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Tissue Substitute Materials for the Human Colorectal Cancer Tissue

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ABSTRACT

Introduction: Due to the high radiation dose used in radiotherapy, the human tissue is usually replaced with tissue substitutes in order to develop new treatment techniques. Tissue substitutes have not been reported for colorectal cancer tissue (CRC). This study aims at developing tissue substitutes for the CRC tissue with respect to the mass attenuation (μ_m) and mass energy absorption coefficients (μ_{en}/ρ) within the energy range of 6 – 15MV.

Material and Methods: Colorectal cancer tissue and four locally sourced materials namely beeswax, gelatine, rice powder, clay, and their mixtures – Clarice, gelarice, gelaclay, and bewaclay were subjected to Rutherford Backscattering Spectrometry (RBS) to determine their elemental composition. Results from the RBS were used in XCOM, a web-based photon interaction software designed by the National Institute of Standards and Technology, USA to determine their theoretical μ_m and μ_{en}/ρ values. Again, these materials were exposed to a narrow beam of x-rays at energies of 6 and 15MV to obtain their experimental μ_m and μ_{en}/ρ values.

Results: Revealed that the ratio of CRC tissue to the test materials ranged from 0.946 (beeswax) to 1.07 (clay) for both theoretical and experimental values with bewaclay having a ratio of 1.01 compared with 1.00 for CRC and a p = 0.541 and p = 0.663 with respect to μ_m and μ_{en}/ρ respectively.

Conclusion: Bewaclay with the closest match can be used as a *tissue* substitute for the CRC tissue between 6 – 9MV with respect to μ_m and μ_{en}/ρ as parameters for matching.

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Introduction

The high radiation dose used to treat cancer and the need to avoid all unnecessary exposure to radiation makes it very unsafe to use human tissue to develop new treatment techniques in radiotherapy. Instead, the human tissue is replaced with tissue substitutes that have similar radiation interaction parameters like the biological tissue. Tissue substitutes are materials that simulate a particular body tissue depending on the set of physical characteristics or radiation interaction parameters [1]. Simulation of the human tissues involves matching the radiation interaction parameters of tissue substitutes with those of the biological tissues. The International Commission for Radiation Units Report 44 [1] recommends the matching of radiation interaction parameters such as the mass attenuation (μ_m) and mass energy absorption (μ_{en}/ρ) coefficients for the simulation of biological tissues [1, 2]. Knowledge of these coefficients allows the quantity of X-ray photons absorbed and transmitted after interaction and the absorbed dose in the human tissue to be theoretically evaluated [3, 4]. Several types of materials have been reported as tissue substitutes for human organs and tissues [1] and for specific tasks [5]. Gelatine, PW1 (paraffin wax + $MgSO_4.6H_2O$) and Rigel (rice + gelatine) for lungs and soft tissues [6]; nylon and modelling clay for the human cerebral tissue [7] have been cited as tissue substitute materials with respect to μ_m.

Radiation therapy is one of the treatment modalities for the colorectal cancer (CRC). It can be used to shrink tumours before surgery (neoadjuvant treatment) or destroy the remaining malignant cells after surgery (adjuvant treatment) or for patients who cannot undergo surgery. Radiotherapy can also be used in conjunction with chemotherapy [8]. The varied treatment techniques used in radiotherapy centres require radiation physicists to have information on the different materials simulating the different human tissues for the purpose of dosimetric measurements [1]. This information on the tissue substitutes for the CRC tissue is currently lacking in the literature. This study aims at simulating the CRC tissue with respect to the μ_m and μ_{en}/ρ in the radiotherapy energy range of 6 – 15MV using four locally sourced materials and their mixtures.

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Materials and Methods

This study was carried out in two parts. First, Rutherford backscattering spectrometry (RBS) was used to determine the elemental composition of the CRC tissue and the locally sourced materials, with the subsequent use of the RBS values as input data in XCOM [9] (Version 3.1) is a web-based photon interaction software designed by the National Institute of Standards and Technology, USA., to obtain theoretical photon interaction values for these materials. The second part involved the use of X-ray attenuation experiments to determine the experimental values of the photon interaction parameters for the CRC tissue and the locally sourced materials.

