SOFT TISSUE IMAGING WITH THE INVISIBLE RAYS: THE PHYSICS AND APPLICATION OF MAMMOGRAPHY IN THE EARLY DETECTION AND THE TREATMENT OF CANCER-A REVIEW

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Abstract: The main objective of this study is to explain the well established theory of mammography in a very crisp manner. Mammography is a method for capturing images of the breast using characteristic x-rays. Compared to conventional radiography, here the prerequisites are somewhat unique and distinct. The breast imaging technology was further improved with a focus on minimizing radiation exposure while maintaining the highest level of diagnostic image quality. In this study, x-ray tube, target materials, image receptors, compression device, scattered radiation and filtration are discussed in the simplest possible manner in relation to the imaging requirements for mammography. Regarding the use of ionizing radiation for breast imaging, there are two schools of thought. Mammography was seen as both a benefit in case of early detection of cancer and a risk as it went through its early stages of development. In order to understand its advantages and disadvantages and to establish its ideal function, numerous studies were conducted. According to various reports, breast imaging raises the risk of breast cancer in asymptomatic women under the age of fifty. Another group of researchers contends that mammography has significant advantages and thus contributes to the welfare of the patients. This review study tries to illuminate the benefits of mammography in the detection of carcinoma, pre-carcinoma conditions like masses, clusters of micro-calcifications, distortion of structure in breast tissue. Mammography contributes in a significant way in the treatment of breast cancer using ionizing radiation. The abstract should appear like this. The abstract should appear like this. The abstract should appear like this. The abstract should appear like this. The abstract should appear like this.

Keywords: Mammography; carcinoma; characteristic x-rays; calcification; conventional radiography; dose

1. Introduction:

The incidence of breast cancer is increasing day by day and the disease grows without pain or any visual symptoms. It gets detected at advanced stages and nullifies the role of cure or radical treatment. The patient remains on palliation, control and care. The most obvious advantages of mammography are early detection of the disease which prompts curative treatment at an early stage and reduces the chance of mortality. Otherwise it is quite difficult to diagnose, since in its formative stage the cancer is asymptotic and often painless. Currently, mammography screening is the only method considered appropriate for mass screening of asymptomatic women [1]. Whenever the term Radiation pops up it brings fear too. There exists a dissent in the community on whether mammography should be made compulsory for every woman entering the age group of forty years. However in order to take such steps the awareness and scientific education demands the highest priority. The first judicious step of avoiding breast cancer is by eradicating or dispelling the myth that mammography triggers the disease itself. For broad usage, careful assessment of potential harmful consequences is required [1]. Screening mammography and adjuvant treatment have improved mortality reduction in breast cancer cases [2, 3]. Several surveys and studies conducted over the last three decades have demonstrated the usefulness of mammography screening for early breast cancer identification [4]. The best method in the struggle against cancer is early detection, which has been universally recognized [4, 5]. Many works have been published in recent years, focusing on technological evolution and changes suitable for physicists with no mammography experience [6], advances in digital detector technology [7,8], contrast enhanced imaging used to enhance the clarity of images [9], prediction of breast cancer risk by advanced deep learning algorithms [10], employing carbon-based composites for in-vivo radiation dosimetry during standard mammography screening [5], objective assessment of clinical mammography using new breast phantom [11], the process of breast compression [12], to mention a few. However, none of these recent researches focuses on the unique procedure of mammography for general public. Inhibition in the mind of the people due to the unique or uncommon procedure of mammography can be minimized by educating them on how the machine works using a non-technical or using a generalized language. In this study, attempts have been undertaken to add a new perspective to mammography screening and awareness.

2. Breast Anatomy:

The female breast is a glandular organ located on the anterior chest wall, extending from the second to the sixth rib and from the sternum to the midaxillary line [13]. However, the female breast undergoes more development and growth due to hormonal changes during puberty, pregnancy, and lactation [13]. The breast is composed of different types of tissue as shown in Figure 1 below, including (i) Mammary gland: - the functional part of the breast producing milk. It is composed of lobes that contain small sacs called alveoli, where milk is synthesized [13]. (ii) Nipple:-the small projection located at the center of the breast. It contains small openings through which milk is released during breastfeeding. (iii) Ducts: - channels that carry milk from the alveoli to the nipple. Several ducts converge at the nipple. (iv) Fat and Connective tissue: - The breast contains an adequate amount of adipose tissue and connective tissue, which provides the breast with its structural support and shape [13]. The breast is also surrounded by a layer of tissue called the areola, which is darker in color and contains small bumps called Montgomery glands that secrete oil to lubricate the nipple during breastfeeding [13]. From infancy until adulthood, the human breast grows at distinct stages. Therefore, any abnormality may occur at various phases. According to studies, women over 40 have a high probability of developing this breast deformity [14]. What could indicate a problem: A lump or thickening inside the breast and underarm region, swelling, breast redness, a change in the size or shape of the breast, an itchy or rashy nipple, nipple discharge, a new discomfort in one location that does not go away, etc., may be signs of breast cancer [15, 16]. Mammography must be able to detect not only minute variations in the density and make-up of breast parenchymal tissue, but also the presence of minute calcifications, or specks of calcium hydroxyapatite, Ca5(PO4)3OH, whether performed for mass screening or on a woman exhibiting symptoms of breast cancer [17]. Most of the aforementioned cancer's early warning signals are painless. These symptoms were often ignored. Therefore, routine breast screening is the greatest method for identifying breast cancer's early warning symptoms.

