Estimating Absorbed Dose to Breast Adipose Tissue from Mammograms

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Abstract

Purpose: Breast cancer usually originates in the glandular tissue of the breast. However, inflamed adipose tissue surrounding glandular tissue may expedite the local growth of cancerous cells. Exposing adipose tissue to radiation during mammography might cause inflammation in adipose tissue. This inflammation depends on the dose, and thus on the energy deposited from the X-ray mammography. Therefore, estimating the absorbed dose to adipose tissue during mammography is essential in breast cancer research. Materials and Methods: Absorbed dose to adipose tissue in the breast is determined using a new geometrical (semi-elliptical) model and Monte Carlo N-Particle transport code (MCNP6). X-ray mammogram images of patient breasts were taken as the basis of the new compressed breast geometry. The source probability density used in the MCNP6 code was generated from a published X-ray spectrum corresponding to tube voltage and air kerma. The relationship between various mammogram parameters such as peak tube voltage, compressed breast thickness, and adipose tissue weight fraction versus estimated absorbed dose is established for analysis. Results: Significant influences of adipose tissue weight fraction on absorbed dose were observed. Conclusion: Estimating the absorbed dose to breast adipose tissue during mammography and patients’ degree of obesity are important factors in breast cancer research.

Keywords: Absorbed dose, adipose tissue, mammogram, Monte Carlo N-Particle, X-ray

INTRODUCTION

Frequent medical screenings in health care have resulted in increased exposure to ionizing radiation. Specifically, annual mammograms have come into wide use to detect breast cancer at an early stage. The two-dimensional digital mammogram procedure consists of taking X-ray images of each breast at two different projections. The female breast has three primary regions: Region (1) is the skin, region (2) is the subcutaneous adipose tissue just beneath the skin, and region (3) is the mixed adipose and glandular tissue [Figure 1]. The thickness of these three regions is dependent upon the woman’s age, degree of obesity, and physical activity.[1,2] The average glandular dose is the average dose absorbed in the glandular tissue. Recommended AGD levels are promulgated by agencies like the International Commission on Radiological Protection and the Institute of Physical Sciences in Medicine.[3]

The breast tissue contains different types of cells including epithelial, glandular, and adipose or fat cells. Radiologists and physicians estimate the risk of radiation in the breast based on the amount of absorbed dose in the glandular tissue. However, the breast also contains adipose tissue that varies depending on the women’s body mass index (BMI). Research shows that obese women (BMI for the obese woman is equal or more than 30) have more fat mass within the breast, increasing the chance of inflammation and oxidative stress as a result of irradiation.[3]

There is evidence of the influential role of adipose tissue in inducing breast cancer.[4] People with higher BMI or who are suffering from obesity are more susceptible to higher radiation doses from exposure to radiation for either diagnostic or treatment purposes. Radiation, apart from targeting cancerous cells, also affects adjacent cells and damages noncancerous cells. Given the high content of adipose tissue within the breast, especially in obese women, it is critical to assess the...
effects of mammography X-ray exposure on adipocytes and how irradiated adipocytes alter other breast tissue cell types, possibly via secreted cytokines and hormones. Factors secreted by adipose tissue in response to radiation include inflammatory cytokines, levels of which are higher following ionizing radiation; the inflammatory cytokines then stimulate a cascade of events that damage surrounding tissues and organs. Hence, irradiation causes inflammation, and adipose tissue is well established as an endocrine tissue that secretes hormones and other inflammatory molecules, irradiated adipocytes may increase breast cancer cell growth via this mechanism.

Very few studies have addressed the effects of low-dose X-ray radiation on the adipose tissue around microtumors found in the breast, especially among obese women. A study has addressed the sensitivity of adipose tissue to radiation, but it was conducted for acute exposure. The risk of low dose radiation has been studied in the breast, but no studies to date have addressed effects on adipose tissue surrounding breast cancer microtumors and only a few studies have focused on breast epithelial cells. Thus, it is critical to understand the effects of low X-ray exposure on adipocytes since irradiation of adipose tissue may cause inflammation; this, in turn, may promote cancer cell growth in glandular tissue surrounded by breast adipose tissue. Irradiation of these adipose tissues may indirectly affect other breast tissues through direct cell-to-cell communication or through factors secreted by adipocytes which affect normal glandular cells or cancerous cells and vice versa.