Theoretical determination of attenuation data

Colorectal cancer tissue samples from the autopsy of previously diagnosed and confirmed patients were obtained from the Histopathology laboratory of the University of Calabar Teaching Hospital, Calabar. These samples were freeze-dried at a vacuum pressure of 10^{-3} Torr, and temperature of −30 to −40°C [10]. After which the samples were grounded into fine powder and allowed to dry overnight in a vacuum cupboard. The dried CRC tissue powder was then made into pellets of 1cm thickness and used as targets in Rutherford backscattering spectrometry (RBS) to determine their elemental composition. The particle accelerator used to carry out RBS was the Peletron Particle Accelerator with Model number 5SDH installed in the Centre for Energy, Research, and Development, Ife – Nigeria. The pelletized CRC tissue was loaded into the particle accelerator and bombarded with helium particle ion ($^4He^+$) of 2MeV backscattered at an angle of about 180^0. Elements in the sample were detected based on the pulse produced from signal on the energy spectrum of the particle accelerator. The elemental composition obtained from RBS was used as input data in XCOM to obtain theoretical values of μ_m for the CRC tissue between 6 – 15 MV.

Four locally sourced materials - beeswax, gelatine, clay, and rice powder were selected to simulate the CRC tissue based on their known photon interaction properties [6, 7, 11, 12, 13]. These materials also fall under the class of wax, plastics, and polymers recommended as the materials of choice for biological tissue substitutes [12]. Using the same method for the CRC tissue, the elemental composition and the theoretical values of μ_m were determined for these locally sourced materials. Also, mixtures of these local materials were theoretically formulated on the XCOM software. This was done by using the percentage option on the XCOM software to combine the different percentage fractions of the local materials and also determine their μ_m in the energy range of 6 - 15MV. Of all the mixtures theoretically formulated, gelatine 20% / rice powder 80% renamed Gelarice, beeswax 50% / clay 50% renamed Bewaclay, gelatine 50% /clay 50% renamed Gelaclay and clay 20% / rice powder 80% renamed Clarice were selected as they were the closest to the CRC with respect to their XCOM attenuation data. The XCOM attenuation data of the locally sourced materials and their mixtures collectively known as test materials were compared to that of the CRC tissue. The μ_m values of the CRC tissue and the test materials was determined from XCOM using equation 1[14]:

$$\mu_m = \sum_{i-1-n}^{n} w_i \left(\frac{\mu}{\rho}\right)_i \quad (1)$$

where μ_m - mass attenuation coefficient for the compound

$\left(\frac{\mu}{\rho}\right)_i$ - Mass attenuation coefficient for the individual elements in the compound

w_i -fractional weight of the elements in the compound

The mass energy absorption coefficient (μ_{en}/ρ) was obtained from mass energy transfer coefficient (μ_{tr}/ρ), which is the mass attenuation coefficient (μ_m) in terms of the theoretical f-factors [15]. The μ_{tr}/ρ was obtained from Equation 2 [16]:

$$\frac{\mu_{tr}}{\rho} = f(\mu_m) \quad (2)$$

where f is the weighted average fraction of the photon energy transferred to the kinetic energy of the charged particles in Compton scattering and pair production. The μ_{en}/ρ was obtained from Equation 3 [16]:

$$\frac{\mu_{en}}{\rho} = \left(\frac{\mu_{tr}}{\rho}\right)(1-g) \quad (3)$$

Where g is the energy loss due to bremsstrahlung

Experimental determination of attenuation data

The theoretically formulated mixtures from the XCOM software - gelarice, bewaclay, gelaclay and clarice were prepared by adding the required percentage fraction of the local materials making up the mixture with warm water (at about 35^0C) in a 1cm thick mould to produce a paste. The warm water enabled good mixing [6] and the mixtures were allowed to dry in a vacuum cupboard, after which they were made into pellets of 1cm thickness. The pelletized CRC and test materials were mounted one at a time on a sample holder and exposed to a narrow beam of X-rays at energies of 6 MV and 15 MV only from the Elektra Precise linear accelerator unit installed in the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria. Three exposures of the incident (I) and transmitted (I_0) X-ray intensities were measured using the Rontgen-Gamma Dosimeter, Type–RGD 27091, with serial number – 7508-PR-208503001 manufactured by the STEP Sensortechnik and Elektronik Pockau GmbH. The mean of 3 exposures of I and I_0 X-ray intensities were used to obtain following experimental values:

The linear attenuation coefficient (μ) for the CRC and the test materials was derived from equation 3 [17]:

$$\mu = \frac{1}{x} In\left(\frac{I_O}{I}\right) \quad (3)$$

where x is the thickness of the materials.

The experimental μ_m for the materials was determined from equation 4 [17]:

$$\mu_m = \frac{1}{\rho x} In\left(\frac{I_O}{I}\right) \quad (4)$$

Where ρ is the density of CRC and the test materials are determined from the direct measurement method of volume and mass. The experimental μ_{en}/ρ for the test materials was obtained from Equation 2.

