (PET) scan

Now describe in brief about the breast cancer price, availability all over the Bangladesh

1.Breast exam

A breast exam involves looking at the breasts physically and checking the lymph nodes in particular. A doctor examines this. Doctors from Bangladesh are able to check this anywhere. There are no additional fees associated with this, including those for doctor visits. **[145]**.

2.Mammogram

A mammogram, as the name suggests, is an instance of mammary X-ray. Mammograms are an established screening technique to detect breast cancer. In the event that a screening mammography reveals an anomaly, the physician will determine the stage, grade, and course

of therapy, among other options **[140**]. This is availability in all major cities of Bangladesh **[135,146].**

3.Breast ultra sound

Ultrasound harnesses sound waves to supply images of inside structures in the body. Ultrasonography can be used to figure out if a new breast lump is a solid mass or a cyst containing fluid **[136].**

5. Removing cancer cells from breast(biopsy)

A biopsy is the only therapy that reliably detects breast cancer. In a biopsy, an experienced needle equipment accompanied by an X-ray or other imaging procedure will be utilized by the medical professional to take a small piece of tissues from an in-doubt location. A tiny metal marker is sometimes put there to help make what's happening inside the breast apparent on future imaging tests **[137].**

Biopsy samples are delivered to a lab wherever experts' investigation them and assess whether the cells are cancerous in nature. A biopsy sample is additionally evaluated in order to identify the type of cells generating the breast cancer, its degree of aggressiveness (grade), and if the cancer cells comprise hormone receptors or other receptors that might modify treatment options. **[146,147].**

5.Breast Magnetic resonance imaging (MRI)

An MRI scanner uses radio waves and a magnet to create pictures of the interior of the breast. Get a breast MRI after receiving a dye injection. Apart from traditional imaging tests, an MRI

provides images without employing radiation. **[138].** The primary goal of breast MRIs is to track anatomic changes in the breast that occur after neoadjuvant therapy. **[141].**

6.Blood test such as Complete Blood Count (CBC)

This test serves only to identify the stages of breast cancer and to medication it. Breast cancer metastases are seen at stage 4 **[148]**. A doctor treating breast cancer would probably want comprehensive blood counts both before and during therapy. These assays determine if the blood has normal concentrations of different blood cell types **[149]**. The quantity of vital blood cells that the body requires to operate correctly can be decreased by both the disease itself and therapies like radiation and chemotherapy **[139].**

7.Bone scan

Perform a scan of the bone to see if the cancer has traveled to the bones. A little quantity of low-dose radioactive material gets injected into the system, mostly accumulating in abnormal bone areas. It can detect tiny regions of cancer spread that are invisible on a standard x-ray and simultaneously display all of the body's bones **[150]**. Tc-99m MDP is used to monitor this bone scan in order to look for metastases in the patient **[142].** This method is particularly useful for detecting skeletal metastases **[151].**

8.Cancer antigen test

Elevations in the cancer antigen 15-3 (CA 15-3) may suggest the existence of breast cancer or its metastasis to other bodily regions **[152].** A recurrence or advancement may be monitored, as well as how the cancer is reacting to therapy, using the CA 15-3 blood test. Numerous cell types achieve a protein dubbed cancer antigen 15-3 (CA15-3), but cells with breast cancer

produce a large amount of it **[153].** After the protein gets to the bloodstream, it could be measured. Higher-than-normal levels of CA15-3 were found in most women whose breast cancer metastasized, or spread to other regions of the body **[154].**

9.Computerized tomography

A CT scan, also known as a computerized tomography scan or CAT scan, is a type of X-ray that provides physicians with two-dimensional cross-sections, or slices, of the body's interior organs **[155].** A CT scan involves the patient lying on a moving table and passing through a machine shaped like a doughnut that captures images of their body from various perspectives. These X-rays are combined by a computer to provide intricate images of the inside of the body **[156].** An intravenous line must be used to inject a contrast solution (dye) into the patient's arm prior to the test **[157]**. Before administering the contrast solution to the patient, the doctor may undergo renal function testing since the dye might have an impact on the kidneys **[144**].

As of the present, breast evaluations do not typically use CT scans. A CT scan may be prescribed by the doctor if the patient has a big breast cancer in order to determine whether the disease has spread to the chest wall. This aids in determining if a mastectomy is necessary to remove the malignancy **[158].**

10.Positron emission tomography

A positron emission tomography (PET) scan is a machineries of diagnosis imaging procedure that looks for possible breast cancer metastases using a radioactive material known as a tracer. This tracer can assist in locating cancerous regions that might not be seen on an MRI or CT scan **[159].**

A tiny quantity of radioactive material (tracer) is needed for a PET scan **[160].** This tracer is administered intravenously (IV), often in a tiny vein in the hand or on the inside of the elbow **[161].** The tracer passes through blood, gathers in organs and tissues, and emits a signal that improves the radiologist's ability to spot specific regions or diseases **[162].** It must wait close by while the body absorbs the tracer **[163].** Usually, this takes one hour or so. After that, lie on a little table that glides into a big scanner in the form of a tunnel **[164].** Signals emitted by the tracer are picked up by the PET scanner. A 3D image is created from the results by a computer **[165].** The doctor views the pictures on a monitor for interpretation. The test requires the patient to lie motionless. Excessive motion might lead to mistakes and blurred photos. The exam lasts for around ninety minutes **[166].** Most PET scans are conducted in conjunction with CT scans. Known as a PET/CT scan, this combined scan enables a thorough evaluation of the whole body in search of any indications of cancerous cells **[167].**

A normal result indicates that the radiotracer has not accumulated abnormally in any places outside the breast. This finding probably indicates that the breast cancer has not progressed to other bodily regions. On a PET scan, very tiny spots of breast cancer could go undetected. Unusual findings might indicate that the breast cancer has migrated to other parts of the body **[168].**

Breast cancer treatment availability in Bangladesh

There are not enough medical facilities in Bangladesh, and most breast cancer treatments need surgery **[169**]. administered radiation and chemotherapy following surgery on occasion **[170].**

1.Breast cancer surgery

For the majority of patients, it is a successful first therapy for breast cancer. Sentinel node treatment involves removing lymph nodes when there is a danger of metastasis, lumpectomy involves removing a small portion of the tumor, and mastectomy involves removing the whole breast **[171].**

Lumpectomy

A lumpectomy is a type of surgical activity that involves removing cancer from the breast. It involves taking out the abnormal tissue and surrounding healthy tissue **[172].** This ensures that the pathological tissue will be completely removed. A lumpectomy is sometimes referred to as broad local excision or breast-conserving surgery since just a portion of the breast is removed. In contrast, a mastectomy involves the whole removal of the breast tissue **[173].** Physicians may sometimes refer to a lumpectomy as a quadrantectomy or an excisional biopsy. One medication option for early-stage breast cancer is a lumpectomy **[174].** A lumpectomy may be performed sometimes to rule out malignancy. In order to lower the likelihood of cancer returning, radiation treatment is typically administered to the breast following a lumpectomy procedure to remove the malignancy **[175].**

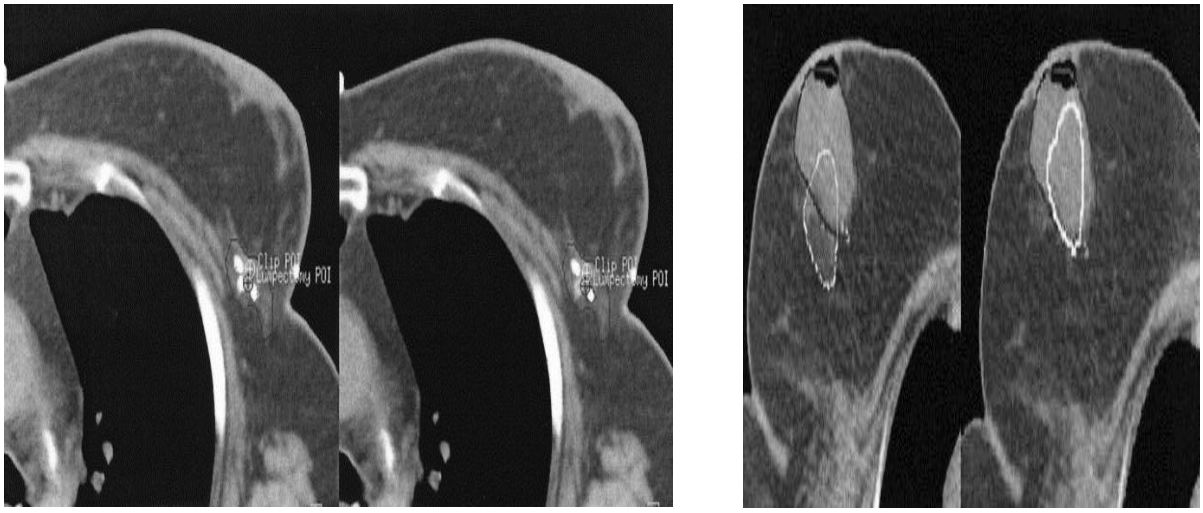

Figure-7: MRI image of patient after and before lumpectomy surgery [176]

Mastectomy

In order to cure or prevent breast cancer, a mastectomy involves removing all of the breast tissue **[177]**. One course of therapy for those with early-stage breast cancer might be a mastectomy. Another possibility is breast-conserving surgery (lumpectomy), in which the breast's tumor is the sole thing removed **[178].** Following the treatment, a more natural-looking breast appearance can be achieved thanks to newer mastectomy procedures that maintain breast skin **[179].** Another name for this is a skin-sparing mastectomy. Breast reconstruction, often known as reshaping surgery, can be performed concurrently after a mastectomy or as part of a follow-up procedure **[180].**

If a patient has breast cancer or is extremely likely to have it, all breast tissue is removed during a mastectomy. A patient may have a bilateral mastectomy, which removes both breasts, or a unilateral mastectomy, which removes just one breast **[181].**

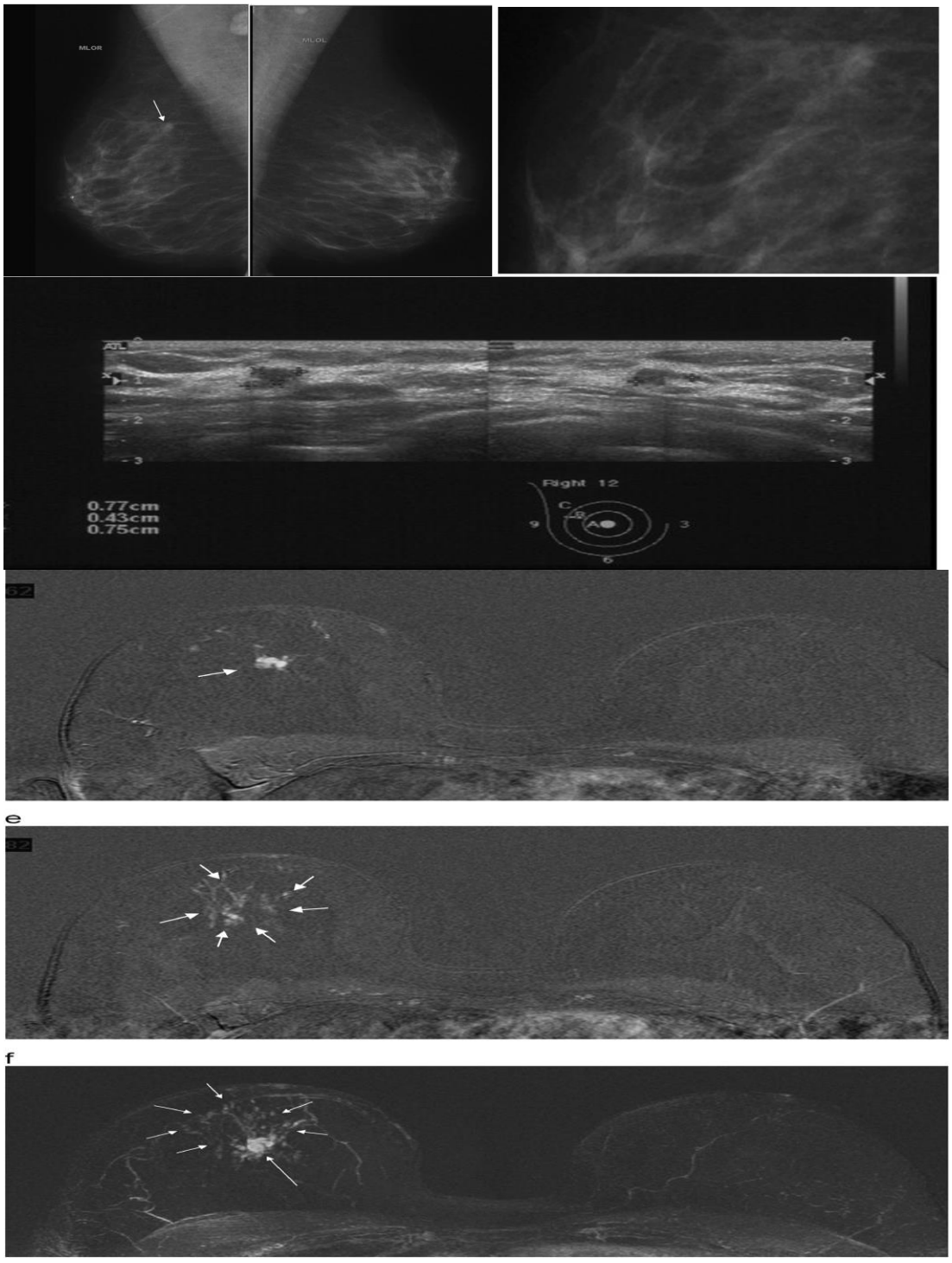

Figure-3(a): -A large cancer cell presents on right breast in MRI images [182].

