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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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BREAST CANCER AND DIAGNOSTIC METHODS: UNDERSTANDING THE ROLE OF BRCA1 AND BRCA2

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Abstract.

Breast cancer is a disease that has a 1 in 8 lifetime risk for women, making it an international burden. Although breast cancer mostly affects women, men have a lifetime risk of around 1 in 1000. The majority of breast cancer instances continue linked to breast cancers that have acquired somatic mutations during a person's lifespan. The mutations that are in the situation do not cluster in families and are not inherited. The particular genetic variables involved in hereditary breast cancer will define a cancer risk due to genetics. Despite fact, Cadherin-1(CDH1), Phosphatase and TENsin (PTEN), Partner and Localizer of BRCA2 (PALB2), serine/threonine kinase 11 (STK11), Checkpoint kinase 2 (CHEK2), and tumor protein 53 (TP53) genes have mutations, a BReast CAncer gene 1 (BRCA1) and BReast CAncer gene 2 (BRCA2) genes, documented to inherit significantly increase a chance of developing BRCA. Recognizing the functional importance of genetic mutations has created avenues to prevent breast cancer and is revealing promising therapeutic approaches.

Key words. Breast cancer, women, diagnostic methods, BRCA1, BRCA2.

Introduction.

In 2020, 2.3 million in 2020, 2.3 million women worldwide will be diagnosed with breast cancer, predicts the World Health Organization (WHO). With 32% of all malignancies in the Egyptian population, the most prevalent cancer among women is breast cancer. By 2050, it is expected to triple in prevalence. Patients with Breast Cancer are now far more likely to survive by recent medical advancements, especially for those with early diagnosis [1]. However, without a thorough comprehension of underlying mechanisms and etiology, the efficacy of prevention and therapy will continue to be constrained. For example, one of the types of cancer is breast cancer that affects breast tissue, cancer in women is the most common kind worldwide the world and may also affect males, but it does so considerably less frequently [2]. Breast cancer can start in some locations in the breast, including lobules that create milk, ducts that deliver milk to the nipple, and other breast tissue. Although there are many distinct varieties of invasive ductal carcinoma is a kind of breast cancer that begins in milk ducts before spreading to adjacent tissue, is the most typical variety. Other varieties are intrusive lobular cancer, injurious breast cancer, and Paget's disorder of the breast. A frequent form of cancer that affects women all around the world is breast cancer. According to estimates, One out of every eight women will get cancer of their breasts at some point in their lives. When aberrant breast cancer happens when breast cells proliferate uncontrollably and create a tumor. Although the exact causes of breast cancer are not yet established, it is known that some genetic alterations enhance the likelihood of getting an illness [3].

Most common BRCA1 and BRCA2 changes include well-known genes related to breast cancer. Breast cancer genetic testing's importance is a subject of ongoing study that is evolving quickly. Increased surveillance and early deployment of risk-reduction measures are made possible by the identification of germline mutations in high-risk people. 2,4 The paper's objective is to evaluate how genetic testing affects breast cancer, especially to advise general surgeons on the uses, implications, and costs of such testing. The clinical environment for breast cancer genetic testing is evolving [4]. The use of genetic testing is fast growing as a result of efficacy with BRCA mutations in certain medications, such as PARP inhibitors. Beyond its typical use genetic evaluation now affects treatment for both terminal and adjuvant diseases in identifying BRCA carriers for secondary prevention circumstances, 1-3 The recent discoveries imply are breast cancer patients' genomic testing is essential for the best possible care [5]. The genes BRCA1 and BRCA2 both works to prevent cancer typically by limiting the development of malignant cells in breast tissue. But if the genes are changed or mutated, they can no longer function normally, which could lead to breast cancer. Women inherited a much more likely breast cancer mutant BRCA1 or BRCA2 genes, and other diseases including ovarian cancer. Mammography, ultrasound, MRI, and biopsy are just a few of the diagnostic techniques used to find breast cancer. A low-dose X-ray technique is mammography to find breast tissue anomalies [6].

While MRI creates precise images of breast tissue using strong magnets and radio waves, ultrasound employs to create images of breast cells, high-frequency frequencies are used. A breast biopsy includes taking a sample of breast tissue and analyzing and examining it under a microscope to look for cancer cells. Breast cancer can only be diagnosed with certainty by biopsy. A biopsy involves taking a tiny sample of breast tissue to check for the presence of cancer cells through a microscope. Surgical, core-needle, and fine-needle aspiration biopsies are only a few of the several types available. Depending on the size and location of the suspicious spot, a particular type of biopsy may be performed [7]. In conclusion, knowing how BRCA1 and BRCA2 genes affect breast cancer might assist in determining

the most at risk for the condition. Early identification by screening and biopsy can greatly increase the likelihood of effective therapy and positive results. People with doctors about genetic testing in the event that breast cancer runs in their family and best-recommended screening procedures [8].