The degree of match in the theoretical and experimental μ_m and μ_{en}/ρ values between the CRC tissue and tested materials was obtained from Equation 5 [18]

$$\frac{\left(\mu/\rho\right)_{substitute}}{\left(\mu/\rho\right)_{tissue}} \quad (5)$$

The percentage (%) difference in the theoretical and experimental μ_m and μ_{en}/ρ values between the test materials and the CRC tissue was obtained from Equation 6

$$\%\ diff = \frac{(PIP)_{tiss} - (PIP)_{subst}}{(PIP)_{tiss} + (PIP)_{subst}} * 100 \quad (6)$$

Statistical analysis was done using the analysis of variance (ANOVA) to determine if there are differences in the mean of the μ_m and μ_{en}/ρ values between CRC tissue and the test materials. Probability value of $p < 0.05$ was considered to be statistically significant

Results

Results of the elemental composition, XCOM, and experimental determination of attenuation data for the CRC tissue and the test materials are presented in table 1 and figures 1 – 13.

Elemental Composition

Figure 1 depicts the elements and their percentage fraction detected in CRC tissue and the test materials by RBS. All the materials contained carbon (C) and oxygen (O). Carbon had the highest percentage fraction in CRC, beeswax, rice, gelarice, bewaclay and clarice while oxygen had the highest percentage fraction in gelatine, clay and gelaclay. Comparison of the test materials to the CRC tissue showed that the mixture – gelarice was the closest in terms of the elemental composition and their percentage fraction. Hydrogen (H) was not detected.

Mass attenuation coefficient and mass energy absorption coefficient

Table 1 depicts the elemental composition, mass attenuation, and mass energy absorption coefficient properties of the CRC tissue and the test materials.

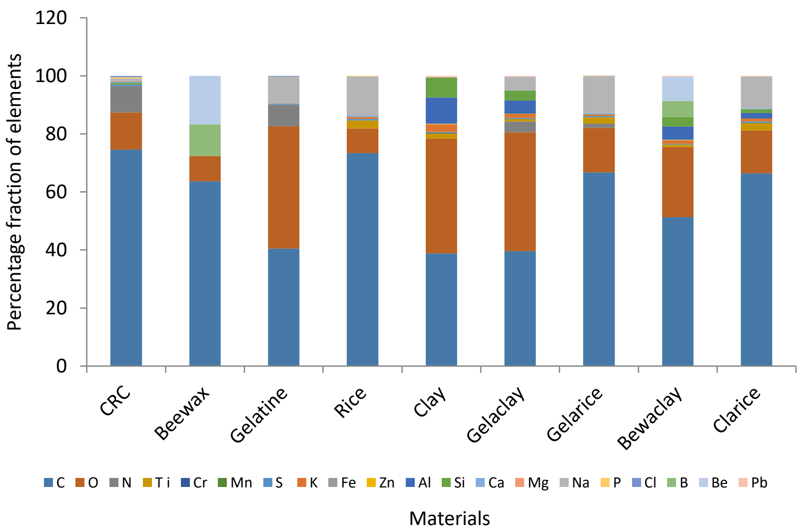

Figure 1. Plot of the elemental composition of the CRC tissue and the test materials

Table 1. Properties of CRC tissue and the test materials

Materials	Elemental composition	Mass attenuation coefficient (cm^2/g)	Mass energy absorption coefficient(cm^2/g)
CRC	C, O, N, S, K, Fe, Zn, Si, Ca, Mg, Na, P, Cl	0.0249 – 0.0175[a] 0.0254; 0.0178[b]	0.0244 – 0.0168[a] 0.0249; 0.0171[b]
Beewax	C, O, B, Be	0.0239 – 0.0163[a] 0.0243; 0.0171[b]	0.0234 – 0.0157[a] 0.0238; 0.0164[b]
Gelatine	C, O, N, Na, S, Fe, Al, Si, Ca, Cl	0.0252 – 0.0182[a] 0.0263; 0.0193[b]	0.0247 – 0.0175[a] 0.0259; 0.0185[b]
Rice powder	C, O, Ti, S, K, Si, Ca, Na, P	0.0251 – 0.0180[a] 0.0263; 0.0193[b]	0.0245 – 0.0173[a] 0.0259; 0.0179[b]
Clay	C, O, Ti, Cr, Mn, S, K, Fe, Zn, Al, Si, Pb	0.0257 – 0.0193[a] 0.0270; 0.0204[b]	0.0252 – 0.0185[a] 0.0264; 0.0196[b]
Gelaclay	C, O, N, Ti, Cr, Mn, S, K, Fe, Zn, Al, Si, Ca, Na, Cl, Pb	0.0255 – 0.0187[a] 0.0264; 0.0194[b]	0.0249 – 0.0180[a] 0.0258; 0.0187[b]
Gelarice	C, O. N, Ti, S, K, Fe, Si, Ca, Na, P, Cl	0.0251 – 0.018[a] 0.0266; 0.0189[b]	0.0246 – 0.0174[a] 0.0260; 0.0182[b]
Bewaclay	C, O, Ti, Cr, Mn, S, K, Fe, Zn, Al, Si, B, Be, Pb	0.0248 – 0.0178[a] 0.0255; 0.0192[b]	0.0243 – 0.0171[a] 0.0250; 0.0184[b]
Clarice	C, O, Ti, Cr, Mn, S, K, P Fe, Zn, Al, Si, Ca, Na, Pb	0.0253 – 0.0184[a] 0.0258; 0.0189[b]	0.0247 – 0.0177[a] 0.0253; 0.0182[b]