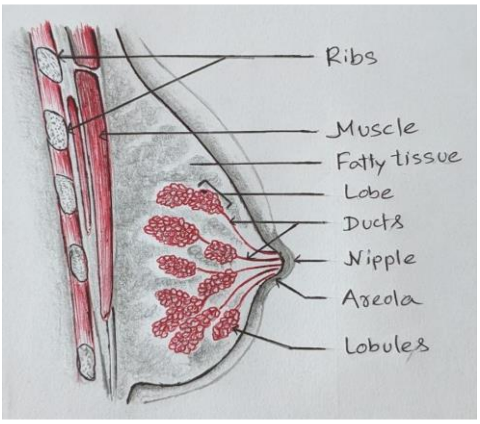

Figure 1: Anatomy of Breast sketched by Mr. Mrigen Rabha

3. Physics of Mammography:

Mammography can also be referred to as soft tissue imaging or soft tissue radiography that differs from conventional imaging in its imaging requirements [18]. The physical density difference between normal tissue and affected tissue is marginal, but the Z values are significant [17, 18]. Radiological differentiation of normal tissue and affected tissue is based on their photoelectric attenuation properties [17, 18]. Mammography was seen as both an advantage and a risk, leading to further development to minimize radiation exposure while maintaining high image quality [18]. Mammography requires a mono energetic beam of 15-25 KeV to reduce patient dose and improve image contrast [17-19]. Molybdenum, Ruthenium, Rhodium, Palladium, Silver and Cadmium provide x-rays suitable for mammography [19]. In 1969, x-ray tubes with 42Mo96 targets were introduced for mammography, replacing conventional tungsten (74W184) targets [18]. Because it produces more low energy photons, achieves good radiographic contrast in the image, and produces the exact energies needed for breast imaging [19, 20, 21]. Low atomic number anodes and low tube voltage reduces bremsstrahlung production, leading to greater importance of characteristic radiation in breast radiography [21]. Characteristic x-rays are produced when high speed incident electrons coming from the filament ionizes a Mo target atom by dislodging one of its bound electrons [17, 19, 20, 21]. Immediately after ionization, electron transition from one of the outer orbits of the atom will take place to fill in the vacancy created by the dislodged bound electron [17, 19, 20, 21]. This electron transition is accompanied by release of energy in the form of characteristic x-rays [17, 19, 20, 21]. The energy of the released radiation will be equal to the difference in the energy levels of the orbits between which the electron transition takes place [17, 19, 20, 21]. The electrons emiting from the filament by the process of thermionic emission is explained by an analogous situation of boiling water as shown in the Figure 2 below.

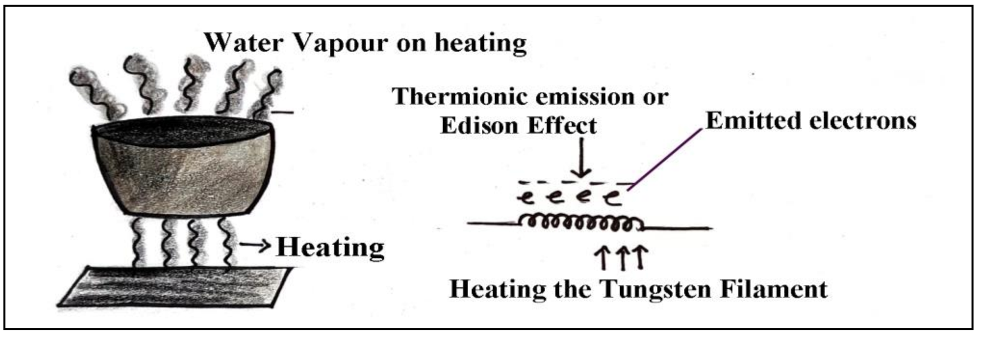

Figure 2: The conceptual diagram of boiling water producing water vapour is analogous to the emission of electrons from the Tungsten filament on heating. Sketched by Miss Nandini Kashyap.

The production of characteristic x-ray can be explained by using a simple example as shown in Figure 3 below.