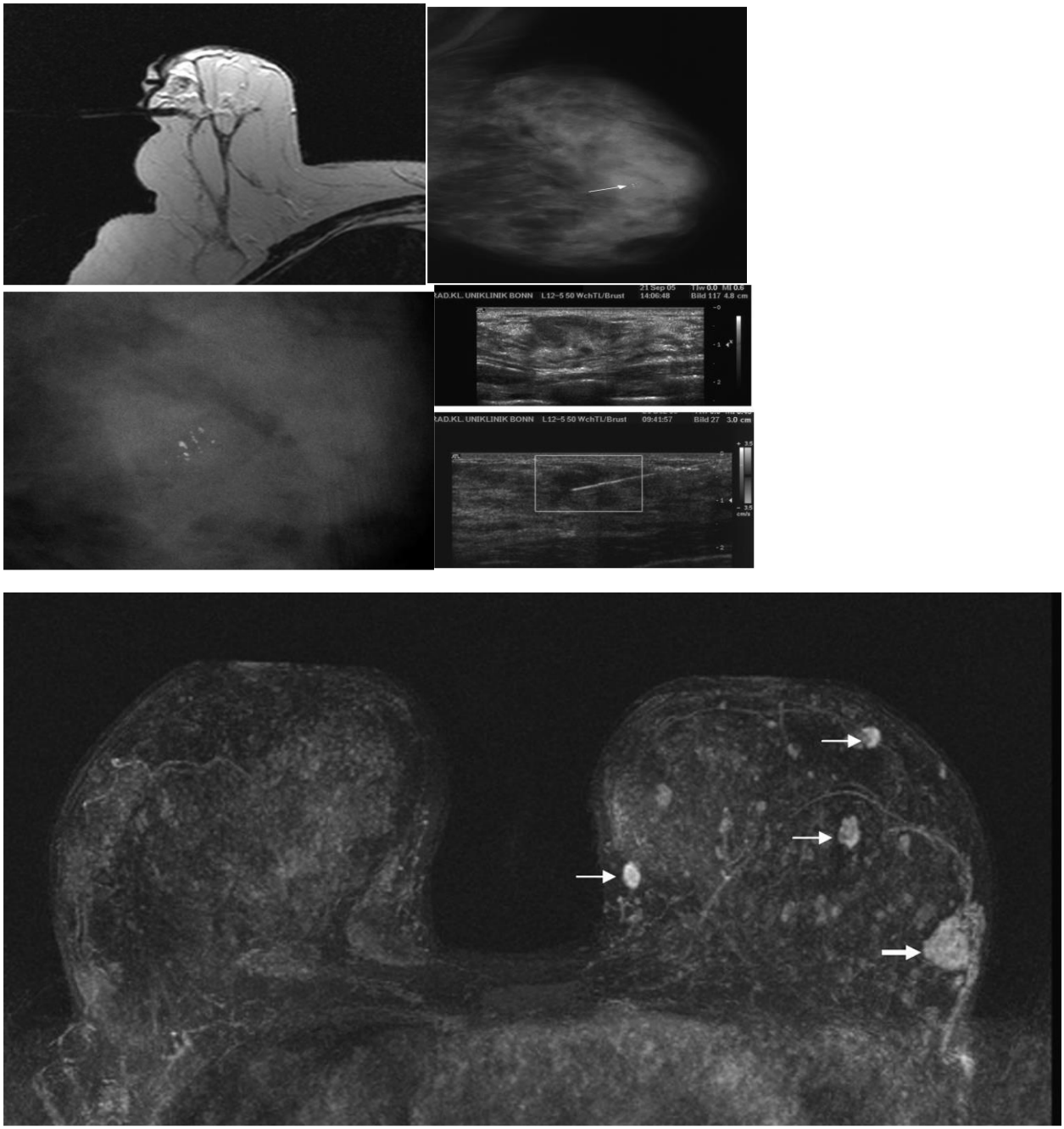

Fig-4(b)After Mastectomy surgery MRI images on breast cancer [182].

Sentinel node therapy

One method to check for cancer spread is a sentinel node biopsy **[183]**. It can ascertain whether the cancer cells have spread from their original place of origin to the lymph nodes. Sentinel node biopsies are regularly carried out on patients struggling with melanoma, breast cancer, and other malignancies **[184].** The first few lymph nodes that cancer spreads to are known as

sentinel nodes **[185].** A tracer substance is utilized in sentinel node biopsy procedures could assist the surgeon during surgery discover the sentinel nodes **[186].** The sentinel nodes were eliminated and inspected at a laboratory [**187]**. It is likely that cancer has not spread if there are no cancerous sentinel nodes. This implies that there's no need to remove any more lymph nodes. Perhaps no more surgery is required **[188].** It could be necessary to remove more lymph nodes for testing if a sentinel lymph node biopsy reveals cancer **[189].**

2.Radiotherapy

Radiation treatment targets cancer cells using powerful radiation beams, such as protons and X-rays **[190]**. Usually, a sizable apparatus that directs energy beams at the body is used to administer radiation therapy (external beam radiation**) [191].** However, brachytherapy—the internal implantation of radioactive material—is another kind of radiation treatment **[192].** High-energy X-rays, protons, or other particles are used in radiation treatment for breast cancer in order to destroy cancer cells **[193].** Radiation therapy has a greater effect on rapidly developing cells than on normal cells, such as cancer cells **[194].** The particles or X-rays are invisible and painless. It is safe for patients, including children, to be around other people if they have had treatment and are not radioactive **[195].**

Breast cancer treatment with radiation can be administered by:

Radiation Form the Exterior.

Radiation from the outside body is delivered to the breast by a machine. According to **[196],** this is the most often utilized kind of radiation treatment for breast cancer

Internal radiation (brachytherapy):

A radiation-delivery device is briefly inserted into the breast in the region where the malignancy was removed after surgery **[197].** Throughout your treatment, a radioactive source is inserted into the apparatus for brief intervals of time **[198].**

Almost every stage of breast cancer can be treated with radiation treatment **[199].** After surgery, radiation treatment is a useful tool for lowering the chance that breast cancer may return **[200].** Furthermore, it is frequently used to relieve the symptoms of metastatic breast cancer, which is cancer that has spread to other regions of the body **[201].**

3.Chemotherapy

Chemotherapy involves drugs to eliminate cells that multiply quickly, such cancer cells. If the person undergoing treatment has a high chance of the cancer relapsing or transmitting to another portion of the body after surgery, the surgeon might prescribe chemotherapy **[202].** Chemotherapy employs drugs that aim at and kill breast cancer cells just. Such medications are frequently administered intravenously (IV) through a needle or consumed orally as pills **[203].**

Chemotherapy is often used in conjunction with other therapies, like hormone therapy, radiation therapy, or surgery, for breast cancer **[204].** Chemotherapy can be used to improve a patient’s life, lessen the likelihood that the cancer will recur, raise the likelihood of a cure, or relieve cancer symptoms **[205].** Chemotherapy may manage breast cancer to extend life if it has spread or returned. Alternately, it may assist in reducing cancer-related symptoms [**206].** The danger of side effects from chemotherapy for breast cancer is also there; some may be modest and transient, while others may be more severe or long-lasting. A patient's physician can advise them on whether chemotherapy is a right option for their breast cancer **[207].**

In the subsequent scenarios, breast cancer patients are eligible for treatment with chemotherapy:

Chemotherapy after surgery for breast cancer

The physician might prescribe chemotherapy during surgery to eradicate any breast cancer particles that were omitted and reduce the likelihood that the disease will recur. This procedure is referred to as adjuvant chemotherapy **[208].** Physician could suggest adjuvant chemotherapy even after surgery if there is no longer any cancer, if there is an elevated likelihood that the illness may return or metastasize, or spread to other parts of body. The patient may have greater likelihood of metastasis if tumor-like cells are found in lymph nodes approximately the breast that is impacted **[209].**

Chemotherapy before surgery for breast cancer

Chemotherapy is occasionally used before surgery to reduce bigger malignancies (known as neoadjuvant treatment or preoperative chemotherapy**) [210].** This might include:

1.Give the surgeon the best opportunity of completely eliminating the malignancy.

2.Permit the surgeon to discharge only the malignancy and not the entire breast.

3.Reduce the amount of illness in lymph nodes, making less invasive lymph node surgery possible.

4.Reduce the likelihood of the cancer returning

5.Assist the doctor in understanding how effectively cancer reacts to chemotherapy, which aids in determining prognosis and the optimum chemotherapy medication option. **[211-215]**

Neoadjuvant therapy is often used for:

1.Breast cancer that is inflammatory

2. Breast cancer that is HER2-positive

3. Breast cancer that is triple-negative

4.Major breast cancers

5.migrates of cancer to the lymph nodes

6.Breast tumors of a larger size **[216-220]**

Chemotherapy can be used as the primary treatment of breast cancer has progressed to other regions of the body and surgery is not an option **[221**]. It can be used with targeted treatment **[222].**

Chemotherapy for advanced breast cancer is often used to enhance quality of life and length of life rather than to cure the disease **[223].**

Risks of chemotherapy

Drugs used in chemotherapy go throughout the body. The drugs are prescribed and how Cancer cell respond to it will determine any side effects **[224].** Side effects might get worse as the treatment is being administered. Most side effects are temporary and go away when treatment is finished. Adverse effects from chemotherapy can be both short- and long-term **[225].**

While chemotherapy drugs primarily target rapidly proliferating cancer cells, it can also damage rapidly proliferating healthy cells, including those found in the bone marrow, digestive tract, and hair follicles **[226].** These side effects usually go away at the end of the treatment or

within a year after the last chemotherapy session. In certain instances, it could persist a long time **[227].**

Common short-term side effects include:

1.Hair loss

2.Fatigue

3.Loss of appetite

4.Nausea and vomiting

5.Constipation or diarrhea

6.Mouth sores

7.Skin and nail changes

8.Increased risk of developing infection (due to fewer white blood cells that help fight infection)

9.Nerve damage (neuropathy)

10.Problems with cognitive function that affect memory and concentration, also known as chemo brain **[228-230].**

Long-term side effects

Certain breast cancer chemotherapy medicines can have long-term negative effects, including: Fertility problems. One likely long-term side effect is infertility. Certain anti-cancer drugs damage the ovaries **[231].** Menopausal symptoms including vaginal dryness and hot flushes

might arise from this. Menstruation may stop or become erratic (amenorrhea). If ovulation ceases, pregnancy cannot occur **[232].**

1.Depending on the age, chemotherapy may cause early menopause **[233].**

2.If continue to menstruate, can still become pregnant, whether during or after therapy. However, the effects of chemotherapy are harmful to the fetus **[234].**

3.Thinning of the bones. Women who go through menopause early as a result of chemotherapy may be more susceptible to the bone-thinning disorders osteopenia and osteoporosis. It is typically advised that these women have frequent bone density testing and, if necessary, therapies to prevent additional bone loss **[235].**

4. heart disease. Chemotherapy has a minor risk of weakening the heart muscle and developing other cardiac complications. Certain chemotherapy drugs have been linked to an increased risk of future cardiac problems **[236].**

5.Leukemia. Chemotherapy for breast cancer can occasionally cause a secondary malignancy, such as cancer of the blood cells (leukemia), several years after the treatment is finished **[237].**

Other side effects

Feelings of fear, sadness and isolation can compound the physical side effects of chemotherapy, both during and after treatment **[238]**.