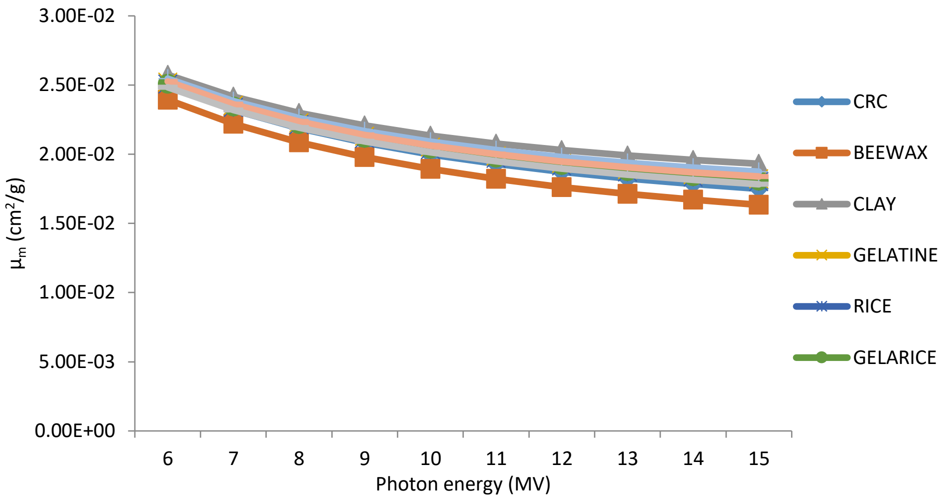

Figure 2. Plot of the theoretical μ_m values of the CRC tissue and the test materials

a – theoretical values between 6 – 15MV; b – experimental values at 6 and 15MV.

Figures 2 - 5 compared the theoretical (XCOM) and experimental μ_m and μ_{en}/ρ values of CRC to those of the test materials against photon energy. The μ_m and μ_{en}/ρ values of all the materials were closer to each other at 6 – 9MV and at 6MV for the theoretical and experimental methods respectively than at higher photon energies. The plots also showed that the μ_m and μ_{en}/ρ values from both methods were decreasing with increasing photon energy for all the materials. Of all the test materials, the μ_m and μ_{en}/ρ values of bewaclay was closest to that of CRC tissue while that of clay was the farthest for both methods.

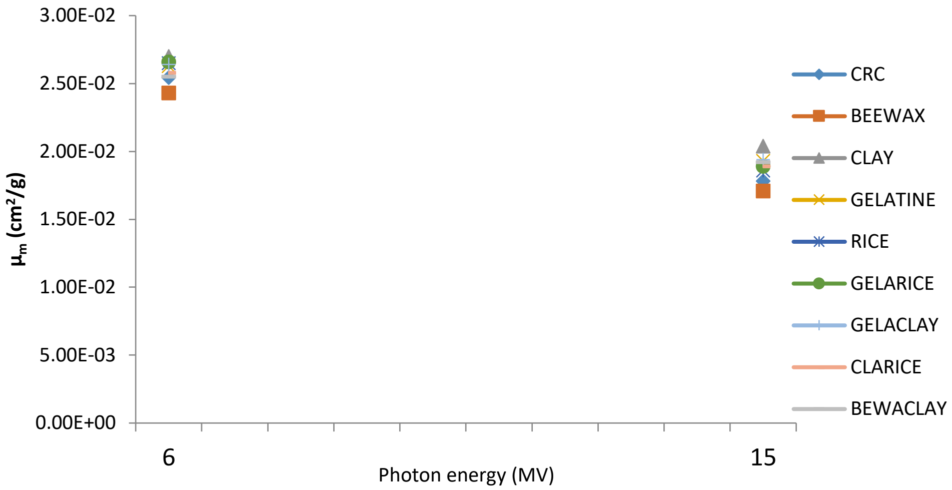

Figure 3. Plot of the experimental μ_m values of the CRC tissue and the test materials