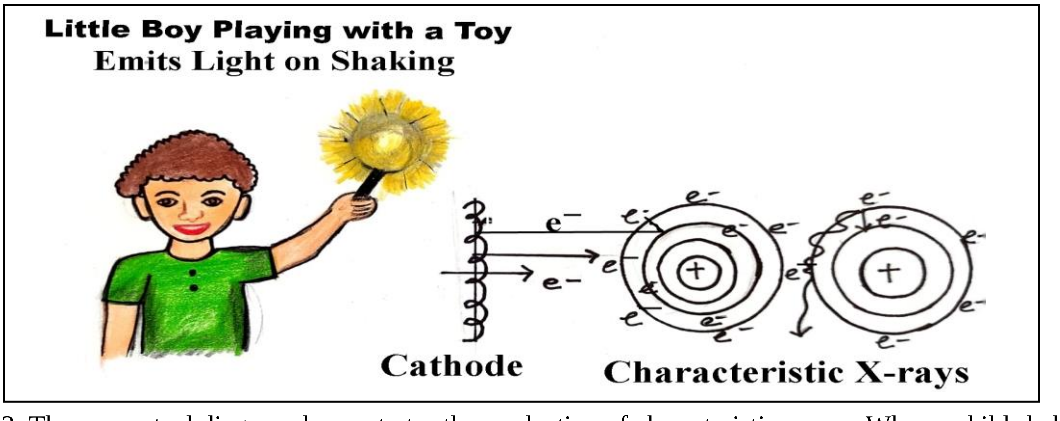

Figure 3: The conceptual diagram demonstrates the production of characteristic x-rays. When a child shakes the toy it produces visible light analogous to the production of characteristic x-rays, where electrons from filament disturb the orbital electrons. Sketched by Miss Nandini Kashyap.

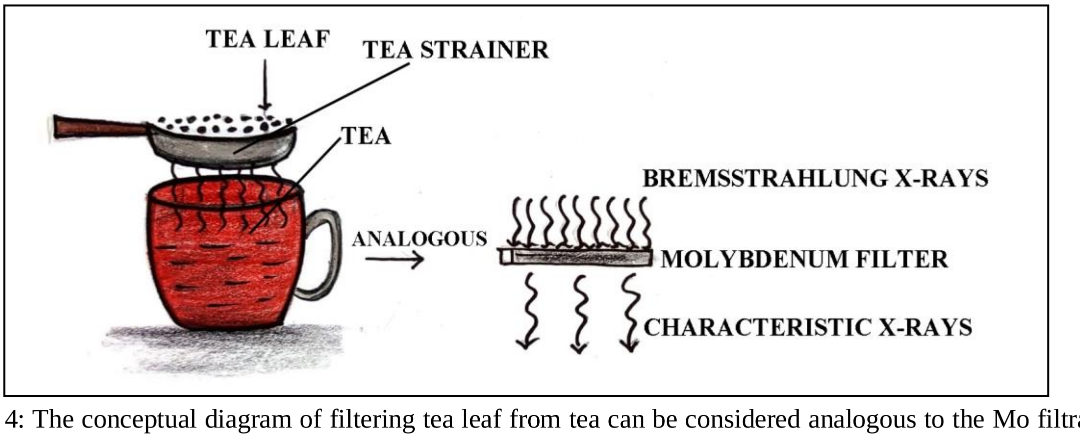

Figure 4: The conceptual diagram of filtering tea leaf from tea can be considered analogous to the Mo filtration of bremsstrahlung x-rays and passing of characteristic x-rays. Sketched by Miss Nandini Kashyap.

The optimal energy for mammography is achieved by the use of specific x-ray target and beam shaping filters [19]. Molybdenum filtration is preferable to aluminum due to its transparency to its own characteristic x-rays, and removes much of the bremsstrahlung radiation above 20 KeV Mo K-absorption edge, which is less effective in imaging [17]. The process of filtration is explained in a very simple manner in the Figure 4.

Mammography tube is oriented with cathode at chest side and anode at nipple side to take the advantage of heel effect to reduce attenuation un-sharpness by making the transmission through thicker and thinner part of the breast uniform [19]. Equipment bulk near the patient's head is also reduced [19]. This facilitates easier patient positioning as shown in the Figure 5 below. Mammography equipment shifts the central beam to the cathode side, allowing the vertical central ray to be directly over the chest wall [19]. This arrangement ensures that the breast is fully covered in the x-ray beam and also avoids the cathode side of the x-ray beam so that effective focal spot size and resolution remains almost uniform [19]. Double focused tubes are used in mammography to yield smaller effective focal spots [19]. Focal spot sizes range from 0.6/0.3, 0.5/0.2 to 0.4/0.1 mm.

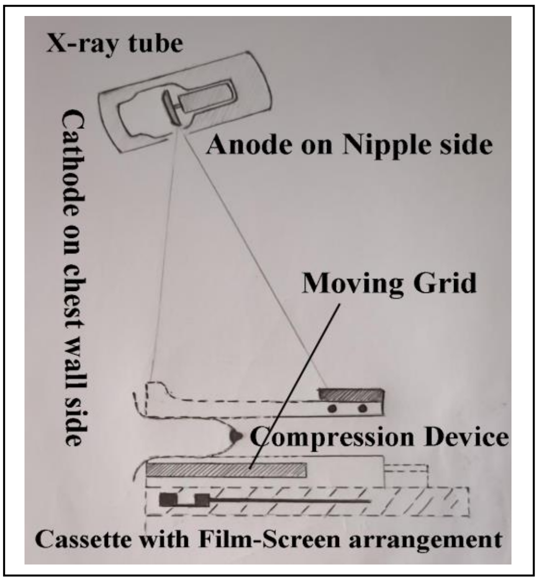

Figure 5: The schematic demonstrates the patient positioning in mammography machine with its important parts. Sketched by Mr. Mrigen Rabha.