4.Hormone therapy

Hormone-sensitive breast cancers are treated with hormone therapy, or maybe particularly with hormone-blocking medication **[239].** These malignancies are referred to as estrogen receptor positive (ER positive) and progesterone receptor positive (PR positive) cancers by doctors

[240]. Certain types of breast cancer have been connected to hormones like progesterone and estrogen. Proteins called receptors are present in breast cancer cells, and they bind to progesterone and estrogen to help the cells grow **[241]**. Treatments that stop these hormones from attaching to these receptors are referred to as hormone or endocrine therapies **[242].** Not only in the breast, hormone therapy may target cancer cells almost anywhere in the body. For females with hormone receptor-positive cancers, it is recommended **[243].** For women whose malignancies are hormone receptor-negative—that is, they do not contain hormone receptors—it is ineffective **[244].**

Cost for treatment breast cancer in Bangladeshi hospital

Breast cancer surgery is exceedingly expensive, and most oncologists do not have enough time for counseling patients before surgery **[244].** This treatment and its cost are mostly determined by the number of sessions required for treatment in chemotherapy, with radiation included in the hospital fee **[245].** This sort of scenario is common when this session cannot function correctly. The most likely cause is a lack of professional people, as well as poor equipment and reagent quality **[246].**

Table-4 for Most of treatment for Breast cancer in Bangladesh **[247,248]**

Treatment name	Public Hospital (per session)	Public hospital Total cost	Private Hospital (per session)	Private Hospital Total coast
Breast surgery	BDT 60,000	BDT6,39,000 annually with medicine	Depend on hospital BDT 1,00,000 to 1,20,000	BDT 10,00,000 annually
Chemotherapy	BDT 20,000	Depend on cost per session and hospital charge. Minimum 5 session takes	BDT 35,000 Without medicine and hospital charge .IN hospital and medicine charge it's up to BDT 50,000	Depend on cost per session and hospital charge. Minimum 5 session takes
Radiotherapy	BDT 25,000	Depend on cost per session and hospital charge. Minimum 7 session takes	BDT 45,000 Without medicine and hospital Charge. In Hospital charge takes to BDT 65,000	Depend on cost per session and hospital charge. Minimum 7 session takes

Table -5 Diagnostic test price for breast cancer in Private hospitals of Bangladesh

No.	Diagnostic Name	Price in BDT
1.	Breast exam	800-1,000
2.	Mammogram	Double breast 2,000-2,500 Single breast 1,000-1,500
3.	Breast ultrasound	Double breast 3,500-4,500 Single breast 2,000-3,000
4.	Biopsy	14,000-16,000
5.	Breast MRI	Double breast 14,000-16,000 Single Breast 9,000-10,000
6.	Bone scan	1,000-5,000
7.	Breast cancer antigen test BCA-15	1,200-1,500
8.	Breast CT scan	6,000-8,000
9.	Positron Emission Tomography (PET)	50,000-55,000
10.	Complete blood count (CBC)	350-450
11.	Mammogram during treatment	1,000-3,000

Table-6 for diagnostic test for breast cancer treatment in Government hospital in Bangladesh

No.	Diagnostics Name	Price in BDT
1.	Breast exam	300-500
2.	Mammogram	Double breast 15,00-2,000 Single breast 1,000-1,200
3.	Breast ultrasound	Double breast 3,000-4,000 Single breast 1,500-2,500
4.	Biopsy	10,000
5.	Breast MRI	Double breast 12,000-15,000 Single breast 7,000-9,000
6.	Bone Scan	1,000-3,000
7.	Breast cancer antigen test BCA-15	400-500
8.	Breast CT scan	4,000-7,000
9.	Positron Emission Tomography (PET)	40,000-45,000
10.	Complete blood count (CBC)	350-450
11.	Mammogram during Treatment	500-1,000

CHAPTER-6 DRUG RESISTANCE IN CANCER

The preceding chapter discussed breast cancer diagnosis, treatment, and cost in Bangladesh. This breast cancer treatment might be highly expensive for certain patients **[249].** Chemotherapy, in particular, is exceedingly expensive, with several sessions required for treatment. As a result, several theories have been developed **[250].** One of the causes is cancer drug resistance. Drug resistance is quite frequent in cancer patients all across the world, including Bangladesh. This chapter discusses the mechanism of drug resistance in order to generate a specific drug **[251].**

Drug resistance in cancer means that chemotherapy drugs are no longer effective **[252]**. When cancer cells, even just a fraction of the cells inside a tumor, undergo genetic changes that make them resistant to a particular medication before treatment starts, resistance might arise **[253].** Because cancer cells within the same tumor usually demonstrate a variety of genetic changes, this so-called intrinsic resistance is prevalent. This applies to all types of cancer. It is a crucial challenge in cancer treatment, and it might be challenging to treat when metastasis occurs. **[254].**

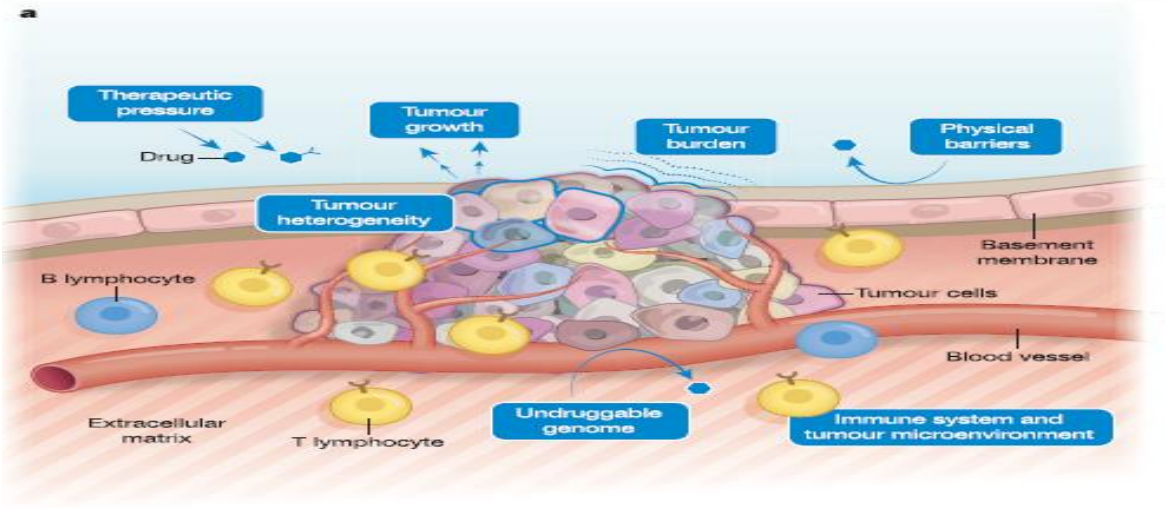

Figure 5- A conceptual model for drug resistance. The biological factors that contribute to medication resistance. Tumors are diverse and exist within an environment that includes the vascular, immune cells, basement membrane, and tumor microenvironment, among other elements. alterations to the tumor's physical characteristics, genetic makeup, and external surroundings **[253].**

Factor of Cancer Resistance to Drug

In today's world, cancer treatment options include radiotherapy, surgery, chemotherapy, targeted medication therapy, immunotherapy, and hormone therapy. However, in 90% of cases, these therapy strategies are not effective in patients. This is the crucial cause of medication resistance in cancer **[255].** Drug resistance in cancer cells is established in a different way **[256].** The major cause of cancer cell survival appears to be Darwinism's notion of natural selection **[257].** Cancer drug resistance factors include

1.Tumor heterogenicity

2.Tumor Microenvironment

3.Cancer stem cells

4.Inactivation of anticancer drug

5.Multi Drug resistance MDR

a) Increasing the release of drugs outside the cell

b) Reducing the absorption of the drugs

6. Inhibition of the cell death (apoptosis pathway blocking)

7. Changing the drug metabolism

8. Changing the chemotherapeutic agents' targets

9. Enhancing the DNA repair

10. Gene amplification

11. Epigenetic altering caused drug resistance

12. MicroRNA in cancer drug resistance **[256].**

13. Metabolism-associated drug inactivation

14. Increased drug efflux

15. Alterations of the drug targets and activation of compensatory pathways

16. Inhibition of cell death

17. Tumor plasticity **[258].**

Tumor Heterogenicity

Tumor heterogeneity refers to tumor growth and form changes that result in medication resistance **[259].** Tumor heterogeneity is a feature of cancer that poses a problem in the area of oncology **[260].** Tumor heterogeneity is the primary source of drug resistance, which results in therapy failure. Tumor heterogeneity either directly affects therapeutic targets or modulates the tumor microenvironment (TME) by producing phenotypic traits and transcriptome changes that

lead to treatment resistance **[261].** Throughout the course of tumor growth, tumor heterogeneity shifts both temporally and spatially, which leads to ongoing TME reprogramming. Thanks to developments in precision oncology platforms and genetic profiling technologies, it has become evident that tumor heterogeneity influences treatment resistance in the TME context **[262].** In this review, we primarily address the mechanisms by which tumor heterogeneity reprograms the TME, hence influencing treatment resistance and prognosis, and the processes by which genomic alterations generate tumor heterogeneity **[263].**

Tumor Microenvironment

TME refers to the environment around a tumor, which includes blood vessels, immune cells, fibroblasts, signaling molecules, and the extracellular matrix (ECM) **[264-267].** The tumor and its surrounding microenvironment are inextricably linked and continually interact **[268].** Tumors can impact the microenvironment by releasing extracellular signals, boosting tumor angiogenesis, and establishing peripheral immunological tolerance, whereas immune cells in the microenvironment can influence malignant cell proliferation and development **[264,269,270].** Oncogene activation causes cancer cells to proliferate and survive indefinitely **[271].** However, the tumor microenvironment must be supported in order for clinically significant tumors to emerge. Recent data suggests that the tumor microenvironment is a crucial controller of cancer immune evasion, progression, and distant metastasis **[272].** Furthermore, the tumor microenvironment is recognized to have a role in tumor acquired resistance to many therapies. Despite major breakthroughs in chemotherapy and radiation, treatment resistance results in decreased effectiveness **[273].**

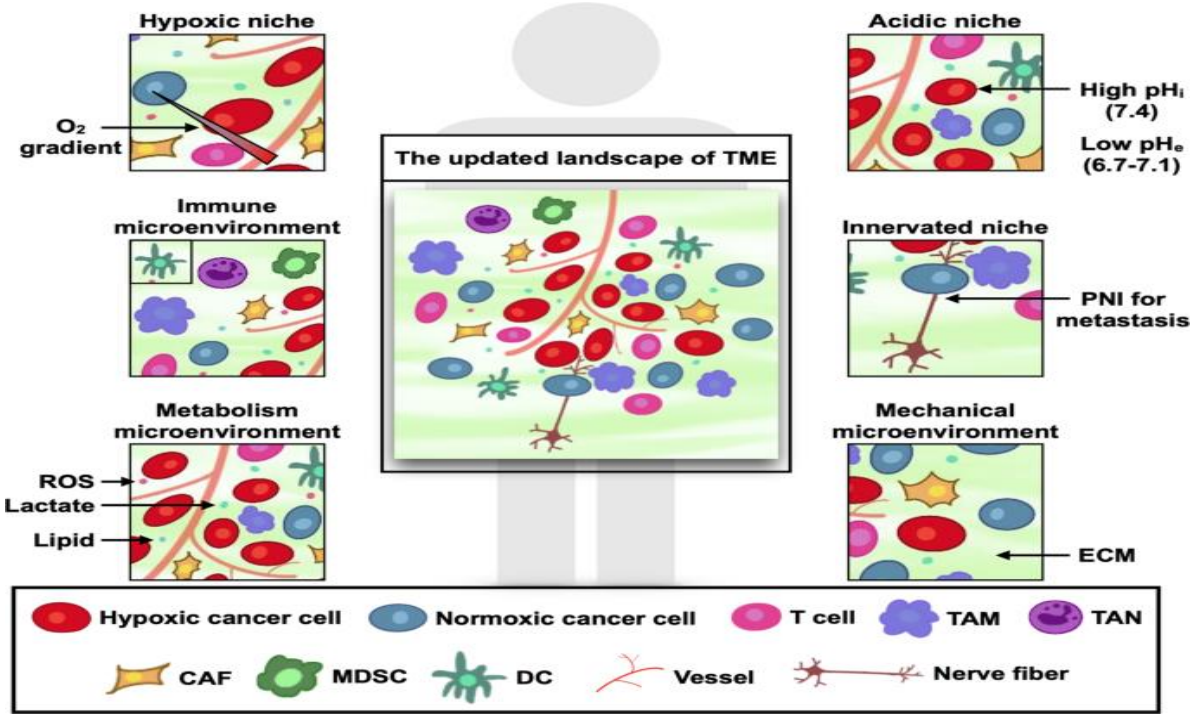

Figure-6 TME is made up of extracellular matrix, blood vessels, nerve fibers, stromal cells, cancer cells, and related acellular components. TME acts as a habitat for cancer cells and a link between the disease and the body as a whole. The six specialized microenvironments that make up TME are the acidity niche, the immunological microenvironment, the metabolic microenvironment, the hypoxic niche, the innervated niche, and the mechanical niche. **[274].**

Cancer stem cell

One type of tumor cell that can start tumors and cause relapses is called a cancer stem cell (CSC) **[275].** At the period of tumor formation, CSCs originate from either differentiated cells or adult tissue-resident stem cells **[276].** The ability of cancer stem cells (CSCs), sometimes referred to as tumor-initiating cells (TICs), to self-renew and specialize into a range of cancer cell lineages is assumed to be the cause of treatment resistance and cancer recurrence. Understanding the characteristics and processes by which CSCs display resistance to therapeutic medications is therefore essential **[277].** This renders a conscious choice to

emphasize the critical traits and mechanisms that regulate CSC activity in drug resistance in addition to current developments in treatment approaches that specifically target CSCs **[278].** This offers new understanding of the role of CSCs in drug resistance as well as improved therapeutic justifications for novel anticancer treatments **[279].**

Inactivation of anticancer Drug

Cancer cells may begin to produce proteins (or larger amounts of proteins) that might inactivate, block, or degrade anticancer medicines, lowering their efficacy **[280].** To prevent the medications from achieving their intended effects, the cells may shuttle them into distinct compartments inside the cell **[281].** Several processes determine the effectiveness and efficacy of anticancer medications. Medication interactions with various protein types (in vivo) can alter the molecular characteristics of drugs and ultimately cause them to become active. Cancer cells become less active when they become resistant to medications **[282].**

Multi Drug resistance MDR

MDR in cancer treatment has been defined as the capacity of cancer cells to survive against a wide spectrum of anti-cancer medications **[283].** An MDR mechanism might emerge as a result of increased drug release outside of the cells. Medication absorption is thus reduced in these cells **[284].**

a) Increasing the release of drugs outside the cell

The extracellular matrix and transporter conformational changes when a drug penetrates the cancer cell wall **[285].** ABC transporters release the medicine outside the cell. Following the

binding of the substance (drug), the phosphate group is freed, ATP hydrolysis releases energy that causes the ABC to change conformation, and the drug is released into the extracellular space **[286].** ATP binding cassette transporter is referred to as ABC transporter. While exporters move lipids, sterols, medications, and a variety of primary and secondary metabolites, ABC uptake porters transfer nutrients, vitamins, trace metals, and biosynthetic precursors. Many of these exporters are linked to inherited human illnesses such as cystic fibrosis, tumor resistance, and other conditions in humans. In both prokaryotic and eukaryotic species (including humans), high expression levels of genes encoding many of these exporters result in drug resistance to a range of medications, including antibiotics and anti-cancer therapies **[287].**

b) Reducing the absorption of the drugs

Anticancer agents can enter tumor cells by passive transfer (e.g., doxorubicin and vinblastine), enhance diffusion, or stimulate transport (e.g., nucleoside analogs) **[288].** On each other hand, only active transportation is involved in the absorption of drugs into cells when there is a significant concentration gradient [289]. Solute carrier SLC transporters, which transport minerals, vitamins, and other materials, make up the bulk of membrane transporters. There are two methods to decrease drug absorption: 1) by decreasing the likelihood that medications will bind, and/or 2) by lowering the quantity of transporters. Certain medications use specific transporters to enter cells. **[290].** Mutations in these transporters decrease the absorption of medications by impeding them. In individuals with acute lymphoblastic leukemia (ALL), a mutation in the human folate carrier (hRFC) gene is the primary cause of methotrexate resistance. The hRFC protein's first transmembrane domain contains a mutation at nucleotide

133 that changes the G point, which reduces the medicine's ability to bind the transporter **[291].** Lysine is replaced with glutamic acid in this region.