That not everyone occurrences of breast cancer are brought on by BRCA1 or BRCA2 gene mutations is disadvantage about using only BRCA1 and BRCA2 testing as diagnosis. Breast cancer development may also be influenced by other genetic abnormalities, environmental variables, and way of life choices. For this reason, it's crucial to correctly identify breast cancer using a variety of diagnostic techniques, such as genetic testing, clinical examinations, and imaging studies. BRCA1 and BRCA2 Assessing can be costly, but hardly all patients' insurance may covers it. This is another disadvantage. In addition, genetic testing can be stressful and upsetting for patients and their families, especially if a mutation is found [9]. The paper [10] detected breast cancer and before surgery, many women were given an option of undergoing Rapid Genetic Testing (RGT) a gene associated with cancer susceptibility. To ascertain RGT for BRCA1 and BRCA2 recipients were diagnosed with breast cancer have psychosocial effects. The paper [11] examined a group of individuals has a greater chance of getting breast cancer assess frequency also mutational spectrum of BRCA1 and BRCA2. There was no need that 1267 patients to be referred for BRCA genetic testing to meet a requirements of mutation probability approaches for molecular screening.

The paper [12] improved genomic stability was played by tumor-suppressor genes BRCA1 and BRCA2 collaborate with DNA repair mechanisms. Developing ovarian and breast cancer was by DNA repair errors brought BRCA1 and BRCA2 missense mutations. Accurate variant identification becomes therapeutically significant since it can help with early discovery and individualized patient care. The paper [13] assisted in nature of carcinogenesis, genetic and molecular pathologies involved in multistep cancer growth, and their interactions with endocrine and environmental variables. Pathologists may be able to better manage breast cancer patients' follow-up care if they are aware of distinctive morphologic and molecular characteristics linked to genetically altered breast cancer. The paper [14] developed that breast cancer is significantly influenced by inherited BRCA mutations (BRCAm). To compare an outcomes of breast cancer in BRCAwt (BRCAwt) and BRCAm (BRCAm) carriers, intended to determine a function of BRCAm testing in afflicted patients. The paper [15] suggested of germline mutations in breast cancer susceptibility genes BRCA1, BRCA2, TP53, CHEK2, PTEN, ATM, and PPM1D cause hereditary breast cancer. There are high- and low-penetrance forms of certain BC susceptibility genes groups based on their interactions with several other genes and environmental factors. The paper [16] discussed recent developments in genetics-based precision treatment for breast cancer, it might be utilized to enhance a capacity to accurately detect and treat breast cancer in each patient. The paper [17] provided a revised loci map for breast cancer susceptibility Single Nucleotide Polymorphisms (SNP) and gene levels, as well as a discussion of cutting-edge techniques for analyzing Genome-wide association studies (GWAS) data used to heredity of cancer. The paper [18] assessed a KIAA0101 gene's expression, diagnostic value, and prognostic/survival utility in BC. The paper [19] evaluated a malignancy of breast cancer using a straightforward layer-based deep-learning technique. That an ANN-based machine learning strategy may achieve over 97% accuracy. The paper [20] assessed the frequency and range of germline BRCA1/2 Copy Number Variations (CNVs) and Single Nucleotide Variations (SNV/indel) in Tanzanian cancer patients, and relationships between patient's sociodemographic and histological features, and discovered variations.

BRCA1.

As proven in Figure 1, the BRCA2 gene's frame of open reading is 10.3 kb, which produces a nuclear protein that is 384 kDa is larger than that of the BRCA1 gene. The produced protein is made of areas with undefinable domain and lacks parts with strong sequences similarity to other recognized genes, as proven in Figure 2. There are 22 exons in the BRCA1 gene,