Previous works estimated the absorbed dose to breast glandular tissue using the Monte Carlo technique, where a semi-circular cylindrical model is used to represent the compressed breast. A voxelized breast model was also used with the Monte Carlo code for the same objective. Moreover, software was developed by Bliznakova et al. in which the breast model consists of seven submodels, including the detailed tissue of the breast; this model was used to calculate the absorbed dose to the glandular tissue. All these studies focused on estimating the absorbed dose to glandular tissue, not adipose tissue.

Although inflamed adipose tissue surrounding glandular tissue may expedite the growth of glandular cancer cells and estimating the absorbed dose to adipose tissue is essential in breast cancer research, little research has been done on estimating the absorbed dose to adipose tissue form X-ray mammogram. This study focuses on the estimation of the absorbed dose to breast adipose tissue using an accurate semi-elliptical model of the compressed breast as shown in Figure 1. This simple geometrical model is used in the MCNP6 code; the dimensions of this model were obtained from 61 X-ray images of different breast sizes.

**Materials and Methods**

Images of 31 patients’ breasts with age group varied from 34 to 74 years was collected from Texas Tech University Medical Centre in Lubbock, Texas (Compact Disc that disabled patient identity), the included image viewing software were used to find the statistical detail of the breast dimensions [Table 1]. The dimensions of different regions of an 8-cm compressed breast in cranio-caudal view are listed in Table 2 and shown in Figure 1. This software show what was the compressed thickness at the time when the mammogram images were taken. The actual X-ray images of 31 anonymous patients (31 images for the right breast and 30 images for the left one) were used to generate different compressed breast thicknesses [Table 3]. An average skin thickness of 0.15 cm, and an average subcutaneous adipose tissue thickness (t) of 0.6 cm were obtained from the 31 patients’ right breast images. In the MCNP6 geometry, the thickness of subcutaneous adipose varied from 0 cm in the major axis direction (a), to 0.6 cm in the minor axis (b) and the compressed thickness (z) directions. The brighter areas in the image [Figure 1] show glandular and fibrous tissues while the darker areas show adipose tissue with a superficial layer of skin.

It is assumed that this compressed thickness (under pressure) is a function of patient’s breast size and degree of obesity. The 31-patient data [Table 1] shows that for large patients this thickness is higher, and it is also evident from the actual patient data. For large breast, compression paddle distance is also higher than medium or small breast. A range of the thickness from 4 to 8 cm is taken to represent small to large size. Furthermore, in the MCNP6 input, it is assumed that the subcutaneous fat (adipose tissue under the skin) thickness is constant for all breast thickness, and = 0.6 cm since its extremely difficult to correlate the fat thickness from one patient to another ($R^2$ value is only 0.29), also, the X-ray image data show no strong correlation between compressed thickness and adipose tissue under skin thickness. However, the percentage of adipose tissue in the mixed region (glandular and adipose tissue) is varied.

All digital copies of X-ray images were incorporated with built-in image analysis tools to measure dimensions and to pan,
zoom, or adjust image brightness. The major and minor axis radii, the average thickness of subcutaneous adipose tissue, and average skin thicknesses were calculated using the built-in dimensioning tool. Two fit equations were developed from those data to calculate the major and minor axis radii \[ a_1 \text{ and } b_1 \text{ in Table 3} \] of the 1st half ellipse as a function of compressed breast thicknesses (Equations 1 and 2). These values were later incorporated into the geometry card of the MCNP6 code to accurately represent different compressed breasts.

\[
\begin{align*}
    a_1 &= -0.0234t^3 + 0.3508t^2 - 0.0943t + 3.667 \\
    b_1 &= -0.0502t^3 + 0.9354t^2 - 4.643t + 15.264
\end{align*}
\]  

where, \( t \) is the compressed breast thickness in cm. The 2nd half ellipse and the radii \[ a_2 \text{ and } b_2 \text{ in Table 3} \] were calculated by subtracting the average skin thickness (0.15 cm) from \( a_1 \) and \( b_1 \), respectively. For the 3rd half ellipse, the radii \[ a_3 \text{ and } b_3 \text{ in Table 3} \] were calculated by subtracting the thickness of subcutaneous adipose tissue from \( a_2 \) and \( b_2 \), respectively. These data in Table 3 were generated from best-fit data of an actual mammogram and utilized in the MCNP6 cell and surface cards to build standard compressed breast geometries.