Inhibition of the cell death (apoptosis pathway blocking)

Instead of inhibiting the drug's action, certain cancer cells may switch off the cell-death mechanism (known as apoptosis), which is what kills the cell. Many medications function by causing harm to cells, forcing them to self-destruct. Cells cannot destroy themselves if the mechanisms that produce this cell death are switched off **[281**]. Necrosis, apoptosis, and autophagy are the three main processes that cause cell death **[292].** The biological characteristics of these processes vary from one another, though. Each of them has a role in cell death. Both external and internal processes can cause apoptosis **[293]**. Its external pathway involves ligands and cell death receptors such FAS, TNF-R, linker proteins, and caspases-3, -6, -7, and -8. Actin and nuclear Lamin protein proteolysis consequently takes place via an external pathway, eventually resulting in cell death **[294]**. Bcl2, AKT, Bax, Bak, and caspase-9 are anti-apoptotic proteins found in the mitochondrial internal pathway, whereas Bax, Bak, and caspase-9 are pre-apoptotic proteins. Increased treatment resistance is associated with up-regulation of anti-apoptotic genes (Bcl2, AKT, etc.) and down-regulation of pre-apoptotic genes (Bax, Bclxl, etc.) in tumor cells **[295]**. Moreover, drug resistance brought on by p53 gene alterations might harm DNA and induce death in stressed cells. These changes might lessen the correlation between apoptotic activation and DNA damage caused by chemotherapy medications **[296].**

Changing the drug metabolism

Cancer cells may alter their interactions with anticancer medications, making them less effective **[297]**. Some medications must be changed within the cell in order to be active and

have anticancer effects. The medications are useless without this cellular metabolism **[281].** Enzymes can participate in the metabolism of chemotherapeutic agents. The most crucial components in establishing agent concentration are enzymes and the inner and exterior walls of cells. Protecting healthy cells from dangerous substances is mostly dependent on agent reactions such phase I reactions, which include oxidation, reduction, and hydrolysis, and phase II reactions, which include consumption and conversion. There are two mechanisms in which these interactions enhance treatment resistance in cancer cells: 1) via increasing drug inactivation (increased activity of certain enzymes) and 2) by decreasing pro-drug activation (reduced activity of some enzymes). Cytochrome P450 detoxification is one of the most well-known examples of a phase I cell process [**298].** Enhancing cytochrome P450 activity has been associated with resistance to drugs in breast cancer; Additionally, increasing cytochrome P450 activity enabled docetaxel to turn inactive **[299].** On the other hand, lowering the activity of this enzyme has resulted in a better response to therapy. Phase II reaction (consumption phase) of the medication lowered its activity and abolished its electrophilic toxicity, converting it to glucuronic acid, sulfate, and glutathione **[300].** Resistance to several alkylating chemicals and platinum-based anticancer therapies like doxorubicin and cisplatin is largely dependent on glutathione transferases, which enhance glutathione production and detoxification **[301].**

Changing the chemotherapeutic agents' targets

Mutations in the target proteins of anticancer treatments can diminish their effectiveness by preventing them from binding as well to their target. The medicine will be less effective if the binding is not as strong **[302]**. Cells may completely stop expressing the target chemical. Hormone treatments, for example, target estrogen or progesterone receptors in breast cancer **[281].** Chemotherapeutic drugs' effects might have been influenced by alterations such as

perturbations in their targets' expression levels and mutations. These sorts of changes in agent targeting will eventually develop to medication resistance **[303].** For example, topoisomerase enzymes are crucial for relieving the compaction in the DNA structure during replication **[304].** Doxorubicin is an anthracycline fungal antibiotic that is primarily used to treat solid tumors (such as breast cancer and lung cancer). It can block Topoisomerase II. Cancer cells with topoisomerase II mutations change the function of the specified medication **[305].**

Enhancing the DNA repair

Many anticancer medications act by disrupting the genes of the cancer cell to the point where the cell kills itself. Cancer cells may make these medications less effective by improving their DNA repair systems **[281**]. DNA repair is a well-known mechanism of medication resistance in the cancer area **[306].** Chemotherapeutic medications in either the direct or indirect way damage cancer cells' DNA, but the damage may be repaired by certain processes. Drugs based on platinum as well like the metal-based chemotherapy damage DNA, which kills tumor cells **[307]**. DNA repair systems such homologous recombination repair mechanisms (RRM) and nucleotide excision repair (NER) mediate drug resistance in cancer cells. Because of this, the effectiveness of these medications depends on preventing cancer cells' DNA repair mechanisms **[308]**. Inhibiting DNA repair processes makes cancer cells more sensitive to these medicines, increasing the efficiency of chemotherapy **[309].** Mutations and epigenetic knockdown in these systems might make it possible to target defects in the DNA repair routes of malignant cells for medicinal reasons **[310].** Furthermore, elevated repairs to DNA and alkyl transferase activity contribute to susceptibility to the alkylating drug doxorubicin **[311].**

Gene amplification

Cancer cells compensate for the medication's effects by generating extra copies of (amplifying) the gene that produces the target protein of the anticancer agent **[281**]. Drug resistance is caused by gene amplification in 10% of malignancies, specially leukemias **[312]**. Methotrexate drug resistance is caused by increasing the number of target genes in various tumoral cells, including leukemia **[313].** Cancer cells produce treatment resistance by expressing numerous copies of the Dihydrofolate reductase gene (a potential methotrexate target enzyme) **[314].** Gene amplification raises the copy number of oncogenes per cell by hundreds of times. Finally, this pathway results in increased synthesis of associated oncoproteins **[315].** The sequences that are amplified in cancer cells during the latter stages of the disease can be identified through extra micro chromosomes that are referred to as homogeneously staining regions (HSR) or double chromosomes (DMs, double minute chromosome) **[316].**

Epigenetic altering caused drug resistance

One of the primary manifestations of drug resistance in cancer therapy is epigenetic modification **[317].** Histone modifications and DNA methylation are the two forms of epigenetic alterations **[318].** When methyltransferase methylates cytosine at the 5' carbon in CpG islands, a key epigenetic process known as DNA methylation occurs (upstream of promoters). On the other hand, methylation may happen at many locations across the genome **[319].** Specific lysine positions at the distal ends of histones and non-histone proteins are acetylated and deacetylated, respectively, by the enzymes histone acetyltransferases (HATs) and histone deacetylases (HDACs) **[320].** These enzymes modify the chemistry and structure of chromatins. Gene expression is dictated by both acetylation and deacetylation of the same unit, lysine, which opens the chromatin structure and triggers chromatin compaction and

stability **[321].** Tumor suppressor genes, for instance, are often silenced by methylation, but their expression is induced by oncogene hyper-methylation **[322].** A multi-drug-resistant phenotype is acquired and anti-tumor drug accumulation within cancer cells is reduced when the multi-drug resistance gene (MDR1) in cancer cell lines is demethylated. Premature myeloid cancer cells overexpress MDR1, while mature myeloid cancer cells downregulate MDR1 **[323].** The epigenetic process may potentially have a bearing on their DNA repair the mechanism **[324].**

MicroRNA in cancer drug resistance

RNAs having 22 nucleotides that are produced from RNA hairpin structures are known as microRNAs, or miRNAs. Because they are far too tiny to code for proteins, microRNAs play essential functions in the control of gene expression **[325].** Most protein-coding genes are under their control, including those linked to cancer and, in particular, the development of resistance to cancer treatments. There are three ways that the miRNA process might silence a gene: 1. splitting the mRNA strand into two parts; 2. destabilizing the mRNA by reducing the length of its poly(A) tail; and 3. translating the mRNA into proteins less efficiently through ribosome translation **[326].**

Metabolism-associated drug inactivation

Drug-metabolizing enzymes (DMEs) control the activation and deactivation stages of a number of chemotherapeutic medicines **[327].** One of the primary contributors of chemotherapy resistance in cancer is a malfunction in the control of DMEs and metabolic signaling systems. This may result in an unwillingness to transform meds into active compounds or drug detoxification **[328].** The triggering of enzymes that breakdown food is required with multiple anticancer medicines **[329].**

Increased drug efflux

Drug efflux, mostly caused by overexpression of ABC transporters, is the main factor resulting in both reduced drug absorption and insufficient intracellular drug concentration. Humans contain 49 members in the ABC transporter superfamily, which is further split into 7 subfamilies (ABCA-ABCG). These subfamilies function to transport a variety of substrates, including lipids, ions, peptides, and foreign substances **[330]**. When ABCB1, commonly referred to as Glycoprotein (Pgp) or Multidrug Resistance 1 (MDR1) protein, was discovered in mouse MDR cell lines in 1976, ABC transporters were first linked to MDR **[331].** As at currently, it was recently determined that at least 13 ABC transporters directly mediate resistance to chemo by anticancer drug efflux **[332]**. These ABC transporters are mostly located on the plasma membrane, and they become activated because they bind to substrate drugs. This conformational shift in the transporter is mediated by ATP hydrolysis, and the substrate drug is extruded **[333].**

Tumor plasticity

It is believed that cancer stem cells (CSCs), a few percent of cells with stem cell characteristics found inside tumors, are in charge of the genesis, growth, and spread of malignancies **[334,335].** These cells have been observed in a variety of cancers, including GBM, colon, and breast. Chemotherapy and radiation therapy may cause partial tumor eradication and subsequent tumor recurrence; however, CSCs are resistant to these treatments due to their capacity to activate DNA damage repair and antiapoptotic signaling pathways. The "CSC theory" was put out by the researchers in light of these discoveries, and they also found evidence of CSCs in a variety of cancer tissues **[336, 337].** The overexpression of MDR transporters, which promotes drug efflux, the tumor's more active DNA repair capacity, and its

propensity to form new microvascular routes are the main causes of CSCs' resistance to therapy **[338].** These characteristics enable CSCs to withstand treatment, provide the tumor with nutrients and oxygen, and quickly repopulate the tumor. Bladder CSCs actively contribute to the development of chemotherapy resistance after several cycles of chemotherapy, which may be explained by a similar procedure to normal tissue stem cells reacting to injury **[339,340].**

What an overcome drug resistance

Tumor resistance to treatment implies the observation because whereas the majority of cancer patients undergoing chemotherapy react at first, some individuals simply fail to react at all or gradually cease responding **[341].** Medication that tackles the resistance determinants can only be generated by comprehending the chemical and biological mechanisms of tumor cell resiliency to toxic drug-induced apoptosis **[342]**. In order to examine options for MDR prevention in human cancer, a model of the mechanism by which resistance develops when sensitive tumor cells are exposed to chemotherapeutic medicines must be established **[343].** Recently, an assortment of experimental techniques has been employed in order to create animals that are tolerant to drugs and to assess the success rate of small-molecule inhibitors in halting the appearance of multidrug resistance (MDR) in a range of malignancy types **[344].**

CHAPTER-7 DIRECTION IN FUTURE FOR CANCER TREATMENT

Different facts concerning cancer, risk factors, diagnosis, and treatment costs was discovered in the preceding chapter. One example of the high cost of cancer therapy is medication resistance in cancer cells **[345].** Sometimes identifying a specific risk factor of cancer cell cannot provide an appropriate remedy to this condition. Finally, the cancer diagnostic procedure is time-consuming and costly **[346,347].** This method discovers a very simple approach that can reduce diagnosis time and expense. In the near subsequent years, it may be a solution for patients to quickly beat cancer.

Different approaches for easy, low-cost, fast, and speedy cancer diagnostics will be developed in the near future. This is a list of therapies.