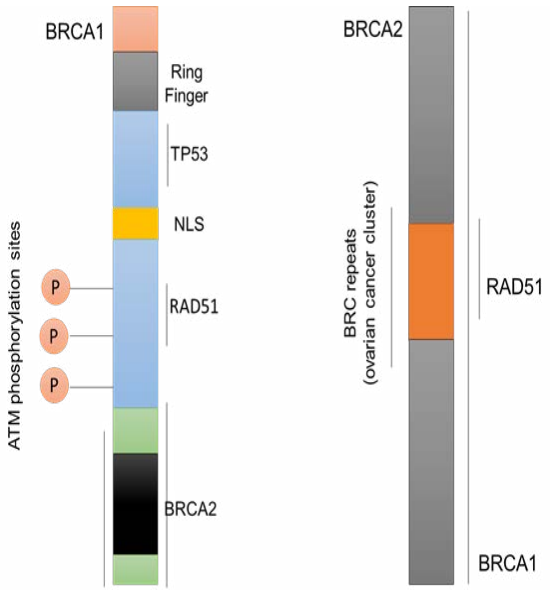

Figure 1. *Diagram showing the BRCA1 and BRCA2 genes.*

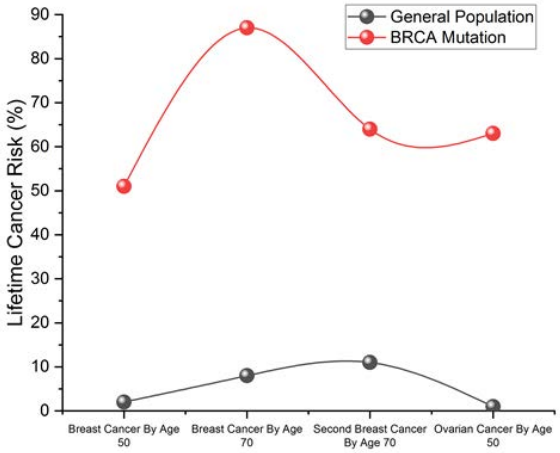

Figure 2. *Lifetime cancer risk for BRCA2.*

which encode a nuclear protein this is 1863 amino acids lengthy and has a mass of 220 kDa. The BRCA1 protein consists of a conserved acidic tail and a zinc-coordinating RING domain. The breast and ovarian cells are two of the many tissues that express the BRCA1 gene. Mutations in the BRCA1 gene can result in various genetic changes, including stop codon insertions, base pair substitutions, missense mutations, deletions, and regulatory mutations.

Precise data on cancers risks: Detailed data at carriers of BRCA1 mutations' lifetime risk of developing breast and ovarian cancer, in comparison to the general population.

Survival rates: The 5-year survival rate of those with BRCA1 mutations in cancer of the breast, as well as a comparison to those without the mutation.

Prostate cancer risk: Clarified the slightly higher prostate cancer risk for men with BRCA1 mutations and mentioned the ongoing investigation into survival rates.

Prognostic implications: Included the impact of PARP inhibitors and other targeted treatments on prognosis and survival, offering an update on the clinical significance of BRCA1 mutations.

There are several tissues that express a BRCA1 gene, including breast and ovarian tissue. The original changes to the BRCA1 gene included a stop codon insertion, a single base pair replacement, a missense substitution, a deletion of 11 bases, and an inferred regulatory mutation. Eighty individuals had a BRCA1 mutation, according to subsequent research from high-risk families, 372 unrelated individuals with breast or ovarian cancer were included. A comprehensive screening of BRCA1 gene revealed 63 alterations, and 38 frequent variants were discovered. Eight, seven, or five times for each of these different changes, and as predicted, 86% of these led to a shortened BRCA1 protein. At this time, more than 1600 BRCA1 gene variations are known, and the bulk of these cause frameshifts that lead to missense or dysfunctional protein. BRCA1 is thought to be a tumor suppressor gene because, in most cases, people with germline BRCA1 mutations have somatic mutations of wild-type alleles. Prostate cancer risk is marginally increased for males with BRCA1 mutations than for women.

Regarding prostate cancer, males with BRCA1 mutations have a slightly higher chance of developing prostate cancer in comparison to the general male population. Studies have shown that men with BRCA1 mutations have a lifetime prostate cancer risk of approximately 20-30%, which is higher than the overall male population risk of around 10-12%. However, the exact survival costs for prostate cancers in BRCA1 mutation carriers are still under investigation. BRCA1 mutations contribute significantly to cancer risk, however, with improvements in genetic screening, personalized treatment, and preventive care, the prognosis for mutation carriers has enhanced. Targeted treatments like PARP inhibitors are providing promising outcomes in improving survival and reducing recurrence in BRCA1-relevant cancers, mainly breast and ovarian cancers.

BRCA2.