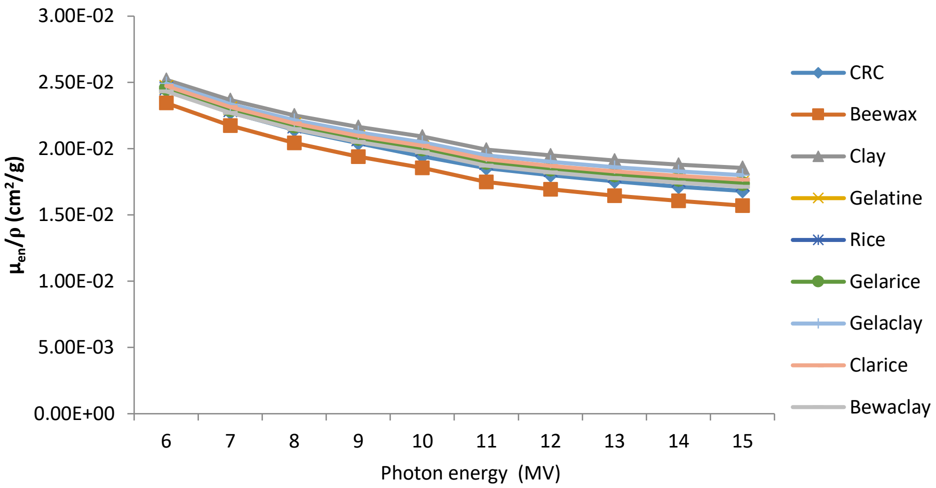

Figure 4. Plot of the theoretical μ_{en}/ρ values for the CRC tissue and the test materials

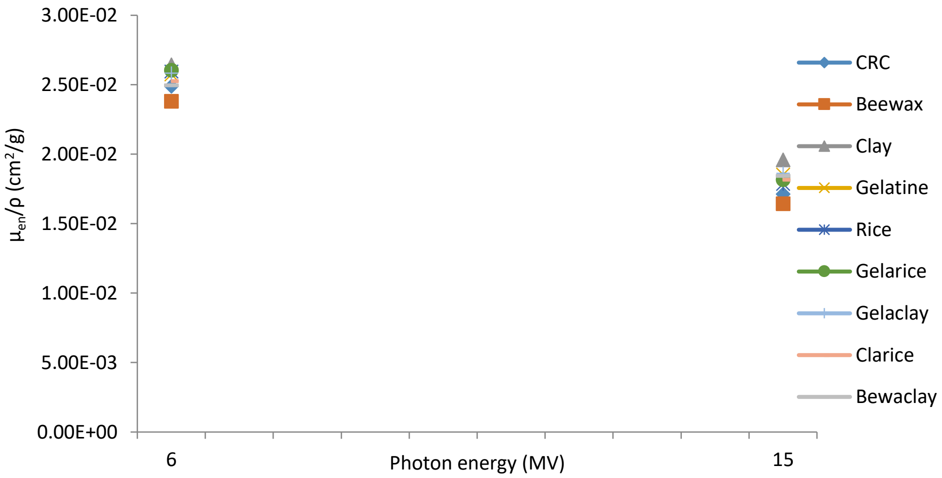

Figure 5. Plot of the experimental μ_{en}/ρ values of the CRC tissue and the test materials

Figures 6 – 9 depicts the degree of match of the μ_m and μ_{en}/ρ values of the test materials to those of the CRC tissue against photon energy. From the plots, the ratios of the μ_m and μ_{en}/ρ values of the test materials to that of the CRC tissue were increasing with increasing photon energy for all the materials for both methods except beeswax which was decreasing for theoretical method. Bewaclay showed the best degree of match to the CRC tissue between 6 – 9MV and at 6MV for the theoretical and experimental methods respectively. Beyond 9MV (theoretical method) and 6MV (experimental method), bewaclay like the other materials was deviating from CRC with increasing photon energy.