1) CRISPER
2) Artificial Intelligence
3) Telehealth
4) Cryo-EM
5) Infinium Assay
6) Robotic Surgery [**348]**.
7) Immunotherapy
8) Targeted drug therapy
9) Peptide Based drug design for Chemotherapy
10) Gene therapy

1.CRISPR

The official name of CRISPR is Clustered Regularly Interspaced Short Palindromic Repeats. Researchers were shocked to see how quickly and effortlessly they could modify the genetic code of living cells. Nowadays, specific DNA portions within cells may be precisely removed, inserted, or altered thanks to CRISPR, which functions similarly to a pair of scissors [349]. The discovery of this novel gene-editing method came about as a side project motivated by an interest in the ways that bacteria fight viruses. For their work related to CRISPR research, Drs. Jennifer Doudna and Emmanuelle Charpentier were granted the 2020 Nobel Prize in Medicine [350]. The first CRISPR-made cancer immunotherapy clinical study started in the United States a year ago, and further research is being done on CRISPR-made cancer medicines **[351].** Moreover, CRISPR is already being tested directly in the body in trials **[352].** Despite its significant advancements, CRISPR has drawbacks, and the morality of gene editing is still up for dispute. However, one thing is certain: CRISPR is an effective technique with the potential to greatly expand studies on cancer and other diseases **[348].**

How CRISPR works

These microbes grab snippets of the invader's DNA and store it as CRISPRs, or clustered regularly interspersed short palindromic repeats, in order to safeguard themselves against predators like viruses **[353].** The DNA segments, which have been fully turned into RNA, enable the Cas enzyme find and cut the DNA of the invader in the event that the same germ strikes again **[354].** Scientists believed this defense mechanism may be a versatile tool for gene editing once they found it **[355].** Numerous organizations effectively altered almost any DNA region in a few of years, initially in microbe cells and then in human cells **[356].** The two primary components of the CRISPR weapon in the lab are a DNA-cutting enzyme, commonly

Cas9, and a guide RNA. Scientists produce guide RNA with the intention of mimicking the DNA of the gene that is to be changed, also known as the target **[358].** Working along with Cas, the guide RNA guides Cas to the target, as the name implies. When the target gene's DNA matches the instructions in the RNA, Cas cuts the DNA **[359].**

2. Artificial Intelligence

The field of precision medicine drug research, and cancer diagnosis have all benefited from the use of computer coding. Guiding a machine to act, think, and learn is known as artificial intelligence **[360]**. It has been particularly helpful in scientific research because of its unparalleled capacity to identify patterns in tremendous quantities of data. The development of digital twins for cancer patients is being advanced by the National Cancer Institute, the Department of Energy, the Frederick National Laboratory for Cancer Research, and a multidisciplinary group of researchers. Others use it to analyze imaging data and electronic health records and tailor chemotherapy for patients. **[361].** Artificial intelligence is even being used to swiftly evaluate population-based cancer statistics and forecast the probability of specific malignancies. And these are only a few of examples of how AI might really enhance cancer treatment **[362].** A computer technique for assessing prostate MRI images was created by NCI intramural investigators and their collaborators **[363].** Routine prostate biopsies haven't always generated the most credible findings in the past. Fifteen years ago, NCI clinicians began utilizing MRI data to guide biopsies, and this enabled them to concentrate on the areas of the prostate deemed most likely to be cancerous in nature. MRI-guided biopsy enhanced diagnosis and treatment when performed by professionals in prostate cancer; however, the technique did not translate well to clinics with a lack of knowledge of prostate cancer **[364].** AI was used by the NCI doctors to capture their diagnostic expertise, and the algorithm was then made available to clinics nationwide as a tool for clinical decision-making and diagnosis **[365].** Thanks to this AI tool, clinics without expertise in prostate cancer are able to fully utilize the

potential of the MRI-guided biopsy developed by NCI researchers. Nowadays, research is concentrated on developing new AI systems that use MRI to predict patient outcomes in an attempt to rival skilled radiologists **[366].**

3. Telehealth

Clinical research and cancer therapy are crucial even in pandemic situations. Telehealth techniques have been effectively applied or extended by several healthcare facilities participating in the NCI Community Oncology Research Program (NCORP) to provide cancer treatment and care to patients remotely **[367].** These hospitals and clinics throughout the nation are maximizing safety and convenience for patients and physicians by utilizing telehealth for in-home chemotherapy, video visits, and remote health monitoring **[368].** Furthermore, telehealth renders cancer care and trials obtainable to a larger geographic range of patients. Someone could have participated in about one-third of virtual health visits and used telehealth services outside of cancer care last year **[369].** Remote care is not fitting for all forms of care, despite its growing popularity. While there are challenges in ensuring egalitarian use of remote health care technologies, scholars are working to find solutions **[370].**

4. Cryo-EM

One type of electron microscopy is cryo-electron microscopy, or cryo-EM **[371].** At previously unheard-of resolutions, cryo-EM imaging produces images of molecules 10 thousandths the width of a human hair. Similar to how individuals choose from a variety of candid images before posting the "good" ones on social media, researchers comb through hundreds of thousands of cryo-EM photos to assess their quality. From there, they reconstruct 3-D models of molecules, enabling scientists to study how they behave. This means learning more about

how cancer cells expand, divide, and engage with therapeutic agents and other cells **[372].** The most detailed view of a human ribosome to date was obtained at the Frederick National Laboratory for Cancer Research using cryo-electron microscopy (Cryo-EM). This achievement could guide the development of cancer and other disease treatments **[373].** The Cryo-EM was used to show how a drug for chronic myeloid leukemia interacts with ribosomes, a molecular machine inside cells.

6. Infinium Assay

Implemented by companies like 23andMe and Ancestry, the Illumina Infinium Assay is a method and suite of instruments that assess millions of single nucleotide polymorphisms, or SNPs, the most common type of genetic variation **[374].** SNPs can provide information on cancer risk, progression, and development in addition to helping map the genes responsible for the disease. The test was created with funds from the National Cancer Institute's Small Business Innovation Research program, and it is a potent example of taxpayer-funded innovation despite early concerns about whether this procedure was technically feasible **[375].** The test has been implemented in numerous other contexts, which includes as cancer research, ancestry reports, the National Institutes of Health's All of Us Research Program, and even genome analysis of plants to figure out factors that affect drought and insect resistance **[376].**

7. Robotic Surgery

Robotic surgery renders it feasible to recuperate and return to normal life more quickly. For instance, a prostatectomy—the removal of the prostate gland—might be necessary for someone with prostate cancer. However, because to robotic arms that enter the body through tiny incisions, procedures that formerly needed a large incision from the midline to the pubic bone

may now be completed **[377].** Using a specially designed console, an orthopedic surgeon may control the arms while displaying a mushroomed, real-time image of the surgery site. Robotic surgery results in less pain and blood loss, and in the event of a prostatectomy, a patient may be freed as early as the next day **[378]**. Despite the fact that the robotic arms look like stuff from a science fiction movie, their precise, delicate movement can make all the difference in situations where millimeters could represent the difference between removing all malignant cells and perhaps injuring healthy tissue **[379].**

7.Immunotherapy

A cancer treatment labeled immunotherapy leverages the immune system of the victim to battle the illness. Immunotherapy has the capability to boost or modify the immune system's capacity to recognize and fight cancerous cells **[380].**

How Immunotherapy Is Used to Treat Cancer

Immunotherapy is an illness treatment which utilizes certain immune system components to treat ailments like cancer. There are many ways to do this **[381]:**

boosting or stimulating the immune system's natural defenses to make it more capable of identifying and combating cancer cells **[382]**. Synthesizing immune system-like chemicals in the lab and using them to enhance or restore the ability of the immune system to recognize and combat cancer cells **[383].** In recent decades, immunotherapy has become an essential element in the treatment of multiple kinds of cancer. Both fresh methods to managing the immune system and novel immunotherapy medicines are being investigated and approved at a

breakneck pace. Certain tumors respond better to immunotherapy than others. For certain cancers, it is utilized in isolation; however, for other tumors, it seems to work better in combination with other treatments **[384].**

What the immune system does

The organs, certain cells, and substances that make up the immune system aid in the defense against infections and other illnesses. The body is defended against disease-causing germs by immune cells and the substances they generate, which travel throughout the body [385]. In a number of other ways, they also help prevent cancer [386]. The body's immune system keeps an eye on every substance. The immune system becomes alert to any novel chemical it recognizes and launches an attack on it. For instance, substances like certain proteins that are absent from the human body are accounted for in germs [387]. The immune system attacks them because it recognizes them as "foreign". Anything that includes foreign material, such germs or cancer cells, can be eliminated by the immune response [388].

On the other side, it is more difficult for the immune system to target cancer cells. This is due to the simple reason that cancer starts when healthy, normal cells encounter mutation or alteration and begin to grow unsupervised. The immune system may not always detect cancer cells as alien as they stem from normal cells [389].

Given that many individuals with healthy immune systems develop cancer, it is evident that the immune system's capacity to combat cancer on its own is limited:

1. Since cancer cells can sometimes be confused for normal cells, the immune system may fail to identify them as alien.

2. From time to time, the immune system finds cancer cells, but the response is not strong enough to eliminate the cancer.

3. Chemicals released by cancer cells can also evade the immune system's ability to recognize and eliminate them.

4. In order to combat this, scientists have developed methods to help the immune system identify cancer cells and fortify its response, enabling it to eradicate them. In this sense, the body may eradicate cancer on its own with the help of science **[390-398].**

Types of cancer immunotherapy

Numerous immunotherapies are used to treat cancer, and more are being studied right now. Depending on the kind of cancer, there may be further information about immunotherapy as a treatment [399].

1. Checkpoint inhibitors: By removing the immune system's "brakes," these medications help the body identify and attack cancer cells.

2. CAR T-cell therapy: In this treatment, T-cells from the patient's blood are combined with a specific virus that teaches the T-cells how to adhere to tumor cells. The patient then receives their own cells back, enabling them to locate, adhere to, and eradicate the cancer.

3. Cytokines: This treatment uses cytokines, which are tiny proteins that carry information between cells, to direct immune cells toward malignancies.

4.Immunomodulators: This class of medications enhances components of the immune system in order to treat some forms of cancer.

5. Vaccines against cancer: Vaccines are substances that are injected into the body to stimulate the immune system against specific diseases. Typically, we think of them as something that healthy individuals take to help them stay healthy. On the other hand, certain vaccines can help prevent or cure cancer.

6. Monoclonal antibodies: Man-made versions of immune system proteins are known as MoAbs or mAbs. mAbs can be particularly helpful in the treatment of cancer because they can be designed to target a very specific area of a cancer cell.

7. Oncolytic viruses: In this treatment, tumor cells are infected and killed by viruses that have been altered in a lab **[400–406].**

Monoclonal Antibodies and Their Side Effects

Among the ways that the immune system of the body fights off foreign substances is by creating a large number of antibodies **[407].** A protein called an antibody binds to another protein called an antigen. Until they identify and attach to the antigen, autoantibodies travel throughout the body. Once linked, they are granted the capacity to force other immune system components to eliminate cells that carry antigens **[408].**

Antibodies directed against a particular antigen, such the one seen in cancer cells, can be produced by researchers. The antibody may then be replicated in a laboratory. These are known as monoclonal antibodies (mAbs or Moabs) **[409].**

Monoclonal antibodies have applications in the medical management of several ailments, including particular kinds of cancer **[410].** The target antigen must be discovered before researchers can generate a monoclonal antibody. It's not always straightforward to pinpoint the

proper antigens for cancer cells, and it's been established those certain cancers response better to mAbs than others **[411].**

Because they hunt for, latch to, and attack a particular target on a cancer cell, certain monoclonal antibodies employed in cancer treatment are known as targeted treatments **[412].** Nonetheless, some monoclonal antibodies function similarly to immunotherapy by enhancing immune system response, which enables the body to identify and combat cancer cells more effectively **[413].**

Targeted drug therapy

Medication is used in "targeted therapy," a type of cancer treatment, to "target" cancer cells while sparing healthy cells **[414].**

Genetic modifications that set cancer cells apart from healthy cells are typically present in cancer cells **[415].** A cell's instructions are contained in its genes, which are sections of its DNA. A cell stops acting normally when its genes are changed. For example, cancer cells may have transformed genes that promote fast cell growth and division. A cancer cell is identified by these types of mutations **[416].** All cancer cells are not produced equally equal, and there exist several types of cancer **[417].** In one case, distinct genetic changes facilitate the growth and/or dissemination of breast and colon cancer cells **[418].** One person's particular form of colon cancer may differ from another's due to distinct gene mutations in cancer cells, even in those with the same critical kind of cancer (e.g., colon cancer) **[419].**

Additionally, studies have shown that certain kinds of tumors may not always begin, initiate, and thrive under the same circumstances **[420].** Specialized proteins or enzymes, for instance, provide instructions to the cancer cell in some types of cancer, telling it to proliferate and divide

[421]. Because of these facts, drugs that "target" certain proteins or enzymes and stop them from delivering signals have been developed. Targeted drugs that inhibit or turn off signals that drive cancer cells to grow can signal the cells to self-destruct **[422].**

Intense therapy is a crucial type of cancer treatment, and as scientists learn more about specific changes in cancer cells, they will develop more targeted drugs. But these drugs are only widely prescribed to treat a small number of cancer types **[423].** Most patients receiving targeted therapy must additionally undergo hormone therapy, radiation therapy, chemotherapy, or surgery **[424].**

How is targeted therapy different from chemotherapy?