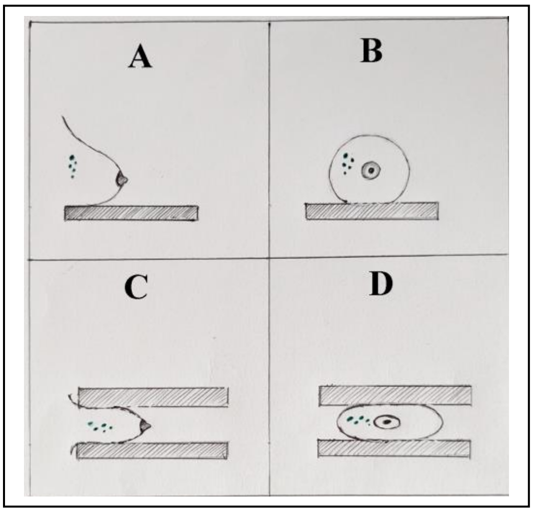

Figure 6: The conceptual diagram demonstrates the usefulness of breast compression. Here the image A & B are breasts without compression and it is clear that the calcifications are lying under one another and will be missed out in imaging. Image C & D are with compression thus proper visualization of tissue structures by spreading out and less superimposition of overlying structures. Sketched by Mr. Mrigen Rabha.

Mammography tubes use special anode positioning that helps to bombard the edge of the anode with electrons to create a small focal spot [19]. Mammography machines use a compression device to reduce geometric un-sharpness, tissue thickness, scatter radiation; increases contrast and facilitate lesser KVp. Reduces radiation exposure, lesser exposure time for thin body part and lesser entrance skin dose. Reduces motion unsharpness, improves visualization by spreading out of tissue structures and less superimposition of overlying structures [18, 19] as shown in Figure 6.

Magnification of the breast reduces resolution, but improves image contrast by reducing quantum mottle and scatter due to air gap [17, 18, 19]. Small 0.10 mm focal spot is used to restore resolution in mammography. Magnifications of the order of 1.5x, 1.8x and as high as 2.0x are employed in mammography [17, 19]. Mammography uses parallel grids with carbon fiber interspacing and moving grids to reduce scatter radiation [18, 19]. The function of moving grid and screen are shown in the Figure 7 & Figure 8 below. Single screens with Gd_2O_2S phosphor are used to reduce noise and increase resolution, while slow films are used to provide highest contrast and resolution [19]. The mammography cassette is loaded with the screen behind the film [17-20]. Single emulsion/single screen combination reduces light diffusion and improves image sharpness [17-20]. Automatic exposure control devices (AEC) are located underneath the image receptor, ensure the image receptor receives the optimum radiation dose and terminate the exposure, avoiding unnecessary patient dose [17-20]. Digital mammography improves performance by optimizing image acquisition, processing, display and storage [20].

Figure 7: The conceptual diagram of moving grid where the first picture shows that a boy took a photo when the train behind him is at rest and the second picture shows that when the train is in motion thus blurring out the train in the picture. This is how moving grid works. Sketched by Miss Nandini Kashyap.

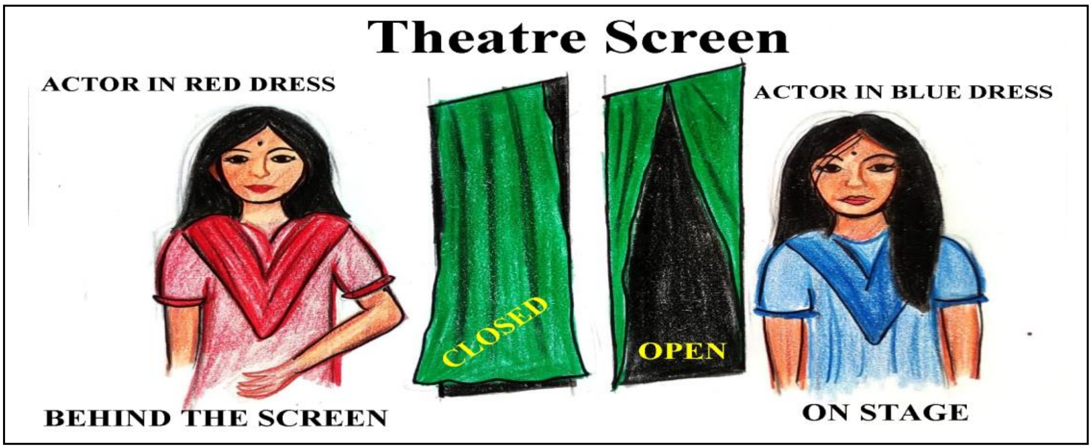

Figure 8: The conceptual diagram of screen demonstrates that an actor with a red dress in back stage with screen closed and in blue dress when screen is open. This can be considered as analogous to screen in mammography. X-rays falls on the screen and comes out as visible light from the screen. Sketched by Miss Nandini Kashyap.

One of the judicious steps of avoiding the breast cancer is by eradicating or dispelling the myth that mammography will cause tremendous pain because of its unique technique of breast compression and will trigger various side effects. But in reality, this is not the case. Breast compression is not as painful as it is thought to be. This is demonstrated in the Figure 9 below.

Figure 9: The conceptual diagram of breast compression shows that mammography is not as painful as it is thought to be. Sketched by Miss Nandini Kashyap.