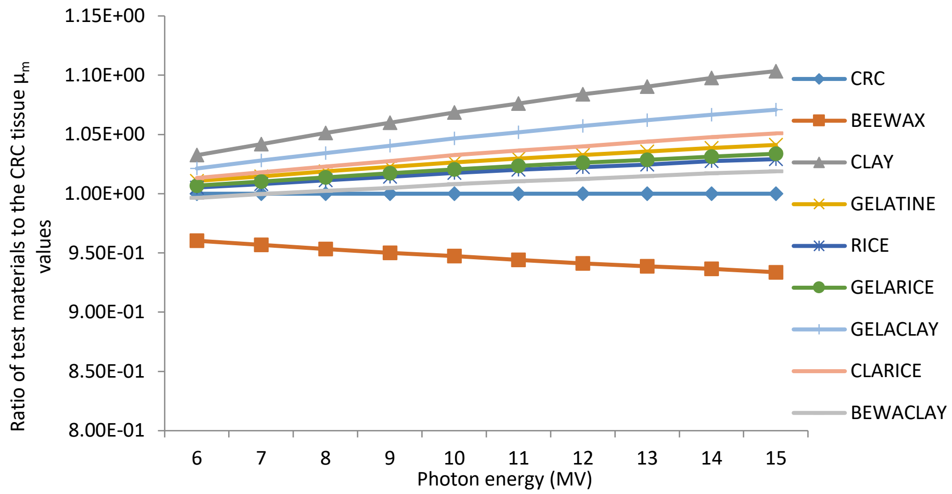

Figure 6. Ratio of the theoretical (XCOM) μ_m values of the test materials to that of the CRC tissue

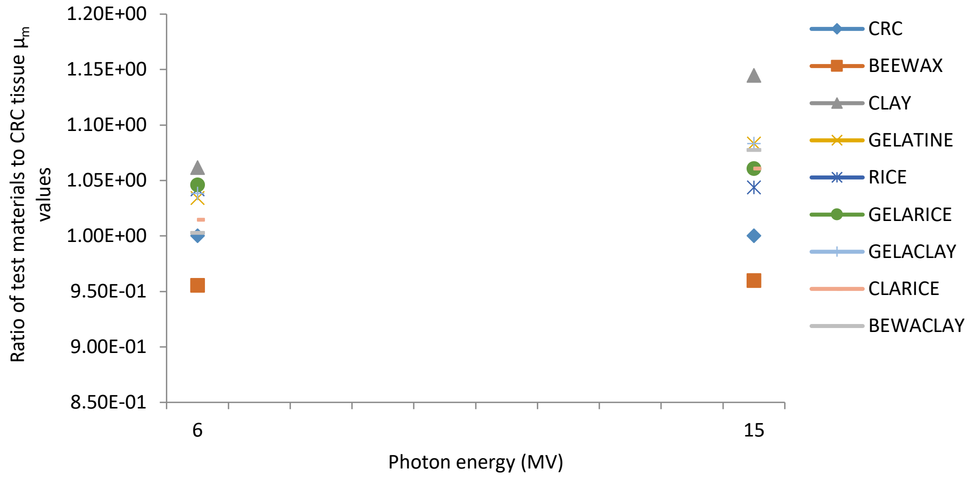

Figure 7. Plot of the ratio of the experimental μ_m values of test materials to that of the CRC tissue

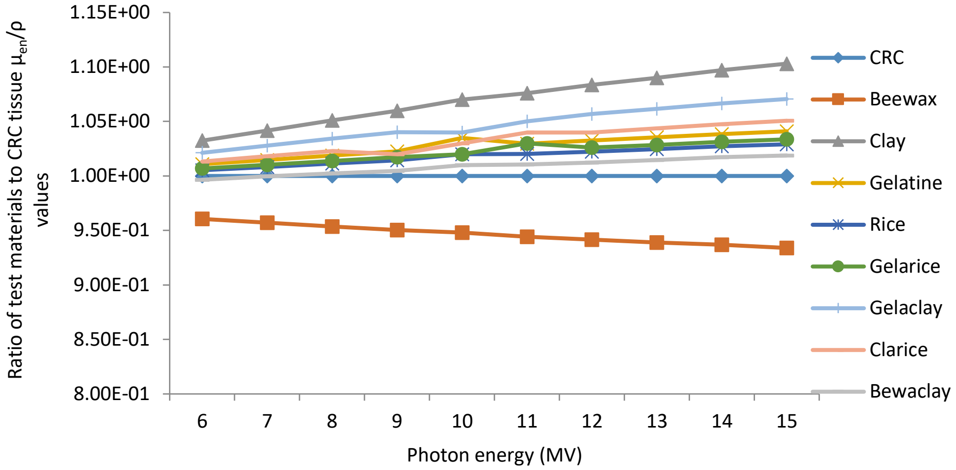

Figure 8. Ratio of the test materials μ_{en}/ρ values to that of the CRC tissue from the theoretical method