The BRCA1 and BRCA2 genes appear to encode proteins with functional similarity, which helps to explain why changes to these genetic factors in a comparable and distinct inherited tendency to ovarian and breast cancer. Early research showed six different germline mutations in families with breast cancer were linked to BRCA2, usually via disrupting of transcriptional unit 17's open reading frame. These mutations involved frameshifts and/or deletions that resulted in premature stop codons, which were associated with the termination of protein translation. A total of more than 1800 alterations, including frameshift BRCA2 have been shown to have deletions, insertions, and nonsense mutations that result in premature protein termination. These occurrences are in line with a predicted dysfunction after changes in cancer suppressor genes. Additionally, carriers of BRCA mutations are more vulnerable to numerous cancers, which encompass ovarian and breast cancer, as shown in Table 1. It illustrates the increased lifetime cancer risks for BRCA mutation carriers as compared to the general population, particularly for ovarian and breast cancer.

Table 1. *Lifetime cancer risk for BRCA2.*

Lifetime Cancer Risk (%)		
	General Population	**Mutation in BRCA**
BRCA by Age 50	2	51
BRCA by Age 70	8	87
Second BRCA by Age 70	11	64
Ovarian Cancer by Age 50	1	63

Role of BRCA in tumorigenesis.

Although around 5-10% of breast cancer cases are hereditary, new estimates suggest that approximately 45% of recipients of BRCA2 mutations and 55–65% of carriers of BRCA1 mutations will have developed breast carcinoma when they are 70 years old. Additionally, BRCA1 or BRCA2 mutation-positive females a demonstrated to have 10-year risks of ovarian cancer of respectively 12.7% and 6.8%. Twenty-four percent of families with a suspected deleterious BRCA mutation (21,401 in total) were found to possess a BRCA1 or BRCA2 change. The tumor-suppressor genes BRCA1 and BRCA2 are held responsible for breast cancer, which are functionally recessive and cannot arise until both copies of alleles are altered in a cell, as shown in Figure 3.

BRCA genes can undergo minor recombination events that are missed by standard screening methods because of a high density of repetitive elements that enable genomic rearrangements mediated by alu. Both BRCA1 and BRCA2 genes are vulnerable to these recombination processes. For instance, high-risk families with BRCA1 and BRCA2 genetic test findings that are negative (wild type) were discovered to have 22 distinct genomic rearrangements with sizes ranging from 1 kb to more than 170 kb. According to, germline BRCA mutations are likely to go undiagnosed. The genetic changes in BRCA1 and BRCA2 genes that can take place have been summarized in several reviews. A homology modulator is BRCA2, while a pleiotropic response to DNA damages protein known as BRCA1 participates in checkpoint activation and DNA repair. Every involvement of BRCA1 in carcinogenesis is connected to some biological processes, including transcriptional control

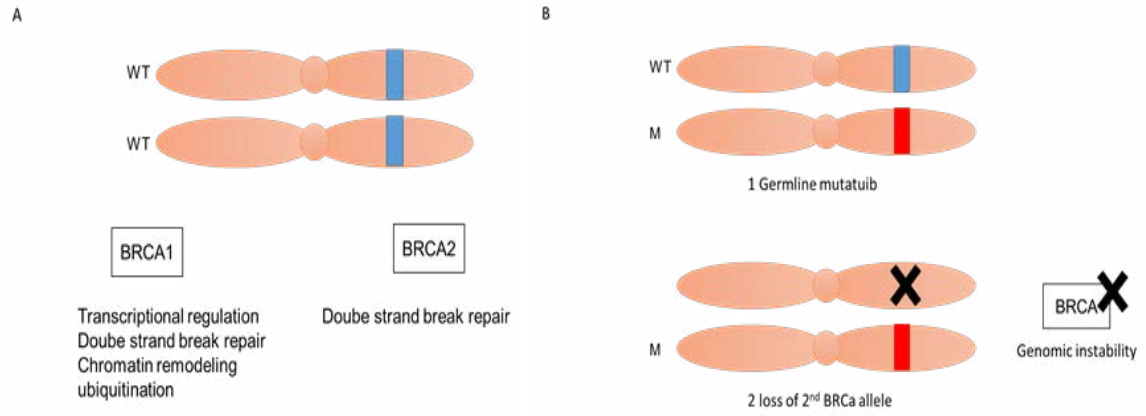

Figure 3. *A) The roles of BRCA1 and BRCA2 are shown graphically, B) Prevention of the 'BRCA1 and BRCA2' genetic factor in a BRCA-mutation carrier.*