Like other cancer therapies, targeted therapy drugs are officially categorized as chemotherapy. However, the way that normal chemotherapy (chemo) medicines work is different from how targeted treatment pharmaceuticals work **[425].** Medications that target specific characteristics between cancerous and healthy cells aim to address some of these discrepancies. They differ from chemotherapy in two ways because of this:

These medications primarily target cancer cells while sparing normal, healthy cells due to their targeted action **[426].** Conventional chemotherapy can damage and destroy cancer cells in addition to normal, healthy cells since it is cytotoxic to the majority of cells **[427].**

A frequent manner in which that targeted therapies perform is by stopping cancer cells from growing **[428].** It suggests that they may be able to help stop the growth and division or cancer cells. The traditional chemotherapy, on the other hand, affects pre-existing cancer cells **[429].**

How targeted therapy works

Targeted therapies aim to identify and target certain molecules or sites within cancer cells, or they detect and block specific instructions that are given inside a cancer cell and direct its growth. The following are some of the compounds that are present in cancer cells and that are "targets" for targeted therapy:

1.Excess of a certain protein on a cancer cell

2.A protein found on cancer cells but not on normal cells

3.A protein on a cancer cell that has been mutated (altered) in some way.

4.Gene (DNA) modifications that do not occur in normal cells. **[430,431,432]**

The action of targeted drugs can work to:

1.Block or disable chemical signals that instruct cancer cells to grow and divide.

2.Modify proteins within cancer cells to cause cell death

3.Stop forming new blood arteries to feed cancer cells

4.Activate your immune system to destroy cancer cells

5. Poisons should only be supplied to cancerous cells in order to sterilize those that are normal.

The activity underlying medications might have an impact on how they operate and the adverse reactions they cause **[434–438].**

It is important to bear in mind that some targeted treatment drugs, such monoclonal antibodies, are known to suppress cancer cells in several ways and can also be referred to as immunotherapy since they boost resilience **[439].**

Targeted therapy as precision medicine

Targeted implementation. is also referred to as tailored medicine or precision medicine **[440].** This is because they are made to specifically target particular mutations or molecules in cancer cells, and even people with the same type of cancer may have distinct objectives **[441].** Some tumor types are screened for specific targets after surgery or biopsy, which can help pinpoint the best course of action. A more precise or customized therapeutic matching can be achieved by identifying a specific target **[442].** More people are "targeted" by certain targeted treatments than by others. Targeted treatment originates in two distinct forms: small and large molecule drugs **[443].** Once they stumble upon cancer cells, tiny molecule drugs are able to penetrate them owing to their small size. They work by pinpointing and blocking a specific molecule in the cell **[444].**

Usually, tremendous molecular drugs are too big to fit within a cell. Their mode of operation involves attacking molecules or enzymes on the cell surface, accompanied by their weakening or removal **[445].** They are commonly referred to as a "lock and key" because the molecule performs like a key to unlock the enzyme or protein on the cell's surface. The prescription medicines works because the key fits beneath the lock **[446].**

Types of targeted therapy

Numerous malignancies can be treated with targeted therapies, and there are several kinds of targeted medications. These are a few instances of types and their applications.**[447].**

Angiogenesis inhibitors are medications that stop new blood vessels from growing, starving cancer cells. Bevacizumab is one example (many cancers). **[448].**

Monoclonal antibodies: These might transport empty molecules or molecules loaded with drugs into or onto cancer cells to kill them. Examples include alemtuzumab (for some chronic leukemias), cetuximab (for specific colorectal, lung, head, and neck cancers), and trastuzumab (for certain breast cancers) **[449].** NOTE: Because some monoclonal antibodies seek out, bind to, and attack a particular target on a cancer cell, they are sometimes referred to as targeted treatments. Nonetheless, some monoclonal antibodies function similarly to immunotherapy by enhancing immune system response, which enables the body to identify and attack cancer cells more effectively **[450].**

Proteasome inhibitors: These disrupt regular cell functions, leading to the disintegration of cancer cells. One example is bortezomib (multiple myeloma) **[451].**

Inhibitors of signal transduction: These sabotage cell communication, changing the actions of cancerous cells. One example is imatinib (in the states of certain chronic leukemias) **[452].**

9.Peptide Based drug design for Chemotherapy

One essential component of cancer therapy is the targeted delivery of chemotherapeutic medicines to cancer cells, which increases treatment efficacy while minimizing damage to healthy tissue **[453].** Because they have anticancer properties, bioactive peptides have become more and more well-known. The application of peptide-based cancer therapeutic approaches offers several advantages, such as enhanced specificity, less toxicity to healthy tissues, and versatility in addressing various biochemical pathways linked to the development of cancer **[454].** In cases of advanced cancer, peptide-based vaccines have been utilized to improve

patients' overall prognosis. Additionally, by enhancing medication transport and sensitivity, the combination of peptides with nanomaterials increases the therapeutic potential of peptides to cure cancer **[455].** Treatments for several disorders, including cancer, are being investigated for peptides at a rapid pace **[456].** Target specificity and low toxicity are two advantages of therapeutic peptides **[457].** The anticancer properties of a peptide may result from the peptide binding its intended target directly, or the peptide may be linked to a radionuclide or chemotherapy drug and used to drive the agent toward cancer cells **[458].** Peptides can be designed to directly permeate the cell membrane or they can be targeted at proteins on the cell surface, where the peptide-protein interaction can result in complex internalization **[459].** Peptides can disrupt cell signaling pathways, cell cycle regulation, necrosis resulting from membrane rupture, apoptosis, immune modulation, inhibit tumor angiogenesis, disrupt cell death pathways, and DNA repair pathways, among other mechanisms that can lead to cell death **[460].** Peptides that are offer a number of benefits when used as therapeutics, but they also have the drawback of being quickly broken down by proteases once given and, depending on how they are administered, occasionally having difficulties entering the bloodstream **[461].** Many peptide changes with excellent stability and efficiency will be created in the future. The list of different peptides [**462]** alterations is shown below.

Peptide modification

In recent decades, there have been significant advancements made in the efficiency and selectivity of therapeutic peptide delivery **[463-466].** The bioavailability and stability of therapeutic peptides have increased due to the development of various formulation and delivery methods, including co-administration of enzyme inhibitors, absorption enhancers, direct chemical modifications, prodrug approaches, and the use of special drug delivery systems

[467–469]. Linear peptide becomes cyclic peptide, and L-peptide becomes d-peptide. Peptide and nanoparticle (peptide-loaded nanoparticle), Peptide and other polymer nanofibrils or micelle **[470].**

Treating Cancer with Cell-Targeting Peptide (CTP) and Cell-Permeable Peptide (CPP)

By directly attaching to their target or conjugating with medications and using the peptide for targeted cargo delivery, peptides can have a therapeutic impact **[471,472].** Cell-targeting peptides (CTP) and cell-permeable peptides (CPP) are the two types of therapeutic peptides. When conjugates are supplied to a particular cell type, CTPs attach to a molecular identifier on the targeted cell, protecting other cells from the often-damaging consequences of the therapeutic payload **[473].** The peptide-therapeutic combination can be internalized as a result of the CTP attaching to its molecular target or acting at the cell membrane. Rather than interacting with molecular markers on the cell surface, CPPs connect with charged components on the cell membrane, which are then internalized through a variety of methods **[474].** Leveraging the fact that the outer membranes of cancer cells are negatively charged in contrast to normal cells, CPPs for anticancer therapy enable a positively charged peptide to concentrate on cancer cells **[475,476,477].** Cell aiming peptides and cell penetrating peptides are the two categories into which delivery peptides fit **[478].**

Possible Mechanisms of Therapeutic Peptides

Anticancer processes including membrane rupture, apoptosis, reduction of tumor angiogenesis, immunological modulation, and blockage of certain internal targets are among the therapeutic peptides **[479,480].** The formation of channels or holes in the cell membrane is one of the many

peptides' modes of action. In addition to causing peptide internalization, the holes have the potential to tear membranes, which can result in cell death **[481]**. Experimental evaluation is necessary to determine the impact of a particular peptide in this regard, as the phenomenon remains incompletely understood. The mechanics involved have been explained by a variety of models, which have been published and debated in a number of papers **[482,483],** including the barrel-stave model, carpet model, and toroidal pore model. These theories, in general, describe how the phospholipid bilayer and the amphipathic nature of the peptides cooperate to produce channels inside the cell membrane **[484, 485].** The peptide can then enter the hydrophobic core of the membrane, where membrane disruption causes the peptide to internalize itself or, in the case of dysregulated osmotic pressure, causes cell rupture and death **[486]**. Membrane disruption can cause cell death independent of growth rate and multidrug resistance mechanisms, which often impede traditional chemotherapy approaches. Additionally, the peptide's cationic residues can facilitate the peptide's preferred targeting to the comparatively anionic cancer cell membrane. Peptides have the ability to change the potential of the mitochondrial membrane as well as the cell membrane, which can cause cytochrome c to be released, caspases to be activated, and apoptosis to be induced **[487,488,489].**

10.Gene therapy

When compared to chemotherapy, which can cause non-specific harm and occasionally lack selectivity, gene therapy, which involves replacing a damaged gene with a functional, healthy copy of the same gene, is a potentially beneficial cancer treatment method **[490].** There are still several obstacles to clinical success, such as non-specific expression, low-efficiency delivery, and biosafety, despite enormous pre-clinical breakthroughs in tumor-selective targeting and

expression **[491].** In order to rebuild vectors/transgenes and make them safer and more effective, a number of innovative genetic approaches are being developed. With the use of innovative delivery techniques, gene expression may now be customized to be unique to a certain tissue or organ **[492].** With these developments in mind, gene therapy is predicted to become an ordinary cancer treatment option and could eventually become the first-line treatment for neoplastic diseases **[493].**

Strategies in Gene therapy

In the past few decades, technological and scientific advances coupled with intriguing clinical data have pushed cancer to one of the primary disease targets for gene therapy, even if the biology and clinical trial objectives in monogenetic sickness are well defined **[494].** Gene therapy is currently being used to target cancer in a number of intriguing ways, such as: (a) communicating a gene to increase tumor sensitivity to radiation or traditional drug therapy, or trigger apoptosis; (b) inserting a wild type tumor suppressor gene to compensate for its loss or dysregulation; (c) using an antisense (RNA/DNA) approach to block the expression of an oncogene; and (d) enhancing tumor immunogenicity to stimulate immune cell reactivity **[495–500].**

Challenges in gene therapy

Gene therapy has to be well understood in order to create strategies to overcome the obstacles in the way of therapeutic intervention and achieve its ultimate goal of long-term therapeutic benefit or, preferably, cure **[501].** Optimal transgenic expression for blocking a cancer-associated gene or delivering a cancer-therapeutic gene to diseased tissue at appropriate doses is a critical barrier to successful cancer gene therapy **[502].** Finding a therapeutic gene or genes that can prevent the onset of sickness will also have an impact on success **[503].** To address

these barriers to successful gene therapy, several techniques, which are outlined in the next sections, are being employed **[504].**

A different way of gene delivery

1.Gene delivery by viruses

2. Immune reactions to vectors: Overcoming Immune Barriers

3. Targeted Transduction: Lowering the possibility of non-specific delivery.

4. Expression of tumor-specific genes by transcriptional targeting **[505-507]**

Success of gene therapy

Fundamental and essential developments in molecular biology and genetic engineering Over the previous two decades have created potential for creating numerous gene treatments; yet, the great majority of cancers are not treated using these techniques **[508].** However, a few of achievements that resulted in long-term survival give hope that this strategy can still deliver in the future **[509].** We will quickly explain a few gene therapy strategies that have effectively made the migration from lab to bedside **[510].**

CHAPTER-8 DISCUSSION

A significant cause of death internationally is cancer. There is no good therapy, no early diagnosis, and no good drug to control this in the modern world. Most cancers pose a hazard when they migrate to other parts of the body, making treatment more difficult. Cancer is derived from the term neoplasia and it seeks to live at any cost. It is similar to Darwinism theory of natural selection in that it seeks to survive, and in order to do so, it consumes an excessive amount of nutrients from the host. If the host dies, cancer has no impact. For this reason, it is very challenging to control it. In present world it cannot control in reason of its not discovered well how it survive, how can its long time stay, how it's can arise from host, how it can spread out all over the body in host. When this all questions are clearly understandable it will control properly. In review try to discuss Top cancer of body in world and how many people are affected with definite factors. In particular, we will review breast cancer risk factors and global treatment options. Different risk variables are responsible, and these risk factors are particularly relevant in the daily lives of women. In daily life style such as eating too much foods that can increase BMI of women and it is one of the significant risk factors of breast cancer, taking tobacco, alcohol can be effected, breast feeding can be prevent breast cancer that's been found from review but modern world for effecting women's life style have less interest in breast feeding that's why its increasing, on the other hand daily uses of television, smartphone, internet highly exposed to radiation, Exposure to X-RAY has been connected to an increase in breast cancer, particularly in mutations of the breast cancer tumor suppressor gene BRAC1/2. All of these variables are linked to changes in the modern world's lifestyle. Breast cancer can be treated genetically in some situations. In conclusion, we will talk about the risk factor

evaluation from a developing nation. It is apparent that assessments in developing countries lack sufficient data to quantify clearly in any risk factor, and there is no major effort in wet lab to find factors connected to mutations that are directly associated to breast cancer. Despite search data from many sites, it is difficult to state anything certain, but one thing is certain: they have always worked in diverse socioeconomic families of women. This data is compared to women from affluent and low socioeconomic backgrounds. It is shown that women from impoverished families have less awareness of healthy living and are more susceptible to cancer on the other hand, wealthy women have a dilemma in that they have a high BMI and breastfeed less frequently, which causes them to be overly affected by breast cancer. In comparison to wealthy and poor nations, menopausal women in affluent countries are more likely to be infected with breast cancer than women in poor ones. It should be noted that during menopause in wealthy countries, women receive an excessive amount of hormone replacement treatment since estrogens multiply to ER and PR receptors. Then, in overview, discuss the therapy and diagnosis of breast cancer in Bangladesh. Bangladesh lacks adequate breast cancer treatment facilities. The incidence rate of breast cancer in Bangladesh was around 22.5 per 100,000 females. Breast cancer has been observed to have the greatest prevalence rate (19.3 per 100,000) among Bangladeshi women aged 15 to 44 **[511].** It is Bangladeshi women's first serious cancer. There are around 400-450 specialized oncologists in Bangladesh. As a result, a substantial number of people do not have access to adequate care. Breast cancer treatment in Bangladesh costs between BDT 10,00,000 and BDT 15,00,000 in a private hospital and BDT 5,00,000 to 6,00,000 in a public hospital, including surgery, chemotherapy, and radiation. Because this treatment is never successful in Bangladesh, a large number of women seek treatment elsewhere. Different approaches to cancer therapy may be developed in the future. Targeted medication therapy, immunotherapy, gene therapy, and CRISPR cas9 may become

more efficient in the near future, reducing costs in cancer treatment. Chemotherapy is particularly effective when peptide-based medication modification is used. Cancer medication resistance will be addressed with a different approach or treatment plan that uses a high-efficiency agent.