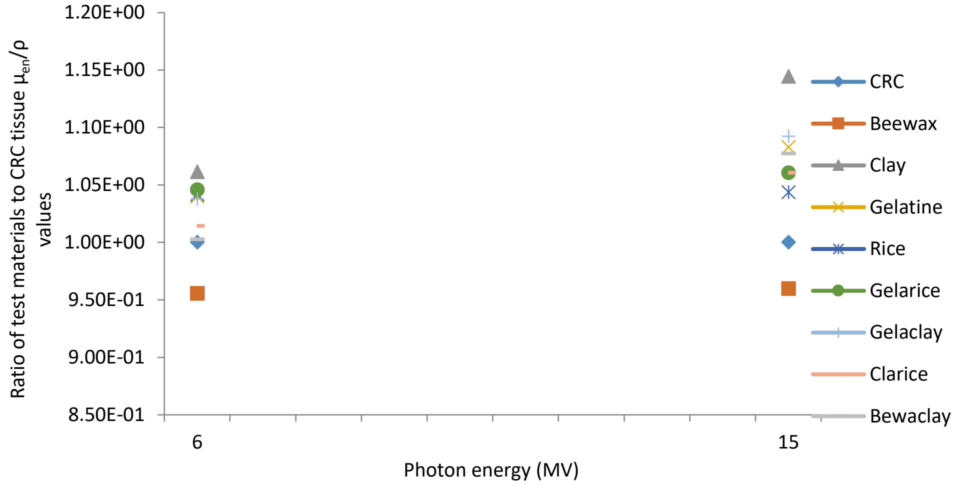

Figure 9. Ratio of test materials μ_{en}/ρ values to that of the CRC tissue from the experimental method.

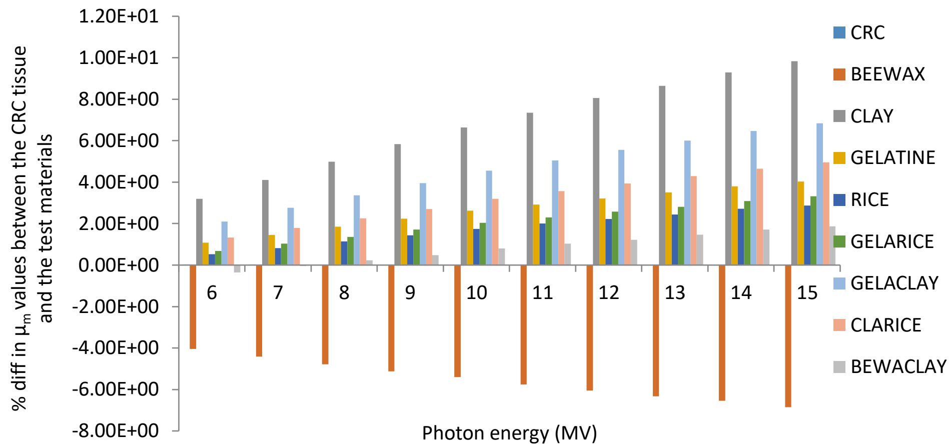

Figure 10. Percentage difference in μ_m values between the CRC tissue and the test materials from the theoretical method

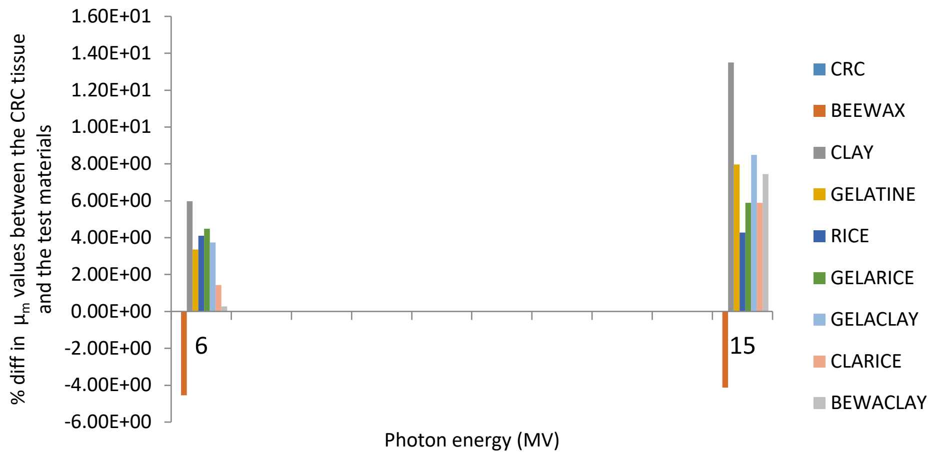

Figure 11. Percentage difference in μ_m values between the CRC tissue and the test materials from the experimental method.