4. Awareness towards Mammography screening:

The rising trend of breast cancer mandates awareness of the topic among the population and demands improvement in accessibility for early clinical diagnosis and prompt treatment in health services. It includes a self-breast examination and mammography. A woman must routinely self-examine her breasts while keeping in mind the signs of breast cancer. Mammography screening is the only method presently considered appropriate for mass screening of asymptomatic women. Only mammography of both breasts is performed during the screening visit. Participants in screening procedures are invited with the implication that they will gain something from taking part [22]. Current guidelines recommend regular (annual or every 2 years) mammography in women aged 50–69 years and in women with a strong familial history of breast cancer, with or without proven BRCA mutations, annual MRI and annual mammography are recommended. Regular mammography may also be done for women aged 40–49 and 70– 74 years, although the evidence for benefit is less well established [23]. Nowadays, the benefits and harms of mammography screening have been a matter of debate. Thus, it is of utmost importance that information about the benefits and harms of mammography screening is balanced to be communicated to the public [24, 25]. Benefits include early detection through mammography screening leading to improved possibilities of treatment. Moreover, early detection allows for a reduced number of mastectomies, better cosmesis in cases of breast conservation surgery, maximum replacement of axillary dissection by sentinel node biopsy, and reduced course of chemotherapy. These trends are being observed in Bavaria and the Dutch screening program, even with a moderate participation rate of up to 50% [26, 27]. Mastectomies are performed today only for extended DCIS, which in general represents a significantly higher risk of developing invasive and sometimes extended invasive breast cancers. Thus improvements in therapeutic options have the potential to greatly benefit women by increasing treatment efficacy along with reducing the negative impact on their physical and emotional well-being.

The use of mammography however involves radiation exposure, which is a known risk factor for breast cancer. But the amount of radiation exposure from mammography is very low and calculated to be 4 mGy per breast. As screening mammography is performed on healthy individuals, strict quality assurance measures are conducted to ensure that the aforesaid benefits are demonstrated. Additionally, some women may be concerned that compression during mammography may cause breast cancer, but there is no evidence to support this concern. There is a relative reduction in mortality from breast cancer ranging between 15 and 25% according to the randomized breast cancer screening trials, for women aged 50 to 69 years [28, 29, 30, 31]. There are also alternative screening methods available for women who may be concerned about radiation exposure, such as breast ultrasound or magnetic resonance imaging (MRI) which is worth noting. Nonetheless, these methods in general are reserved for women who have dense breast tissue and who are at high risk for breast cancer. Ultimately, a person should decide whether to have a mammogram or any other sort of breast cancer screening, after speaking with a healthcare professional about their specific risk factors and preferences.

The risk of false-positive recalls is one of the potential hazards of screening mammography. A false-positive result occurs when a mammogram seems to display an abnormality, but further testing shows the absence of cancer. This may lead to additional testing and unnecessary biopsies, which can be uncomfortable and confusing for patients as they have to carry out those at their own risk. While it can be stressful and anxiety-provoking to receive a false positive call but it is important to account that the majority of women who are recalled after a screening mammogram will ultimately be found to have benign findings. Approximately 1% of the recalled women undergo a histopathological assessment to detect malignancy, and in rare cases, open surgery may be necessary and breast cancer is confirmed in 4-5 of 1,000 screened women [32, 33]. There are researches indicating that most women can tolerate stress for a short while and that it has no overall negative effects on compliance with subsequent screening invitations [34]. The majority of women prefer being recalled and value thorough investigation rather than taking unnecessary risks. Quality assurance measures, such as double and consensus reading help to ensure that the number of false alarms is as low as possible. Since the benefits of early detection far outweigh the potential risks and stress associated with a false alarm so patient should undergo mammography screening. The prevalence of interval cancers, which include tumours that exist and spread quickly but are mammographically occult or were overlooked owing to a reader error, is another drawback of screening mammography. Among women who take part in screening, 28 to 33% of breast cancers found are interval cancers [35], and this proportion remains stable in subsequent screening rounds [36]. It has been found that with the increasing use of digital mammography, detection rates of ductal carcinoma in situ (DCIS) and invasive cancers are higher than that of screen-film mammography. However double-blinded and consensus reading, special training, and continuous feedback can help optimize the sensitivity of screening mammography. As a result, women with interval cancer do not have a worse prognosis than women who choose not to have mammography of breast cancer, a statistical concept that describes the detection of breast cancers through screening that would not have caused harm to the patient if left undetected and untreated. The use of mammography screening has been found to increase the incidence of breast cancer; it poses a substantial ethical dilemma, as it burdens both the patient and the healthcare system. Over diagnosis may result in the diagnosis and treatment of breast cancer with no possible survival benefit for the individual woman but may cause increased mortality by other causes besides breast cancer. Despite these challenges, most calculations suggest that over diagnosis represents a relatively small proportion of breast cancer diagnoses, with estimates typically ranging from 5 to 10%. This means that for every 10-100 diagnosed breast cancers, one may be over diagnosed. It is important to note that Duffy et al.'s [38] calculations suggest a relatively low rate of over diagnosis. While some studies [26, 38] have suggested that a small proportion of breast cancers may regress or remain stable without treatment, this phenomenon is not common and is difficult to predict. It is not recommended to rely on this assumption as a basis for deciding against treatment. The standard of care for breast cancer remains early detection, accurate diagnosis, and appropriate treatment based on individual patient characteristics and tumor characteristics.