This research can complete the goals that's are to find specific on risk factor for breast cancer, cost treatment in Bangladesh and discuss about that particular reason to high treatment cost in cancer treatment this are drug resistance of cancer cell.

Future limitation to treatment in breast cancer and Bangladesh

In breast cancer treatment have a lot of limitation in future treatment in Bangladesh. In future of world have a probable chance to cure breast cancer, but Bangladesh cannot improve on this. In future targeted drug therapy with vaccination is more improved, but this facility cannot improve in Bangladesh. In reason of lack of budgets in improved drug in cancer, insufficiency of enough expertise on drug development, sometimes have a problem in sample collection in cancer patient for research purpose, ethical issue ,lack of interest in research of cancer drug design .On the other hand one problem is find to expert oncologist in critical condition of cancer that gives proper suggestion to improve treatment .This reason Bangladesh cannot get improvement in cancer treatment that developed country to thinking.

CHAPTER-9 CONCLUSION

An illness in which aberrant cells divide without control and have the ability to infect neighboring tissues **[8].** Cancer cells can potentially move to other regions of the body via the circulatory and lymphatic systems. Cancer is the second leading cause of mortality in the United States **[11].** Cancer is a hereditary illness caused by a mutation in the DNA. Most harmful mutations are either produced by mutagen exposure or occur naturally as part of aging. Some cancers are characterized by epigenetic alterations such as localized increases in DNA methylation and changes in histone modifications. These epigenetic modifications may regulate functions like as growth, survival, and aging. Heritable genetic alterations in cancer cells are passed down to daughter cells during cell division. As a result, individuals that have these mutations are vulnerable to Darwinian selection (survival of the fittest, possibly the most significant scientific principle in Biology). Cells with survival mutations alter to benefit from nutrients in another cell. Darwinian selection continues to affect cancer evolution, and it has gotten more aggressive. As a result, the host is malnourished. Cancer is commonly referred to as "NEOPLASIA" **[10].** The term neoplastic refers to new growth. Cancer biology, on the other hand, refers to uncontrolled cell growth and division. Neoplasia is frequently associated with tumors. A mass of tissue that occurs when cells divide or gore more than they should or do not die **[8].**

Epidemiology is a discipline of medicine that studies the occurrence, distribution, and potential control of illness and other health-related factors. Cancer epidemiology is the study of variables impacting cancer in order to determine likely patterns and causes **[24].** Cancer is most likely caused by a lack of knowledge, tobacco use, alcohol and drug use, and many types of air

pollution. Cancer is caused by a continual mutation in DNA caused by a mutagen, while the DNA repair system is unable to function **[15].** Early cancer detection might be improved by developing cancer markers that can be detected using serum **[16],** Sweat, plasma, urine, stool, and other bodily fluids. Cancer can be avoided by the study of cancer immunology, which identifies the specific antibody of cancer cell antigen. Finally, everything is dependent on public understanding of good eating habits and pollution control**.[27]**

Breast cancer is the world's second most frequent cancer and the most prevalent cancer among women. Every woman in the United States has a 12.4% lifetime risk of having breast cancer, or one in every eight women.18 Breast cancer was responsible for 1.67 million new cases globally in 2012, accounting for 25% of all malignancies **[39].** Gender, Age, Blood Group, Reproductive Factors, Age of Menarche, Age of Menopause, Full Term Pregnancy, Abortion, Full Term Pregnancy, ovulatory menstrual cycle, pregnancy characteristics, Hormonal factors, contraceptive methods, ovulation stimulating drugs, post-menopausal drugs, post-menopausal hormonal therapy, genetic factors, family history, lactation, obesity, overweight, smoking, alcohol consumption **[45].**

In breast cancer going to four different stages. Stage o to stage 4 **[56].**

In present time treatment and diagnosis of breast cancer

Biopsies, screening, cancer antigen tests, and mammograms are now used to diagnose breast cancer. Breast surgery, radiation, chemotherapy, and hormone therapy are all common therapies.

Critical condition of breast cancer

Breast cancer is dangerous when it spreads to other organs such as the ovaries, lung, liver, colon, and blood. Chemotherapy is essential at this time; however, it is not working as effectively in this state.

Probable successful treatment in near future

Cancer treatment utilizing CRISPR case 9 in the near future will include targeted drug therapy, immunotherapy, gene therapy, and peptide drug therapy. In the near future, several procedures and approaches for therapy are being developed, and some are in the trial phase **[348].**

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Appendix-A

Figure-1

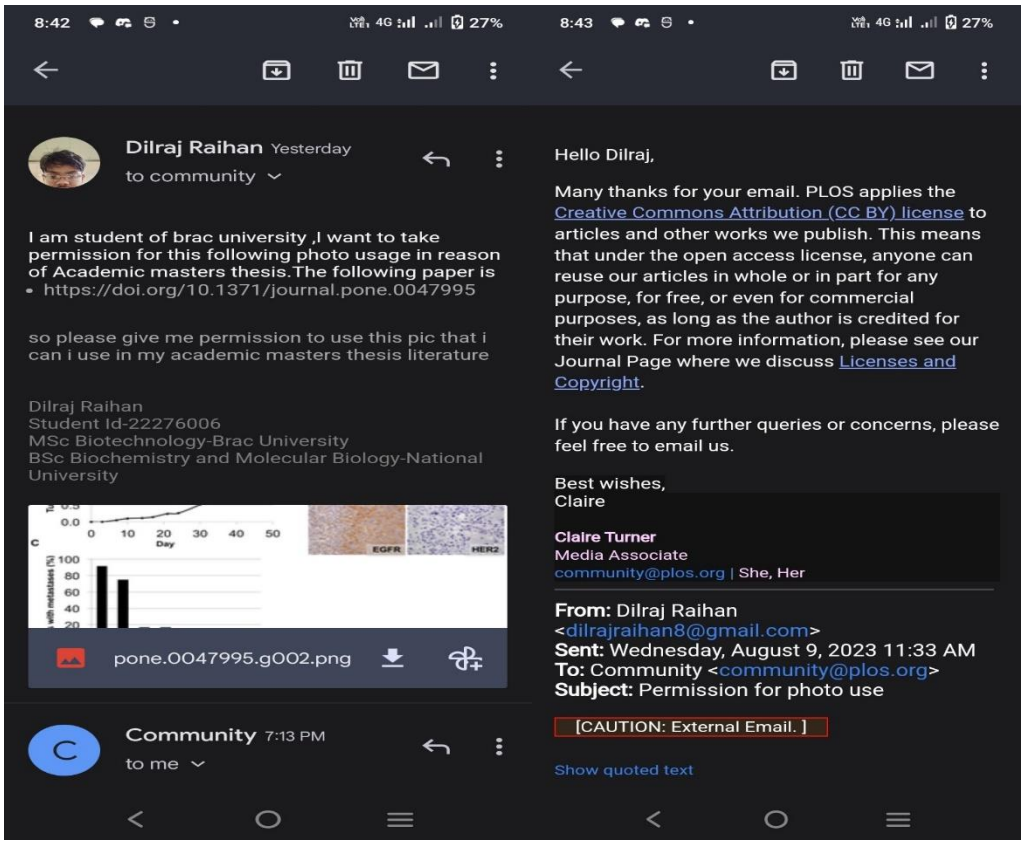

Figure-1 Figure 1 Fibromatosis of the left posterior neck. (a) Coronal (lesion depicted by arrows) and (b) axial STIR MRI shows an infiltrative lesion in the

region of the left brachial plexus. The axial image shows tumour infiltration into the C7 neural exit foramen (arrow).