Table 2 was for one single image (not used in MCNP6), whereas Table 3 was generated from the best-fit data of 31 anonymous patients (61 images of right and left breast). To simulate the X-ray image of the compressed breast in Figure 1, the MCNP6 geometry shown in Figure 2 was created. The whole model consists of three concentric semi-elliptical cylinders characterized by major and minor axes. The region between the first and second semi-elliptical cylinders represents a skin layer of 0.15 cm thickness. This skin thickness was considered based on the average breast skin thickness noted in the literature and obtained from actual mammogram data.

The region between the second and third semielliptical cylinders represents subcutaneous adipose tissue, a 0.6 cm thickness is considered for all compressed thickness. The third, innermost semieliptical cylinder represents mixed adipose and glandular tissue. There is no correlation developed so far between the adipose tissue mass in the breast and the obesity degree, the percentage by mass of adipose tissue in the breast is chosen from 20% to 60%. Hence, the modeling considered the following percentages of mixed adipose and glandular tissue in the innermost semieliptical cylinder: (1) 20% adipose and 80% glandular; (2) 40% adipose and 60% glandular; (3) 50% adipose and 50% glandular and (4) 60% adipose and 40% glandular. The four types of materials defined in MCNP6 were: (a) skin, (b) adipose tissue, (c) mixed adipose and glandular tissue, and (d) air. The material elemental compositions for air and skin were taken from the material handbook recommended for radiation transport modeling and the adipose and glandular tissue compositions from similar past studies of Hammerstein. The volume fraction of the glandular tissue and adipose tissue in the mixed region can be calculated using the following equations:

\[
\begin{align*}
    v_a &= 1 - \left( \frac{f_g \rho_g}{f_a \rho_a} + 1 \right)^{-1} \\
    v_g &= f_a - v_a
\end{align*}
\]  

where \( \rho_a, \rho_g, v_a \) and \( v_g \) stand for the density of 100% adipose (0.93 g/cm³) and 100% glandular tissues (1.04 g/cm³) and their volume fractions, respectively. And \( f_a \) and \( f_g \) represent mass fraction of glandular and adipose tissue. Furthermore, the mixture density can be obtained using the rule of mixture equation:

\[
\rho_{mixture} = \rho_a v_a + \rho_g v_g
\]  

For example, for a mixture of 60% glandular and 40% adipose tissue, \( f_a = 0.6, \) and \( f_g = 0.4 \); from equations 3 and 4, \( v_a = 0.43 \) and \( v_g = 0.57 \); and from equation 5, the density of the mixture is 0.993 g/cm³. Table 4 shows the elemental compositions of different breast tissues and Table 5 shows...
Table 3: Different parameters of compressed breast geometry used for Monte Carlo N-Particle 6

| CB thickness, t (cm) | 1st half ellipse (outer) | 2nd half ellipse (middle) | 3rd half ellipse (middle) | Assumed skin thickness, t_s (cm) | Assumed adipose thickness under skin, t_a (cm) | Thickness of mixture region = (t-2t_a-2t_s) (cm) |
|---------------------|-------------------------|--------------------------|--------------------------|-------------------------------|---------------------------------------------|-----------------------------------------------|
| 4                   | 7.4                     | 8.4                      | 7.25                     | 8.25                          | 7.25                                       | 0.15                                          | 0.6                                           | 2.5                                          |
| 6                   | 10.7                    | 10.2                     | 10.55                    | 10.05                         | 10.55                                      | 0.15                                          | 0.6                                           | 4.5                                          |
| 8                   | 13.4                    | 12.3                     | 13.25                    | 12.15                         | 13.25                                      | 0.15                                          | 0.6                                           | 6.5                                          |
| 10                  | 15.3                    | 12.9                     | 15.15                    | 12.75                         | 15.15                                      | 0.15                                          | 0.6                                           | 8.5                                          |

CB: Compressed breast

Table 4: Elemental composition (weight fraction) of different breast tissues

| Elements                | H   | C   | N   | O   | P   | S   | Cl  | K   | Ca  |
|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Adipose tissue          | 0.112| 0.619| 0.017| 0.251| 0.001| 0   | 0   | 0   | 0   |
| Glandular tissue        | 0.102| 0.184| 0.032| 0.677| 0.005| 0   | 0   | 0   | 0   |
| Skin                    | 0.10059| 0.2283| 0.04642| 0.619| 0.0033| 0.0016| 0.0027| 0.0009| 0.00015|