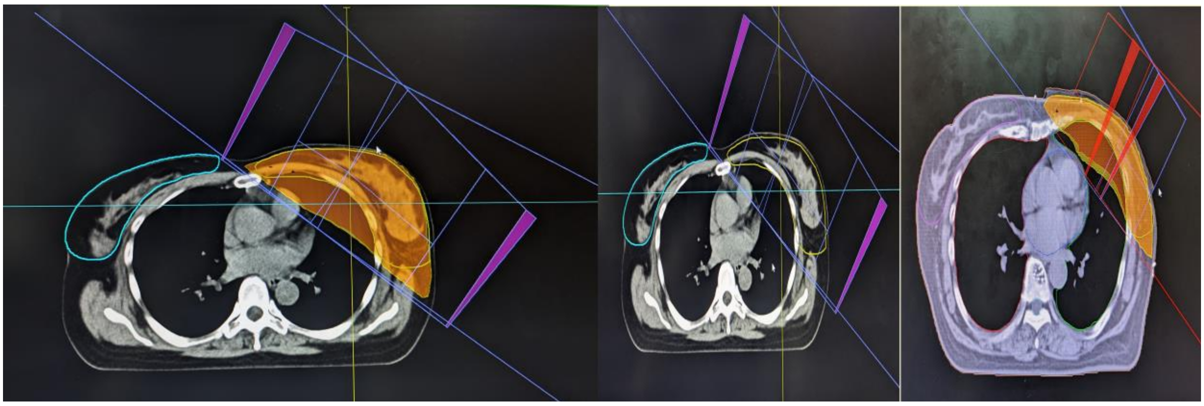

Figure 10: This is how the breast treatment planning is done on the treatment planning system. (State Cancer Institute, Gauhati Medical College).

5. Treatment of Breast Cancer:

Breast cancer treatment requires an individualized multidisciplinary approach that includes both local and systemic therapy. Local therapy involves surgery and radiation, with breast-conserving therapy (BCT) and mastectomy being the surgical options. BCT has been shown to be safe and equally effective as mastectomy in stage I and II breast cancer. Systematic therapy includes chemotherapy and hormonal therapy tailored to the biology of the tumour. Other approaches that may be considered include targeted therapy, immunotherapy, neoadjuvant and adjuvant therapy, radiation therapy, and supportive care [39-43]. CT Simulation is the first step to radiotherapy. CT Simulation involves immobilizing the patient in a simulator couch with an immobilization device or thermoplastic mould. X-rays are used to localize the malignant tumour, and lead markers are used to act as reference points. Radiotherapy involves matching the malignant tumour with the body surface. Images are transferred to the Treatment Planning System (TPS). The body contours, target volumes and organs at risk were delineated and reconstructed into three-dimensional images. Target volumes and organs at risk are delineated using RTOG and ICRU recommendations. EBRT has four types of planning techniques: conventional 2D radiotherapy, 3DCRT, IMRT, and VMAT. Conventional 2D and 3DCRT is the most common type of breast treatment planning. 6MV, 15MV photon beams are used depending on the patient contour and tangential beams are used with appropriate wedges. Low weightage beams are also used to remove overdose regions. Wedges are used to push the dose in the lung to prevent under dosage while breathing. The images of breast planning done in the treatment planning system are shown in the Figure 10. The approved treatment plans were then sent to the machine for the treatment.

6. Result:

Now it is a fact that awareness can lower the incidences of disease. To illustrate that it can be cited that the number of cervical cancers has reduced and one of the factor is awareness drive prompting people to change their hygiene behaviour. The incidence of cervical cancer has decreased as a result of organised vaccinations and screening programmes in developed countries [44]. Awareness should be built so that people can come forward to access the available medical help i.e. mammography in order to combat breast cancer by allowing early detection.

7. Conclusion:

The risk of radiation-induced breast cancer risk is negligible in comparison to the anticipated mortality reduction achievable with screening for the mammographic screening regimens under consideration that start at age 40 [45]. Women over the age of 40 should not be discouraged from mammographic screening due to the risk of radiation-induced breast cancer [45]. Regarding the amount of malignancies caused and probable fatalities, mammographic screening is projected to have a minimal risk of radiation-induced breast cancer [45]. Mammography can detect malignant diseases early, reducing mortality, but may lead to carcinogenesis [46]. In light of the possible advantages of screening, the carcinogenic risk is viewed as being low [46]. Annual mammographic screening has a significant benefit over radiation risk for women starting at age 50 [47]. According to Law's calculations [48, 49], a single mammogram per breast at a dose of 1 mGy would uncover 186 times more breast cancers than it might cause the same in women aged 40 to 49 [48, 49]. Randomized control trails involving women of 40-49 age groups have shown that screening mammography can be beneficial [50]. There is evidence that screening mammography can reduce the mortality rate from breast cancer by 25% for women aged 50 and older [51]. According to this study, the risk of ionizing radiation should not be considered when deciding whether to undergo annual mammographic screening. However, the choice of participating in screening is ultimately up to each woman.