Table 2. *The function of BRCA-interacting proteins.*

Protein	The function of interacting protein
BASC complex	Mismatch repair
RAD50	Fixing a broken double-strand
RAD51	Fixing a double-stranded break
H2AX	Signalling of DNA damage
pRB	Cell-cycle regulating tumor suppressor gene
c-myc	Transcribing Oncogenes
TP53	Tumor suppressor gene – Transcription factor
E2F	A Transcription Factor Regulating Cell Division
STAT1	Signal Transducer – Transcription factor
Estrogen Receptor	Ligand responsive transcription factor
RNA Pol II	Transcription
SWI/SNF	Chromatin remodelling complex
Androgen Receptor	Ligand responsive transcription factor
BRAP2	Cytoplasmic retention
HDAC	Histone deacetylation – chromatin remodelling
ARD1	Ubiquitin ligase
PALB2	Double-strand break repair

including genes involved in DNA repair, production on the X chromosome of heterochromatin, healing of double-strand breaks, and ubiquitination. In addition, other proteins connected to BRCA1 interact with DNA damage response mechanisms, a cell cycle, BRCA2, TP53, and RAD51, as shown in Table 2.

Cells without functional BRCA1 proteins cannot prevent the cell cycle in the phase known as G2 in an instance of damaged DNA and are not capable of transcription-coupled repair. Further, BRCA1 engages in interactions with γH2AX to modify structure chromatin, enabling DNA repair proteins to get to damaged areas. BRCA2 contributes to the preservation of chromosome stability and the recombination-based restoration of DNA breaks in double-strands, comparable to BRCA1. In the absence of BRCA2, the separation of chromosomes is compromised, and unexpected chromosomal defects show up after a few sections, including tri-radials, four-armed structures, and two-stranded. There is no effective restoration system, Therefore, DNA damage can happen in a variety of locations, including genes that are essential for the phases of the cycle of cells to develop. For example, cells lacking BRCA may not undergo cell death and continue to grow if they have TP53 gene alterations, which would block p21 expression. It is thought that people with TP53 mutations typically have BRCA1 or BRCA2 mutations, suggesting that BRCA insufficiency leads to mutation of several oncogenes.

Additional possible breast cancer genes.

Rare mutant susceptibility alleles with varying penetrance levels, there are more BRCA genes that account for a small percentage of inborn breast cancer occurrences along with BRCA1 and BRCA2. For instance, a serine-threonine kinase STK11/LKB1 is responsible for pigmented macules and hamartomata's polyps in small intestine are features of Peutz-Jegher syndrome. When compared to non-carriers, it has a 20.3 relative breast cancer risk. Cowden syndrome is associated with Phosphatase and Tensin Homolog (PTEN) and also has a highly penetrant mutation. There is a 20 to 30% lifetime risk increase for breast cancer related to this mutation. Breast cancer penetrance reaches 100% in individuals with inherited TP53 mutations, associated with Li-Fraumeni disorder, if mutation carriers live through infancy. The position of moderate penetrance genes as hereditary breast cancer genes has just lately been recognized, and they are frequently linked to BRCA function. Breast cancer risk is higher in people who carry ATM gene mutations (ataxia-telangiectasia). The cell cycle checkpoint kinase CHEK2, which is necessary for DNA repair pathways including TP53 and BRCA1, contains pathogenic mutations that double the chance of getting breast cancer. However, BRCA mutation carriers are not at increased risk because of it. Another illustration is the PALB2 gene, also referred to as the localizer of the BRCA2 gene, which is connected to the synthesis of useful protein that assists BRCA2 in repairing faulty DNA. Extremely low amounts of red, white, and platelet blood cells are hallmarks of Fanconi anemia type N, a condition brought on by the inheritance of two defective PALB2 genetic factors.

Extensive genomic analysis reveals previously unknown genetic variations.

Complex hereditary mutations can be uncovered by cutting-edge genomic research that uses whole-exome sequencing. SNPs (single nucleotide polymorphisms) in genes including FGFR2, TNRC9, and MAP3K1 were shown to be connected

with an improved substantial number of people's risk of developing breast cancer, including both people with breast cancer and healthy controls (4,316). Genotyping was done to evaluate SNPs found, and results were used further also connected to their chance of acquiring breast cancer are these locations in carriers of BRCA1 and BRCA2 mutations. Minor allele carriers of the SNPs rs2981582 and rs889312 compared to those who acquired a BRCA1 mutation had a higher risk of developing breast cancer, however, this was not the case for those who inherited a BRCA2 mutation. In people with changes to BRCA1 and BRCA2, the SNP rs3803662 enhances the possibility of having breast cancer. In 2009, a substantial linkage disequilibrium block on chromosome 1p11.2 including NOTCH2 and FCGR1B genes revealed a pericentromeric SNP. A large-scale genotyping investigation that discovered and genotyped 29807 SNPs found 41 additional loci linked to a higher chance of developing breast cancer. Together, these results show that cutting-edge sequencing research will probably keep discovering novel loci that increase the risk of breast cancer. Clinical decision-making may soon undergo a major change as a result of genomic technology' falling costs and their capacity to accurately and affordably identify patients' genetic diversity.