Table 5: Change in elemental weight fraction with different percentages of adipose and glandular tissue

| Elements                          | H   | C   | N   | O   | P   |
|-----------------------------------|-----|-----|-----|-----|-----|
| 20%-80% adipose + glandular       | 0.104| 0.271| 0.029| 0.5918| 0.0042|
| 40%-60% adipose + glandular       | 0.106| 0.358| 0.026| 0.5066| 0.0034|
| 50%-50% adipose + glandular       | 0.107| 0.4015| 0.0245| 0.464| 0.003|
| 60%-40% adipose + glandular       | 0.108| 0.445| 0.023| 0.4214| 0.0026|
| 80%-20% adipose + glandular       | 0.11| 0.532| 0.02| 0.3362| 0.0018|

X-ray output data used in MCNP6

The mammogram X-ray image in Figure 1 was produced by a selenia dimensions full-field digital mammography (FFDM) system (Hologic, Inc.). In general, this system has a target anode made of tungsten (W), and optional rhodium (Rh) or silver (Ag) filters that are 0.052 mm thick for scanning.[20] The Rh filter is recommended for compressed breasts 1-5 cm in thickness, and the Ag for those 6-15 cm in thickness during manual exposure control. In automatic exposure control (AEC) mode, the machine decides on the optimal filter for best image quality and the lowest absorbed dose for the patient. The system’s X-ray generator has a maximum tube current of 200 mA and an operating tube output voltage ranging from 20 to 49 kV.[23] In practice, the clinical range of energy varies from 25 to 39 kV. The system’s maximum source to image distance (SID) is 70 cm, with an air gap of 2.5 cm between the bottom support plate and the detector, and the maximum field-of-view size of the X-ray detector is (29 × 24) cm. In MCNP6 simulation, the X-ray source is considered a point source with a spectrum of energy distributions. The W anode spectra similar to the Hologic Selenia Dimensions FFDM system were generated by using Tungsten Anode Spectral Model Interpolating Cubic Splines (TASMICS).[27] The TASMICS is a free distributable Spreadsheet by Hernandez et al., capable of generating X-ray spectral data for the tube output voltage peak...
kV between 20 and 640 kV, given the desired air kerma (mGy), filter, and HVL of the system. The TASMICS is chosen because of its simplicity and also TASMICS demonstrated no statistically significant differences from Birch and Marshall and Poludniowski’s spectral computational model over the wide range of tube potentials compared by Hernandez et al. Absorbed dose in the air (Air kerma) can be calculated using equation 6 where is the mass energy transfer coefficient of the material and is the energy fluence, which is energy passing through a unit cross-sectional area and can be derived by multiplying the photon fluence \( \phi \) with photon energy \( E \).

\[
K_{air} = \psi \left( \frac{\mu E}{\rho} \right) [J/kg]
\]

Figure 4 shows example plots of X-ray spectra of 25–39 kV spectrums for both tungsten-silver (W/Ag) and tungsten-rhodium (W/Rh) anode-filter combinations. The horizontal axis of the spectra denotes the photon energy (keV) with 2 kV increments and the vertical axis denotes the fluence (number of photons per mm\(^2\)). Spectra similar to these were generated with TASMICS to calculate the output photon energy and its probability distribution [Table 7 for example] for MCNP dose calculations.

**Verification of MCNP6 calculations**

**Air kerma verification**

Air kerma values were calculated using the calibration chart [Table 6] for the Selenia Dimensions digital mammogram system; this table lists the tube voltage, the HVL, the type of filter used, and the air kerma per mAs (in µGy/mAs) at 100 cm from the source (the X-ray focal spot). In turn, the calculated air kerma were used in the TASMIC program to obtain the input parameters of the source card in MCNP6 (fluence probability vs. energy). To verify the MCNP6 result with the calibration data given in Table 6, the X-ray energy spectrum corresponding to air kerma of about 3.17 mGy, 28 kV, 86 mAs, and 0.52 mm Al HVL was considered as an input in the TASMIC program, where we adjusted the Rh filter to a thickness of 0.0586 mm, to obtain output spectra corresponding to an HVL of 0.52 (mm Al); This output spectra were used as a source card in the MCNP6 after normalizing each fluence to a source probability (fluence probability) corresponding to each energy. The estimated absorbed dose \( D \) in the thin air cell (20 cm × 24 cm × 0.1 cm) (air kerma) from MCNP6 using one million particles history was \( 1.663 \times 10^{-6} \) MeV/particle passing all statistical checks; this value was converted to milli-Gray (mGy) by multiplying the total fluence per \( 1 \times 10^{-6} \) MeV/kg.