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References:

[1] S. H. Heywang-Köbrunner, A. Hacker, S. Sedlacek, Advantages and disadvantages of mammography screening. Breast care, 6, 199-207, 2011.
[2] N. A. Wadden, C. Hapgood, Canadian association of radiologists' mammography accreditation program—clinical image assessment. Canadian Association of Radiologists Journal.,73, 157-63, 2022.
[3] D. A. Berry, K. A. Cronin, S. K. Plevritis, D. G. Fryback, L. Clarke, M. Zelen, J. S. Mandelblatt, A. Y. Yakovlev, J. D. Habbema, E. J. Feuer, Effect of screening and adjuvant therapy on mortality from breast cancer. New England Journal of Medicine, 353, 1784-92, 2005.
[4] S. Di Maria, S. Vedantham, P. Vaz, X-ray dosimetry in breast cancer screening: 2D and 3D mammography. European Journal of Radiology, 151, 110278, 2022.
[5] D. A. Bradley, S. N. Nawi, S. A. Sani, M. U. Khandaker, K. S. Almugren, Characterisation of graphite-based material for dosimetry in the mammographic energy range. Radiation Physics and Chemistry, 201, 110405, 2022.
[6] J. Law, The development of mammography. Physics in Medicine & Biology, 51, R155, 2006.
[7] M Mahesh, AAPM/RSNA physics tutorial for residents: digital mammography: an overview. Radiographics, 24, 1747-60, 2004.

[8] M. J. Yaffe, Basic physics of digital mammography. In: U. Bick, F. Diekmann, (eds) Digital mammography. Medical Radiology. Springer, Berlin, Heidelberg. 2010 https://doi.org/10.1007/978-3-540-78450-0_1.
[9] A. Kornecki, Current status of contrast enhanced mammography: A comprehensive review. Canadian Association of Radiologists Journal, 73, 141-56, 2022.
[10] H. T. Nguyen, S. B. Tran, D. B. Nguyen, H. H. Pham, H. Q. Nguyen, A novel multi-view deep learning approach for BI-RADS and density assessment of mammograms. In 44th Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), 11, pp. 2144-2148, 2022.
[11] C. Zhang, J. Fu, A new breast phantom suitable for digital mammography, contrast-enhanced digital mammography and digital breast tomosynthesis. Physics in Medicine & Biology, 68, 045015, 2023.
[12] M. Hertel, R. Makvandi, S. Kappler, R. Nanke, P. Bildhauer, S. Saalfeld, M. Radicke, D. Juhre, G. Rose, Towards a biomechanical breast model to simulate and investigate breast compression and its effects in mammography and tomosynthesis. Physics in Medicine & Biology, 68, 085007, 2023.
[13] G. Zucca-Matthes, C. Urban, A. Vallejo, Anatomy of the nipple and breast ducts. Gland surgery, 5, 32, 2016.
[14] P. L. Fitzgibbons, D. E. Henson, R. V. Hutter, Benign breast changes and the risk for subsequent breast cancer: an update of the 1985 consensus statement. Archives of pathology & laboratory medicine, 122, 1053, 1998.
[15] M. Morrow, Chapter 3: Physical Exam of the Breast. Diseases of the Breast. 5th ed. Philadelphia: Wolters Kluwer Health. 2014.
[16] M. S. Sabel, Clinical manifestations, differential diagnosis, and clinical evaluation of a palpable breast mass. UpToDate. Post TW (ed): UpToDate, Waltham, MA. 2022.
[17] A. B. Wolbarst, Physics of Radiology, Prentice-Hall Internationals., United States of America, pp-219-225, 1993.
[18] E. Seeram, X-ray imaging equipment: An Introduction, Charles C Thomas, USA, pp-204-214, 1985.
[19] J. A. Seibert, E.M. Leidholdt Jr., J.M. Boone, The Essential Physics of Medical Imaging, Lippincott Williams & Wilkins, USA, pp-191-224, 2002.
[20] D. R. Dance, S. Christofides, A.D.A. Maidment, I.D. McLean, K.H. Ng, Diagnostic Radiology Physics: A Handbook for Teachers and Students, International atomic energy agency Vienna, Austria, pp-209-235, 2014.
[21] T. S. Curry III, J. E. Dowdey, R. C. Murry, Christensen's Physics of Diagnostic Radiology, Williams & Wilkins, USA, pp-10-35, 1990.
[22] W.W. Holland, S. Stewart, Screening in Disease Prevention. What works? Oxford, United Kingdom: The Nuttfield Trust/Radcliffe Publishing Ltd; 2005.
[23] F. Cardoso, S. Kyriakides, S. Ohno, F. Penault-Llorca, P. Poortmans, I.T. Rubio, S. Zackrisson, E. Senkus, Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of oncology, 30, pp-1194-220, 2019.
[24] K. J. Jorgensen, P. C. Gøtzsche, Content of invitation for publicly funded screening mammography, BMJ.; 332, 538–541, 2006.
[25] K. J. Jorgensen, P.C. Gøtzsche, Information in practice. Presentation on websites of possible benefits for breast cancer: cross sectional study, BMJ, 328,148, 2004.
[26] P.H. Zahl, J. Maehlen, H.G. Welch, The natural history of invasive breast cancers detected by screening mammography. Arch Int Med, 168, 2311, 2008.
[27] Health Council of the Netherlands: The benefit of population screening for breast cancer with mammography. The Hague: Health Council of the Netherlands, publication no. 2002/03E, 2002, ISBN: 90–5549–420–8,.
[28] P. Gøtzsche, K.J. Jorgensen, Screening for breast cancer with mammography, Cochrane Database Syst Rev., 6, CD001877, 2013.
[29] U.K. Independent Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review, Lancet, 380, 1778, 2012.
[30] H. Vainio, F. Bianchini, IARC Handbook of Cancer Prevention, Volume 7, Breast Cancer Screening. Lyon, France: IARC Press; 2002.
[31] L.L. Humphrey, M. Helfand, B.K. Chan, S.H. Woolf, Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force, Ann Intern Med., 137, 347–60, 2002.
[32] Heywang-Köbrunner, A. Hacker, S. Sedlacek, J. Engel, Mammographie-Screening – eine Zwischenbilanz, Gyn und Gebhilfe, 7, 31–8, 2010.
[33] Qualitätsbericht des Mammographie -Screening- Programms von 2005–2007. www.mammo-programm.de/service/infomaterial-fachservice.php.
[34] N.T. Brewer, T. Salz, S.E. Lillie, Systematic review: the long-term effects of false-positive mammograms. Ann Intern Med., 146, 502–10, 2007.
[35] S. Törnberg, L. Kemetli, N. Ascunce, S. Hofvind, A. Anttila, B. Sèradour, et al, A pooled analysis of interval cancer rates in six European countries, Eur J Cancer Prev., 19, 87–93, 2010.