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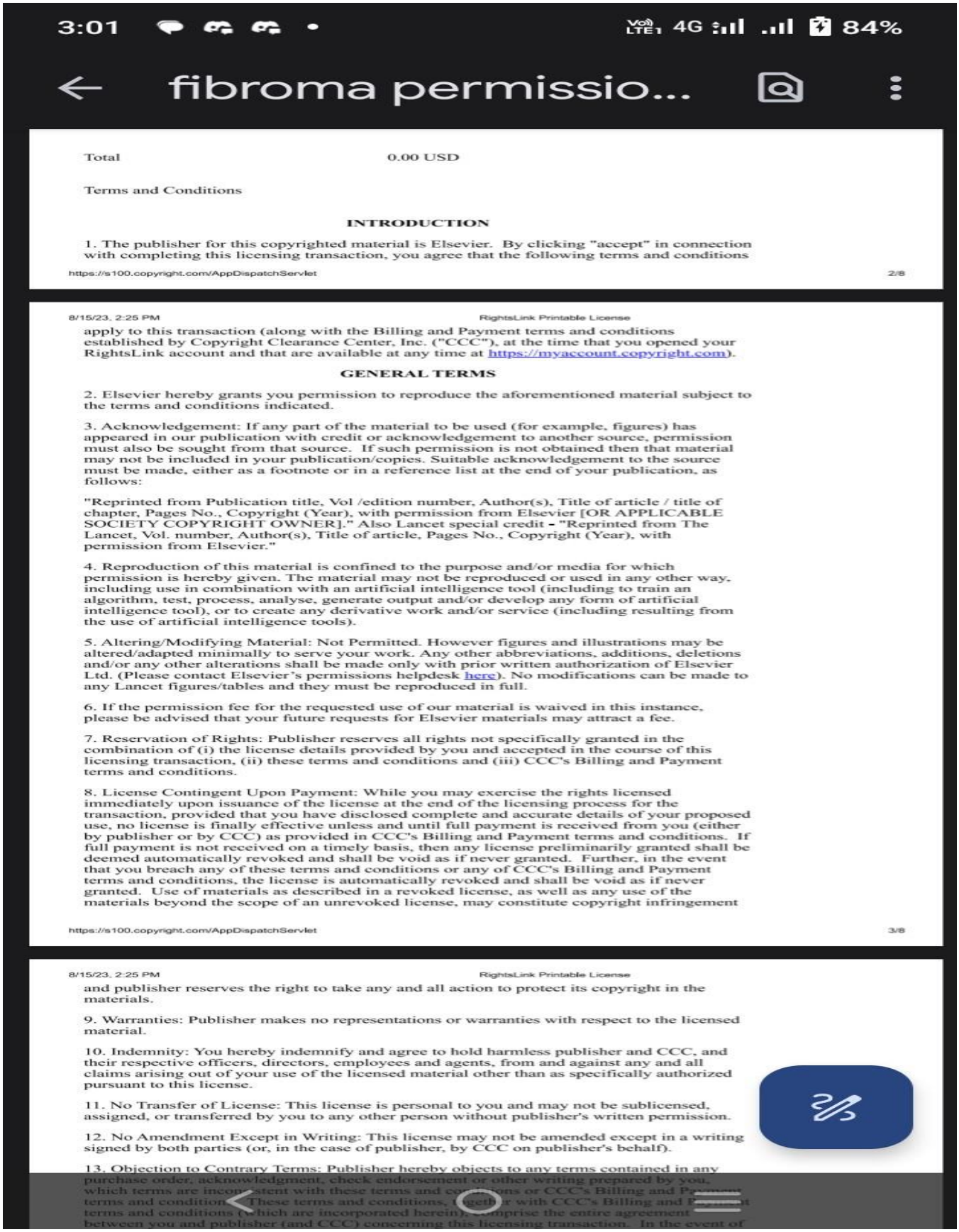
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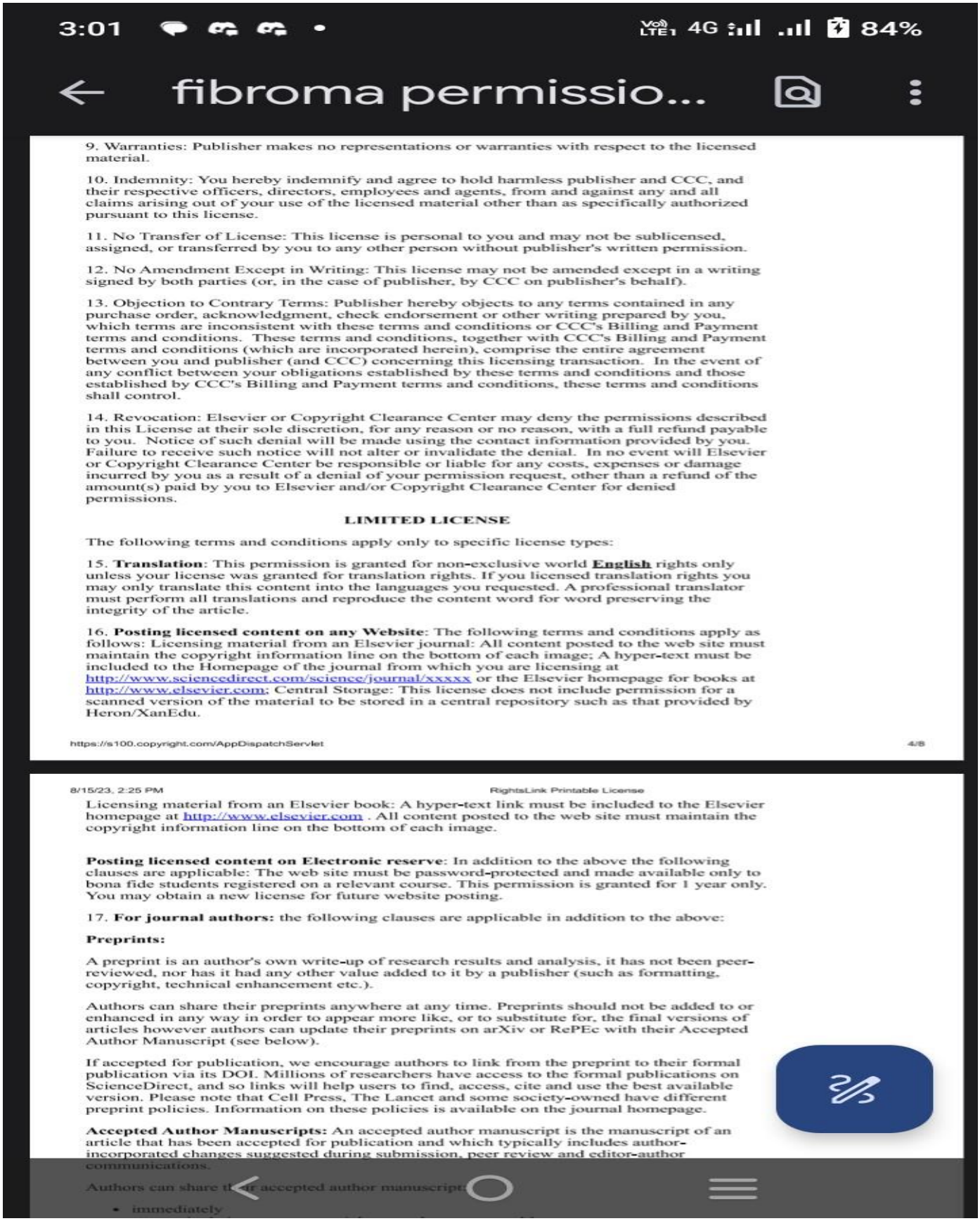
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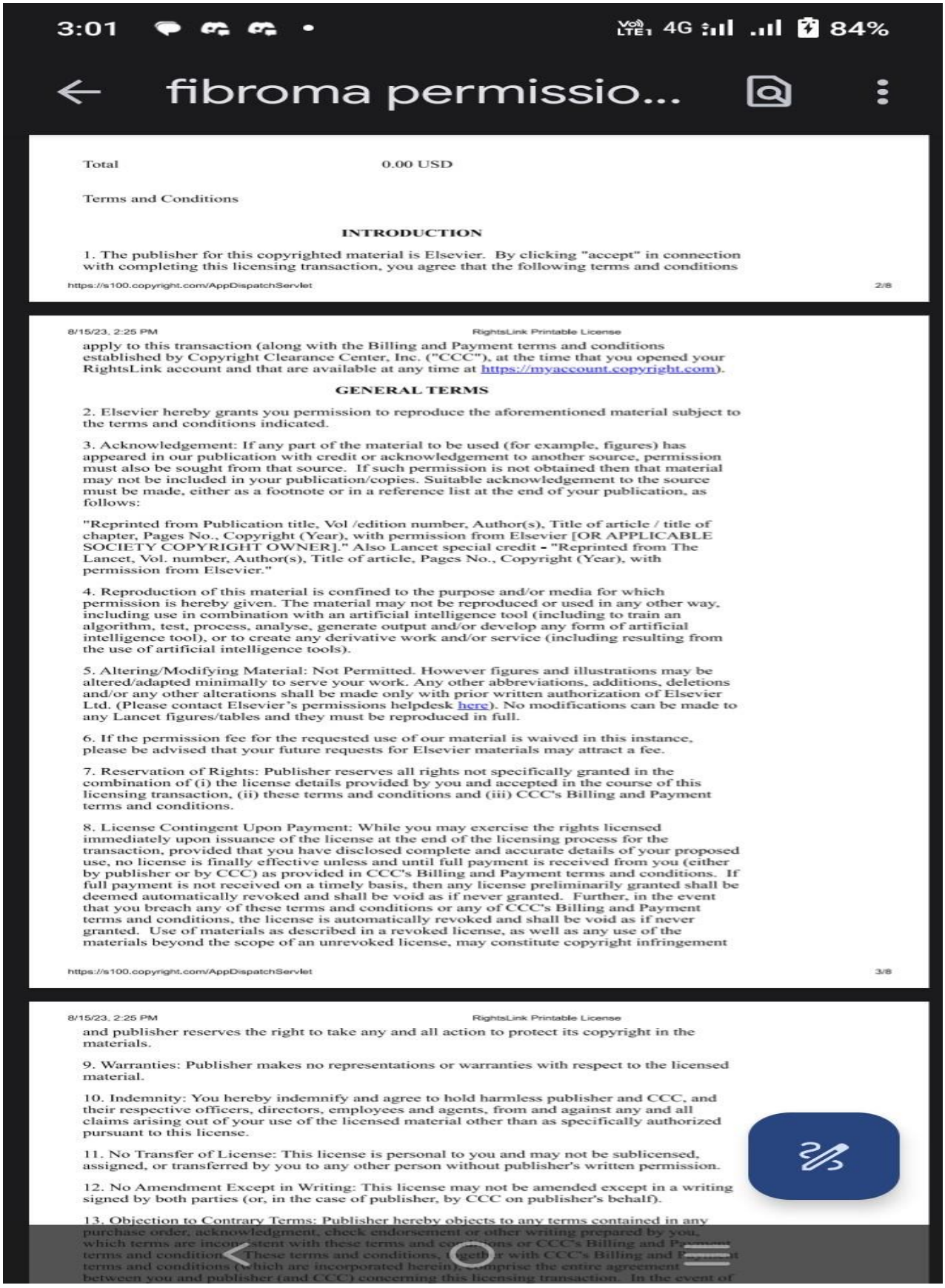
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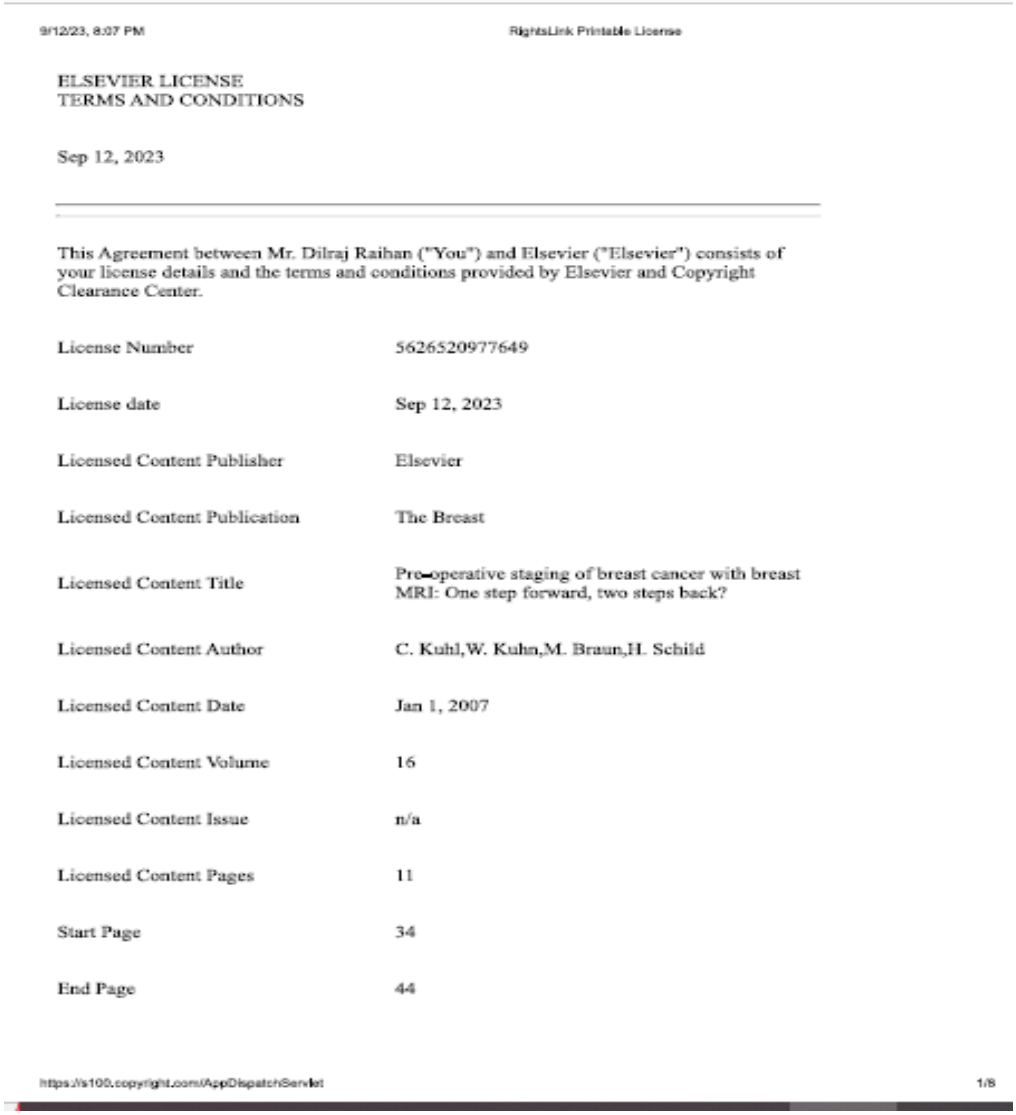

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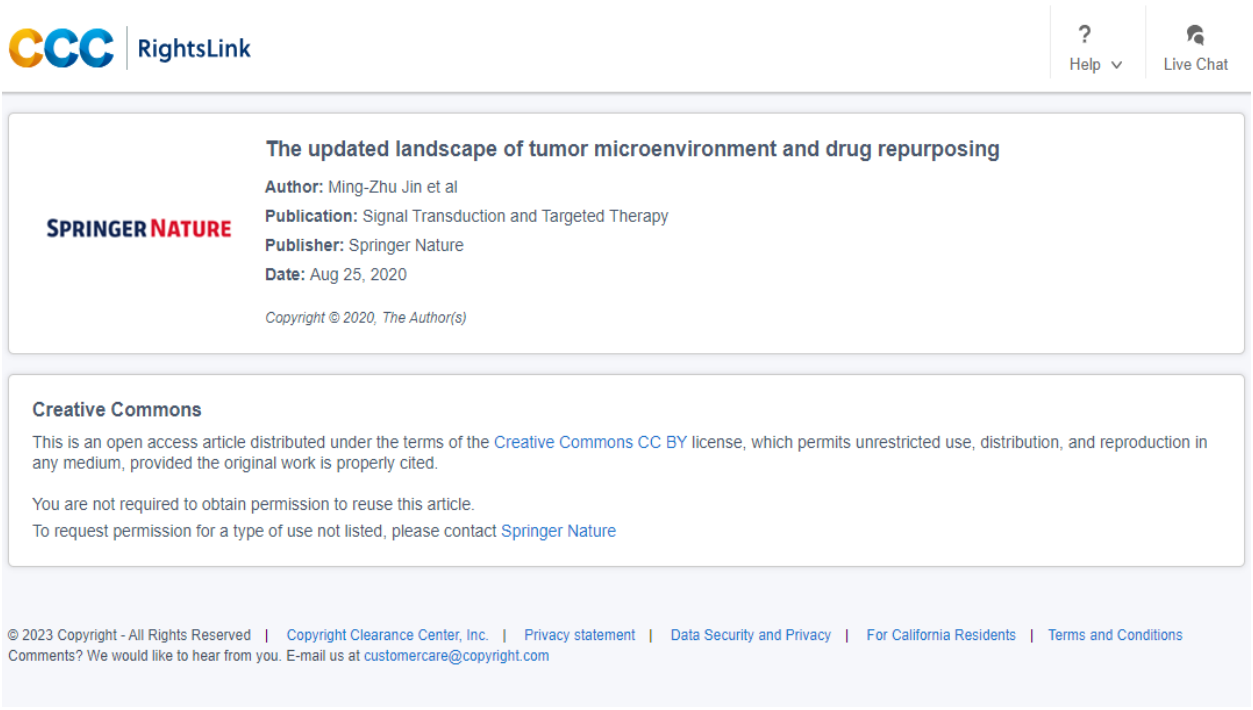

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