\[
D = \left( \frac{1.663 \times 10^{-6} \text{MeV}}{p} \right) \times \left( \frac{7.399 \times 10^{13} \text{P}}{48 \text{cm}^3 \times 1.293 \times 10^{-3} \frac{g}{\text{cm}^3}} \right) \times \left( \frac{\text{kg}}{1000 \text{g}} \right) \times \left( \frac{1 \text{Gy} \times \left( \frac{1000 \text{mGy}}{\text{Gy}} \right)}{6.242 \times 10^{12} \frac{\text{MeV}}{\text{kg}}} \right) = 3.1766 \text{mGy}
\]

where 1 Gy is equal to \( 6.242 \times 10^{12} \) MeV/kg. Comparing the estimated air kerma obtained from MCNP6 code (3.1768 mGy) to the air kerma used to generate the spectra in the TASMIC program, the percentage difference is <0.21%.

**Absorbed dose verification**

To verify the absorbed dose \( D \) to adipose tissue in the mixed region, the following parameters were used. A broad, parallel photon spectrum corresponding to 29 kV and a current of 100 mAs, incident on 6 cm compressed breast that consist of three layers: skin, subcutaneous adipose tissue, and mixed adipose and glandular (80% adipose and 20% glandular) tissue. Analytical and stimulated (MCNP6) calculations were performed. For this purpose, the absorbed dose to

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**Table 6: The tube output, air Kerma at 100 cm as a function of tube voltage, half value layer, and anode/filter combination**

| Tube voltage (kV) | Target (anode) | HVL (mm Al) | Filter | Air kerma (µGy/mAs) at 100 cm |
|------------------|----------------|-------------|--------|-------------------------------|
| 25               | W              | 0.48        | Rh     | 11.4                          |
| 28               | W              | 0.52        | Rh     | 16                            |
| 31               | W              | 0.56        | Rh     | 20.4                          |
| 31               | W              | 0.63        | Ag     | 27.4                          |
| 34               | W              | 0.66        | Ag     | 33.8                          |

HVL: Half-value layer

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**Figure 3: Pyramid-shaped air cell built around the compressed breast defined in the geometry card of MCNP6**
absorbed dose to breast adipose tissue by mammograms

adipose tissue in the mixed region were calculated for each mono-energetic photon from the spectrum. The fluence to the mixed tissue region was considered as those photons that penetrated the skin and subcutaneous adipose tissue without interactions using Equation 8. The absorbed dose to adipose tissue in the mixed region was utilized using equation 9.

\[
\Phi_m = \Phi_s \times \left( e^{-\mu_{s,\text{eff}} t_s} \right) \times \left( e^{-\mu_{a,\text{eff}} t_a} \right) \times \left( e^{-\mu_{m,\text{eff}} t_m} \right)
\]  

where subscript s, a, and m stand for skin, adipose, and mixture respectively, \( \Phi \) is the photon fluence, \( \mu/\rho \) and \( \mu_{\text{en}}/\rho \) were mass-attenuation and mass-energy absorption coefficients as a function of the elemental composition of each material and photon energy in the spectrum; the photon energy, mixture density, breast thickness, mass of the mixture and its area were expressed with symbols \( E_i, \rho, t_m, \text{mass} \), and \( A_m \) respectively.

The estimated absorbed dose to 60% adipose tissue in the mixed tissue region from the above analytical solution was 0.351 mGy compared to the MCNP6 calculated absorbed dose of 0.482 mGy, which brought a relative error of 27%. This error was encountered due to simplifying assumptions of parallel broad beam radiation and neglecting the contribution of bremsstrahlung and the scattering and double scattering photons to the absorbed dose. Moreover, while photons that interacted with the skin and subcutaneous adipose tissue were removed from further calculation of the dose to the mixed tissue region in the analytical solution, the contributions of photons–which need to be considered—that interacted with the skin and subcutaneous adipose tissue to the absorbed dose in the mixed tissue region are included in the MCNP6 results.