[36] M. Kalager, R. Tamimi, M. Bretthauer, H.O. Adami, Prognosis in women with interval breast cancer: population based observational cohort study. BMJ., 345, e7536, 2012.
[37] S.R. Hoff, A. L. Abrahamsen, J.H. Samset, E. Vigeland, O. Klepp, S. Hofvind, Breast cancer: missed interval and screening-detected cancer at full-field digital mammography and screen-film mammography - results from a retrospective review, Radiology, 246, 378–86, 2012.
[38] S. W. Duffy, L. Tabar, A. H. Olsen, et al., Absolute numbers of lives saved and over diagnosis in breast cancer screening, from a randomised trial and from the breast screening programme in England. J Med Screen; 17, 25–30, 2010.
[39] B. Fisher, S. Anderson, J. Bryant, R.G. Margolese, M. Deutsch, E.R. Fisher, et al, Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Eng J Med., 347, 1233–41, 2002.
[40] U. Veronesi, N. Cascinelli, L. Mariani, M. Greco, R. Saccozzi, A. Luini, et al, Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med., 347, 1227–32, 2002.
[41] M.M. Poggi, D.N. Danforth, L.C. Sciuto, S.L. Smith, S.M. Steinberg, D.J. Liewehr, et al, Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial, Cancer, 98, 697–702, 2003.
[42] A.C. Voogd, M. Nielsen, J.L. Peterse, M. Blichert-Toft, H. Bartelink, M. Overgaard, et al, Differences in risk factors for local and distant recurrence after breast-conserving therapy or mastectomy for stage I and II breast cancer: pooled results of two large European randomized trials. J Clin Oncol. 19, 1688–97, 2001.
[43] S. Darby, P. McGale, C. Correa, C. Taylor C, R. Arriagada, M. Clarke, et al, Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet. 378, 1707-16, 2011.
[44] M. Vu, J. Yu, O.A. Awolude, L. Chuang, Cervical cancer worldwide. Current problems in cancer, 42, 457-65, 2018.
[45] M. J. Yaffe, J. G Mainprize, Risk of radiation-induced breast cancer from mammographic screening. Radiology, 258, 98-105, 2011.
[46] E. K. Pauwels, N. Foray, M. H. Bourguignon, Breast cancer induced by X-ray mammography screening? A review based on recent understanding of low-dose radiobiology. Medical Principles and Practice. 25, 101-9, 2016.
[47] F. A. Mettler, A. C. Upton, C. A. Kelsey, R. N. Ashby, R. D. Rosenberg, M. N. Linver, Benefits versus risks from mammography: A critical reassessment. Cancer: Interdisciplinary International Journal of the American Cancer Society, 77, 903-9, 1996.
[48] S. A. Feig, R. E. Hendrick, Radiation risk from screening mammography of women aged 40-49 years. JNCI Monographs. 1997, 119-24, 1997.
[49] J. Law, Risk and benefit associated with radiation dose in breast screening programmes—an update. The British Journal of Radiology, 68, 870-6, 1995.
[50] R. E. Hendrick, R. A. Smith, J. H. Rutledge III, C. R. Smart, Benefit of screening mammography in women aged 40-49: a new meta-analysis of randomized controlled trials. JNCI Monographs, 1997, 87-92, 1997.
[51] S. A. Feig, C. J. D'orsi, R. E. Hendrick, V. P. Jackson, D. B. Kopans, B. Monsees, E. A. Sickles, C. B. Stelling, M. Zinninger, P. Wilcox-Buchalla, American College of Radiology guidelines for breast cancer screening. AJR. American journal of roentgenology, 171, 29-33, 1998.