Mutation in BRCA and Prognosis.

Approximately 80% of BRCA1 mutation cases result in triple-negative breast tumors, which commonly exhibit an inherited BRCA1 mutant transcriptome signature characterized by elevated regulation of genes in the basal layer. According to histological characterization, inherited BRCA1 mutant cancers have high histological grades, rare medullary features, higher growth indices, intrusive restrictions, and lymphatic infiltration. Carriers of contralateral breast cancer are more likely to develop in those with BRCA2 mutations and frequently have tumors that are estrogen-receptor positive. Survival rates for sporadic and BRCA1 mutant carriers were significantly different, as were survival rates for BRCA2 mutation carriers and sporadic cases when patients were matched for age and year of diagnosis. According to a second paper using a cohort of 491 patients, when diagnosed with breast cancer, patients with BRCA2 mutations were older and had tumors having a nuclear grade that was higher than that of the other two groups of patients than BRCA1 mutants and also no mutants.

The BRCA mutations' impact on breast cancer prognosis was the subject of two recent studies, both of which produced different findings. BRCA1 mutation carriers showed a shorter employed database improved overall survival compared to those with a non-mutated BRCA1 allele in 105,220 breast cancer patients with mutation status and 3.4% BRCA carriers. The overall survival of people with a BRCA2 variation is comparable, but their disease-specific compared to people whose BRCA1 gene is not altered. Identical year, researchers examined data from 10,180 individuals across 16 trials and concluded showed BRCA mutations did not correlate with a decrease in overall survival. The combined results suggest that the BRCA alteration may not be a good predictor of independent outcomes.

Genetic Analysis and Preventative Measures.

A clinical diagnosis of hereditary breast and ovarian cancer can be made based on the following family characteristics: i) early detection of breast cancer, includes both in situ and invasive ductal carcinoma; ii) two primary breast cancers also associated cancers in one person, or two initial breast cancers or other malignancies that are connected in same side a family, first- to third-degree relations; iii) populations at risk; iv) a relative who carries a BRCA1 or BRCA2 mutation; and v) any type of male breast cancer; vi) any age for primary peritoneal, ovarian, or fallopian tube cancer. To examine possible genomic rearrangements in BRCA1 or BRCA2 genes, molecular genetic testing is used to identify BRCA mutations. The NCCN has revised its genetic testing, counseling, and risk assessment recommendations should be part of guidelines for genetic/familial high-risk assessment.

Those with a BRCA1 or BRCA2 mutation may reduce their chance of acquiring breast cancer with a combination of prophylactic mastectomy, regular monitoring, and chemoprevention. Every probability of getting contralateral breast cancer was shown to be 50% lower when tamoxifen was used as an adjuvant 1504 people with hereditary BRCA1 or BRCA2 mutations participated in a recent experiment. Every option to provide tamoxifen medication to postmenopausal women depends on the patient's age, sickness stage, risk of recurrence, and personal desire. Additionally, during anti-estrogen medication, ASCO recommendations advise switching to an aromatase inhibitor. Tamoxifen medication administered to premenopausal women for ten years may lower their chance of breast cancer recurrence.

Breast cancer treatment.

Surgery: Multiple studies have shown distinctions between breast tumors brought on by mutations in BRCA1 and BRCA2. BRCA that recurs is more frequent in females who have a BRCA variation or a secondary malignancy. Bilateral mastectomy is recommended for those who are BRCA1/2 mutation carriers since research has indicated that this procedure lowers the chance of acquiring breast cancer death compared to unilateral mastectomy.

Chemotherapy.

Taxanes: Taxanes are chemotherapeutic drugs that stabilize microtubules and stop cell division, causing apoptosis. In 1993 and 1995, respectively, docetaxel and paclitaxel were given use approval, respectively, are taxanes most often used to treat breast cancer. Compared to hormone-negative individuals without BRCA1 mutations, BRCA1 mutation carriers in subgroups with hormone-negative tumors demonstrated poorer susceptibility to taxane treatment. On the other hand, in both hereditary and sporadic instances a subset of hormone-positive tumors has comparable sensitivity to taxane treatment, as shown in Figure 4.