**Table 7:** Tungsten anode spectral model interpolating cubic splines spectral data for 28 kV and 3.17 mGy air kerma, 0.52 half-value layer, and Rh filter

| Photon energy (keV) | Fluence (photon/mm²) | Probability |
|---------------------|----------------------|-------------|
| 5.5                 | 9.83E-10             | 6.38E-17    |
| 6.5                 | 7.13E-4              | 4.63E-11    |
| 7.5                 | 1.55E00              | 1.01E-07    |
| 8.5                 | 2.06E+2              | 1.33E-05    |
| 9.5                 | 3.48E+3              | 2.26E-04    |
| 10.5                | 2.07E+4              | 1.34E-03    |
| 11.5                | 7.77E+4              | 5.04E-03    |
| 12.5                | 1.88E+5              | 1.22E-02    |
| 13.5                | 3.90E+5              | 2.53E-02    |
| 14.5                | 6.68E+5              | 4.34E-02    |
| 15.5                | 9.97E+5              | 6.57E-02    |
| 16.5                | 1.32E+6              | 8.53E-02    |
| 17.5                | 1.60E+6              | 1.03E-01    |
| 18.5                | 1.85E+6              | 1.20E-01    |
| 19.5                | 2.00E+6              | 1.30E-01    |
| 20.5                | 2.06E+6              | 1.30E-01    |
| 21.5                | 2.03E+6              | 1.30E-01    |
| 22.5                | 1.99E+6              | 1.30E-01    |
| 23.5                | 4.00E+4              | 2.59E-03    |
| 24.5                | 5.13E+4              | 3.33E-03    |
| 25.5                | 5.47E+4              | 3.55E-03    |
| 26.5                | 4.57E+4              | 2.97E-03    |
| 27.5                | 3.23E+4              | 2.09E-03    |
| Total               | 1.54E+7              | 1.00E00     |

**Figure 4:** (a) The X-ray spectra of 25-39 kV spectrums for tungsten-silver (W/Ag); (b) The X-ray spectra of 25-39 kV spectrums for tungsten-rhodium (W/Rh)

\[
D_a = \sum \left[ 1 - e^{-\left( \mu_{s,\text{eff}} / \rho \right) t_s} \right] \times \Phi_s \times \frac{A_m}{\text{mass}} \times G_a
\]

where subscript s, a, and m stand for skin, adipose, and mixture respectively, \( \Phi \) is the photon fluence, \( \mu/p \) and \( \mu_{\text{en}}/p \) were mass-attenuation and mass-energy absorption coefficients as a function of the elemental composition of each material and photon energy in the spectrum; the photon energy, mixture density, breast thickness, mass of the mixture and its area were expressed with symbols \( E_i, \rho, t_m, \text{mass} \), and \( A_m \) respectively. Finally, G factor (\( G_a \)) was utilized to separate the absorbed dose to adipose tissue in the mixed tissue only.

**Results**

MCNP6 codes were utilized to calculate the absorbed dose to compressed breast thicknesses: 4 cm represents a small breast, 6 and 8 cm represents a medium breast, and 10 cm represents a large breast. In the MCNP6 simulations, energy deposition in adipose tissue was estimated as MeV per gram per particles (F6 tally output in MCNP6 code) and converted to the absorbed dose in the unit of mGy using equation 10.
where the total number of photons that interacted with the breast tissue (fluence multiplied by the ESA) was computed by the procedure mentioned in the air kerma verification section.

To separate the absorbed dose to adipose tissue alone from the total absorbed dose to the mixture region, a factor $G_a$ expressed in equation 11 was utilized.

$$\frac{F_{\text{MCNP6}}}{\text{gm}*p} \times \phi \times \frac{P}{\text{mm}^2} \times \text{ESA} (\text{mm}^2) \times (1.602 \times 10^7) \frac{\text{mGy}}{\text{MeV}} \times G_a$$

Equation 10 and the MCNP6 results, where all different thicknesses of breasts with 60% adipose weight fraction in the mixed tissue region were exposed to a fixed 100 mAs X-ray energy and 29 kV fluence with the tungsten anode and Rh filter. When exposed to the same X-ray generated from identical current and same tube voltage for 60% adipose tissue in the mixed tissue region, smaller breasts had a higher absorbed dose to adipose tissue compared to larger breasts. For the same X-ray current and tube voltage, the absorbed doses in adipose tissue gradually decreased as the compressed breast thickness increased from 4 cm to 10 cm (the compressed breast thickness is automatically determined by the mammogram machine for specific patient).

Figure 5 illustrates the absorbed dose to adipose tissue using Equation 10 and the MCNP6 results, where all different thicknesses of breasts with 60% adipose weight fraction in the mixed tissue region were exposed to a fixed 100 mAs X-ray energy and 29 kV fluence with the tungsten anode and Rh filter. When exposed to the same X-ray generated from identical current and same tube voltage for 60% adipose tissue in the mixed tissue region, smaller breasts had a higher absorbed dose to adipose tissue compared to larger breasts. For the same X-ray current and tube voltage, the absorbed doses in adipose tissue gradually decreased as the compressed breast thickness increased from 4 cm to 10 cm (the compressed breast thickness is automatically determined by the mammogram machine for specific patient).

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**Table 8: Mass energy absorption coefficients for adipose and glandular tissue**

| kV  | Weighted average energy, $E$, keV | For glandular, $(\mu_{en}/\rho)_g$, cm²/g | For adipose, $(\mu_{en}/\rho)_a$, cm²/g |
|-----|----------------------------------|----------------------------------------|---------------------------------------|
| 25  | 18.5                             | 0.64                                   | 0.39                                  |
| 27  | 18.9                             | 0.60                                   | 0.37                                  |
| 29  | 19.1                             | 0.58                                   | 0.35                                  |
| 31  | 19.4                             | 0.54                                   | 0.33                                  |
| 33  | 19.9                             | 0.51                                   | 0.31                                  |
| 35  | 20.3                             | 0.47                                   | 0.29                                  |
| 37  | 20.9                             | 0.43                                   | 0.27                                  |
| 39  | 21.5                             | 0.40                                   | 0.24                                  |

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**Table 9: G factor calculations for 29 kV tube voltage and different weight fractions in the mixture**

| $f_a$ | $f_g = 1 - f_a$ | $\rho_a$ | $\rho_g$ | $\nu_a$ | $\nu_g = 1 - \nu_a$ | $\nu_{\text{mixture}}$ | $(\mu_{en}/\rho)_a$, cm²/g | $(\mu_{en}/\rho)_g$, cm²/g | $G_g$ | $G_a$ |
|-------|----------------|----------|----------|---------|---------------------|---------------------|--------------------------|--------------------------|-------|-------|
| 0     | 1              | 1.04     | 0.93     | 0       | 0.93                | 0.35                | 0.35                     | 1                        | 1     | 0     |
| 0.1   | 0.9            | 1.04     | 0.93     | 0.91    | 0.09                | 0.94                | 0.35                     | 0.15                     | 0.85  | 0.71  |
| 0.2   | 0.8            | 1.04     | 0.93     | 0.82    | 0.18                | 0.95                | 0.35                     | 0.29                     | 0.71  | 0.48  |
| 0.3   | 0.7            | 1.04     | 0.93     | 0.72    | 0.28                | 0.96                | 0.35                     | 0.41                     | 0.59  | 0.35  |
| 0.4   | 0.6            | 1.04     | 0.93     | 0.63    | 0.37                | 0.97                | 0.35                     | 0.52                     | 0.48  | 0.35  |
| 0.5   | 0.5            | 1.04     | 0.93     | 0.53    | 0.47                | 0.98                | 0.35                     | 0.62                     | 0.38  | 0.35  |
| 0.6   | 0.4            | 1.04     | 0.93     | 0.43    | 0.57                | 0.99                | 0.35                     | 0.71                     | 0.29  | 0.35  |
| 0.7   | 0.3            | 1.04     | 0.93     | 0.32    | 0.68                | 1.0                 | 0.35                     | 0.79                     | 0.21  | 0.35  |
| 0.8   | 0.2            | 1.04     | 0.93     | 0.22    | 0.78                | 1.02                | 0.35                     | 0.87                     | 0.13  | 0.35  |
| 0.9   | 0.1            | 1.04     | 0.93     | 0.11    | 0.89                | 1.03                | 0.35                     | 0.94                     | 0.06  | 0.35  |
| 1     | 0              | 1.04     | 0.93     | 0       | 1                   | 1.04                | 0.35                     | 1                        | 0     | 0     |
Tube output voltage kV and the current (mA) of the X-ray tube in the mammogram machine determine the energy and fluence of the output photons to be used.\(^{[25]}\) At a fixed product of X-ray tube current and exposure time 100 mAs with peak voltage of 29 kV, the average absorbed dose to the adipose tissue in the mixed tissue region increases as the weight fraction of adipose tissue increases from 20% to 60% [Figure 6]. This is due to the accompanying increase in the elemental weight fraction of carbon and hydrogen atoms [Table 5].

Figure 7 shows the relation between peak tube voltage and corresponding absorbed dose to adipose tissue in the mixed tissue region for an 8 cm compressed breast with 60% adipose tissue at a constant 100 mAs using the Rh filter. The general trend of the absorbed dose shown in Figure 7 is to increase as peak tube voltage kV increases. A higher voltage in the X-ray tube will generate photons with higher kinetic energy and increases exposure since exposure is approximately proportional to the square of kV in the clinical energy range.\(^{[25]}\) As a result, higher exposure due to increases in kV resulted in higher absorbed dose for the same mAs, filter, and compressed breast thickness [Figure 7].