When anthracyclines and Taxanes were used for neoadjuvant chemotherapy, 46% of BRCA1 mutation carriers had compared to 22% of individuals with sporadic breast cancer, a Pathological Complete Response (PCR). However, a recent meta-analysis paper found that for individuals with advanced breast cancer, a Taxanes-based treatment may be better than an anthracycline Taxanes regimen Taxanes are less toxic and both therapies provide equivalent clinical results.

Table 3 shows the distribution of different chemotherapy regimens used over the years, which includes anthracycline-

Table 3. *Chemotherapy for breast cancer.*

Years	Percentage				
	Anthracycline-based (without Taxanes)		**Anthracycline-and Taxanes-bases**		**Others**
2014	24.13994	2011.96874	4.52551	2011.14965	60.25278
2015	37.37194	2012.67904	7.05482	2011.79809	43.97624
2016	49.73743	2014.1615	0.45052	2012.67904	23.976
2017	59.40968	2014.9486	10.22876	2013.35735	16.17731
2018	66.85707	2016.44599	20.06495	2014.23829	10.74399
2019	40.06518	2017.18616	37.18459	2014.9166	28.02757
2020	51.42363			2015.67383	10.90793
2021	35.14709			2016.44599	22.78161
2022	22.43031			2017.24801	17.69958

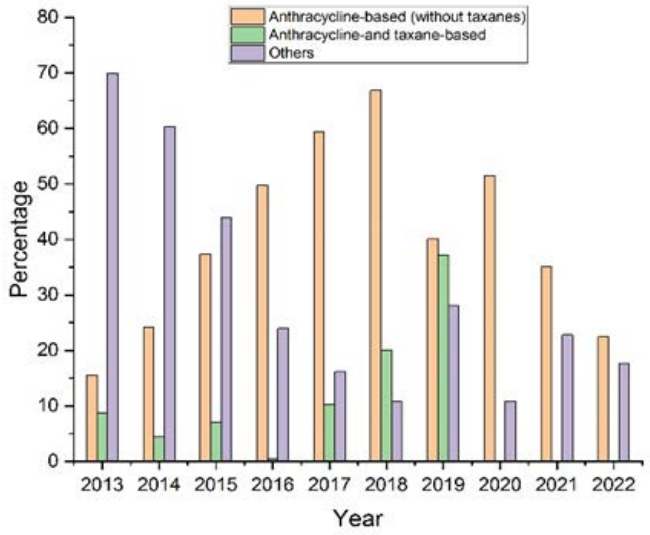

Figure 4. *Chemotherapy for breast cancer.*

based (without Taxanes), anthracycline-and-Taxane-based, and different treatments. While the table does not particularly focus on neoadjuvant chemotherapy for BRCA1 mutation carriers, it highlights the trends in chemotherapy usage. A recent meta-analysis suggests that for advanced breast cancers, Taxane-based treatments can be less toxic and as effective as anthracycline-Taxane regimens, even though Table 3 does not directly correlate with this finding.

Platinum agents: Direct DNA binding of platinum compounds, generating platinum-DNA adducts that because of double-strand breaks also inter-strand DNA crosslinks. In biological neoadjuvant chemotherapy for BRCA1-associated breast cancer improves a response to platinum compounds while decreasing of response to Taxanes. Despite having a small patient base, cisplatin had a pCR of 83% as opposed to 8% for women receiving doxorubicin and docetaxel. The use of a combination treatment involving doxorubicin, chemotherapy, and sometimes fluorescent yet only showed a 22% pCR is intriguing. Reduced BRCA1 expression might help to distinguish cisplatin-sensitive subgroups of triple-negative tumors, in accordance with studies on neonatal cisplatin therapy. A subsequent clinical experiment employing cisplatin, which demonstrated that individuals with BRCA1 mutations were especially susceptible to chemotherapeutic drugs, added more support to the argument. A systematic research and meta-data analysis of all published studies using platinum agents in addition to conventional neoadjuvant chemotherapy in triple-negative cancer found that their use significantly increases the probability of complete response (PCR). In contrast, recent research found that a patient with newly discovered triple-negative breast cancer underwent 18 weeks of platinum-based neoadjuvant therapy before developing a BRCA1 reversion mutation, leading to a poor response, an early recurrence, and death.

PARP inhibitors: The DNA damage repair process depends heavily on poly (ADP-ribose) polymerases (PARPs). DNA damage, especially from PARP-1 through PARP-3, DNA damage response's starters, often encourages PARP activation. ADP-ribose polymer, which PARP produces, draws assembling DNA repair complexes at damaged regions.

Chromosome instability results from PARP inhibitors' prevention and repair of DNA damage, which leaves the DNA lesions that are typically repaired by homologous replication intact, cell cycle arrest, and ultimately death. Through a process known as synthetic lethality, PARP inhibitors target cancers with BRCA1 or BRCA2 gene defects. DNA Single Strand Breaks (SSBs) are increased by PARP inhibitors, and in cells with BRCA1/2 deficiency, these SSBs replicate into hazardous, irreversible DNA Double double-strand breaks (DSBs). Patients who carry genetic BRCA mutations can benefit from PARP inhibitor therapy, according to clinical research. Additionally, those who carry mutations other than BRCA may benefit from PARP drugs.

Multiple clinical studies are now investigating the use of PARP inhibitors in adjuvant treatment for ovarian cancer, BRCA-mutated breast cancer, and other malignancies, as well as in neoadjuvant and metastatic situations. Iniparib, developed by Sanofi-Aventis and the most advanced PARP inhibitor in clinical tests in 2011, did not extend the lives of patients with triple-negative breast cancer despite high hopes for the new class of medications. According to a 2013 study, failure was linked to a resistance event when patients began showing clinical indicators of resistance to PARPs-blocking pharmaceuticals around the same time they had a later BRCA2 mutation. Every function of protein in a wild-type state will probably be restored by this mutation, undermining a synthetic lethality strategy.

Limitation.

A possible drawback is that the emphasis on somatic mutations may obscure the potential impact of inherited genetic variables, even though the great majority of cases of breast cancer cases are associated with acquired somatic mutations. If inherited genetic variables are overlooked, the true magnitude of the risk of breast cancer may be underestimated. In addition, a thorough understanding of the interaction between inherited genetic variables and acquired somatic mutations has yet to be achieved, which may lead to an incomplete picture of cancer's etiology. A person's risk profile may be better understood with the help of their family history and genetic counseling, but this may be overlooked if more attention is paid to mutations that are not inherited.

Discussion.

The psychosocial impact of Rapid Genetic Testing (RGT) was explored [10], for BRCA1 and BRCA2 in breast cancer patients, suggesting that while it aids in treatment decisions, it might also introduce emotional stress, highlighting the psychological burden. The research [11] highlighted specific mutations in BRCA1 and BRCA2 populations and highlighted the need for tailored genetic screening strategies for cancer prevention, contrasting global universal screening with regional genetic profiles requiring more localized approaches. The role of BRCA1 and BRCA2 in genomic stability was discussed [12] and their interaction with DNA repair mechanisms. It emphasized the therapeutic significance of identified mutations in those genes for early detection and personalized treatment, aligning with precision medicine advancements. The complex interaction between genetic mutations was highlighted [13] and environmental factors in breast cancer development, suggested a more integrated approach to both genetic and environmental risk factors, potentially improved patient outcomes, diverging from more genetic-centric studies. The breast cancer outcomes in BRCA mutation carriers (BRCAm) and non-carriers (BRCAwt) were compared [14], finding that BRCAm patients had more aggressive disease courses but responded better to targeted therapies.

The genetic transmutations in BRCA1, BRCA2, and related genes linked to hereditary breast cancer [15], suggested genetic testing could identify high-risk individuals for preventative interventions, but highlighting the need for refined screening tools. The genomics-based precision treatments for breast cancer were discussed [16], highlighted their potential for improved detection and treatment, but argued that financial and technical barriers hinder their widespread implementation. A revised map of breast cancer susceptibility loci, revealing a more complex genetic susceptibility, involving multiple low-risk variants, challenging the traditional view of high-penetrance mutations as the sole risk factor was presented [17]. The prognostic significance of the KIAA0101 gene in breast cancer was explored [18], suggested it could be a valuable biomarker for early detection and survival rates, enhancing cancer treatment plans. Machine learning models could achieve over 97% accuracy in diagnosing breast cancer using deep learning techniques were suggested [19], indicating the potential of AI and machine learning in cancer diagnosis. BRCA1/2 mutation frequency was explored in [20] and variations in Tanzanian cancer patients, highlighted the need for genetic screening in underrepresented populations and suggested understanding African genetic diversity could improve global risk assessments.

Conclusion.

The understanding of a person's BRCA mutation status is crucial for making informed choices about therapy and prevention. Those with the BRCA mutation who receive appropriate care and monitoring may be able to prevent cancers or detect them at an earlier, more treatable stage. Knowing a person's BRCA mutation status is valuable for guiding treatment and preventative measures, particularly for breast and ovarian cancer, as regular screenings and medical attention can reduce the risk of developing these cancers.

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