The absorbed doses in Figure 8 were estimated using MCNP6 with input data generated using the AEC settings [Table 10] for the Hologic Selenia Dimensions FFDM system.\(^{[29]}\)

In Table 10, as the compressed breast thickness increases, the machine automatically selects optimized settings for kV and mAs, and the correct filter to obtain the best image quality and minimize the X-ray dose to the patient. In automatic mode, the machine tends to choose higher kV and mAs as the thickness increases; for thicknesses greater than 7 cm, the Ag filter is usually selected.\(^{[24]}\) When the AEC selected parameters [Table 10] were used in MCNP6, the absorbed dose to the adipose tissue in the mixed tissue region increased as the compressed breast thickness increased. As both kV and mAs increase, the photon energy and total photon fluence also increase, and consequently, the absorbed dose to the adipose tissue increases.

For 4 cm compressed breast thickness with 60% adipose weight fraction, the absorbed dose to adipose tissue in the mixed tissue region was 1.107 mGy [Figure 5] where the total absorbed dose for that region was 2.306 mGy. The G factor for 60% adipose tissue was calculated as 0.48 [Table 9] meaning that 48% of the total absorbed dose to the mixed tissue region was to the adipose tissue. Hence, women with breasts characterized as “fatty” have more risk of inflammation from mammogram X-ray exposure.

### Discussion

The low absorbed dose may produce inflammation in adipose tissue. Given the amounts of adipose tissue within the glandular tissue of the breast, adipose tissue inflammation may also enhance cancer growth. Our study has parted away from conventional mammogram dosimetry study where the mean glandular dose is the primary metric of absorbed dose to the breast. Our primary goal was to estimate the absorbed dose in adipose tissue inside the third region (mixed adipose and glandular tissue) from various low energy X-ray during mammogram procedures, where in future research, we can correlate these absorbed doses in breast adipose tissue with inflammation, and subsequently with cancer and cancer risk. Using a dosimeter, we can easily measure the air kerma (entrance absorbed dose) for a given source; however, we cannot place the dosimeter inside the breast to measure the absorbed dose. Ultimately, using MCNP code to estimate the absorbed dose to adipose tissue inside the breast is a very practical and convenient way of simulating millions of particle interactions and consequently energy deposition.
Since it is difficult to estimate the skin thickness (first region) and the adipose tissue thickness (second region), we assumed an average thickness of 0.15 cm for the skin and 0.6 cm for the adipose tissue in the second region. Our elaborate study showed that with increased weight fraction of adipose tissue in the adipose-glandular region, absorbed dose also increased when we kept the breast compressed size, kV and mAs constant [Figure 6]. In other words, if two patients’ breasts with the same age, exposed to the X-ray beam from mammogram machine with the same kV and mAs, the absorbed dose will be higher for the patient who has more adipose tissue in the breast.

Although AEC of the mammogram machine adjusts the X-ray kV and mA dynamically for each patient to optimize the dose received by patients and achieve best signal-to-noise ratio, it does not consider the percentage of adipose tissue in the breast. Thus, our approach, in considering fat mass is innovative and provides more accurate dosimetry estimates.

**Conclusion**

Research on adipose tissue inflammation is still in its rudimentary stage and has yet to be explored from a dosimetry perspective. In this work, we presented tabulated data of the absorbed dose to adipose tissue in the mixture region of compressed breasts during mammogram screening in the craniocaudal view for a commonly used mammogram system with MCNP6. These data will serve as a supplement to dosimetry characterizations and the role of adipose tissue irradiation on breast cancer initiation and tumor growth.

When current, exposure time and peak voltage were kept constant, the average absorbed dose in the adipose tissue of the mixed tissue region increases as the weight fraction of adipose tissue increases; therefore, women who are obese are the most vulnerable group to mammogram radiation exposure. Detailed dosimetry analysis will aid the researchers in this field in terms of exploring the cellular mechanism of low absorbed dose radiation to adipose tissue and its effects on adjacent cells.

In our work we theoretically estimated absorbed dose in adipose tissue for different tissue composition of adipose tissue and X-ray energy range. Moreover, an empirical work can be performed in the form of animal studies to better understand whether these low absorbed doses can initiate inflammation and the degree of inflammation with *in vitro/in vivo* studies for mammogram risk assessment.

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**Conflicts of interest**

There are no conflicts of interest.

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