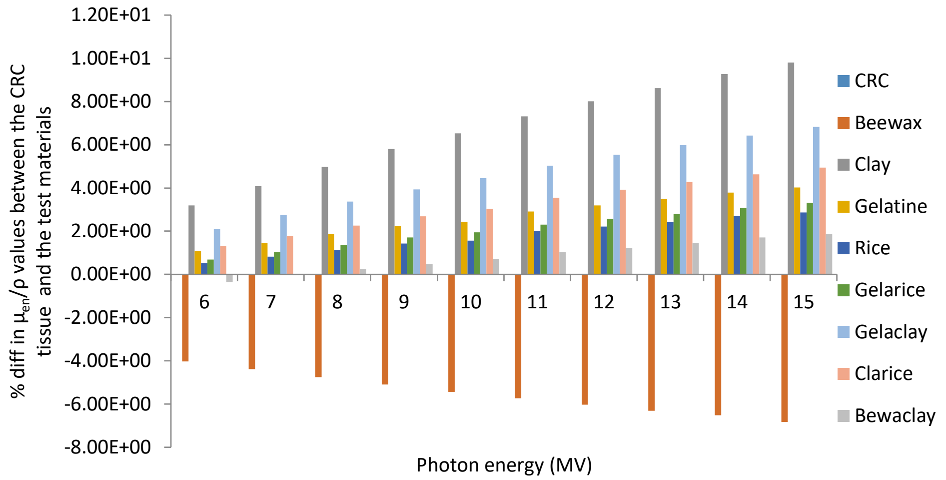

Figure 12. Percentage difference in μ_{en}/ρ values between the CRC tissue and the test materials from the theoretical method

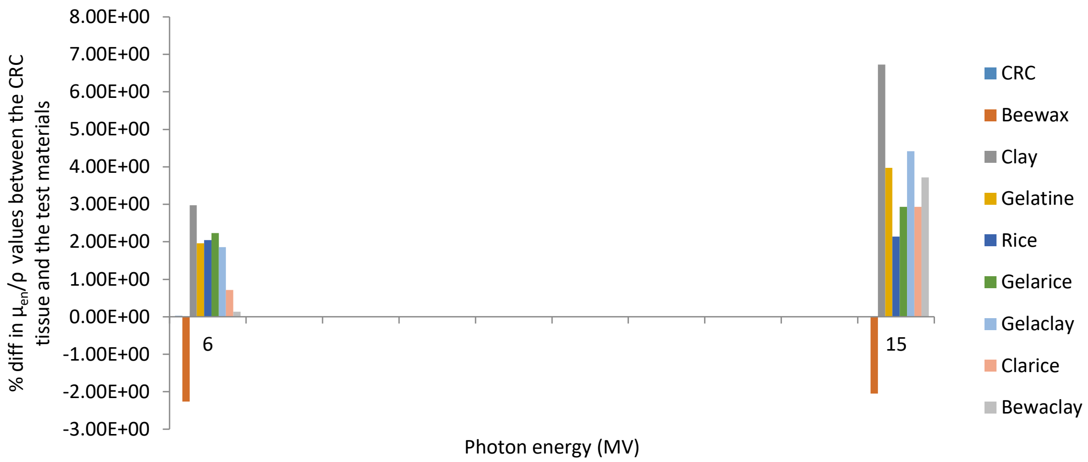

Figure 13 Percentage difference in μ_{en}/ρ values between the CRC tissue and the test materials from the experimental method

Figures 10 – 13 shows the percentage difference in μ_m and μ_{en} values between the CRC tissue and the test materials against photon energy Bewaclay had the lowest percentage difference in μ_m values of about 2% between 6 – 15MV and at 6MV for the theoretical and experimental methods respectively. With respect to the μ_{en}/ρ values, bewaclay still had the lowest percentage difference of less than 3% for both methods. The percentage difference of the μ_m and μ_{en}/ρ between the CRC tissue and the test materials was within 10% and 14% for the theoretical and experimental methods respectively.

Analysis of variance (ANOVA) carried out for CRC tissue and the test materials showed a Probability value of $p = 0.542$ and 0.663 for μ_m and μ_{en}/ρ respectively for the theoretical values, and $p = 0.999$ for the experimental values for both coefficients.

Discussion

In this study, the elemental composition, the mass attenuation and mass energy absorption coefficients of 8 locally sourced materials were matched with those of the CRC tissue. Five of these materials – gelatine, beeswax, rice powder, clay and gelarice (mixture of gelatine and rice) have been previously reported as tissue substitutes for different body tissues [6, 7, 11, 12, 13, 19]. The other materials – gelaclay, clarice and bewaclay are new in tissue simulation studies.

Comparatively, figure 1 revealed that the number of elements detected in beeswax, gelatine, rice powder, and clay were less than those in CRC tissue. This confirms that no single chemical compound can match the atomic composition of body tissues [1, 20]. The combination of these local materials to correct this deficiency resulted in the formulation of the following mixtures – clarice, gelarice, bewaclay and gelaclay. Though the number of elements in these formulations increased, no mixture contained all the elements found in CRC tissue. Gelarice (mixture of gelatine and rice powder) was the closest in terms of the number of elements detected, but still lacked two elements zinc (Zn) and magnesium (Mg) found in the CRC tissue. The elemental composition of gelatine and rice powder from RBS may have accounted for this closeness as CRC tissue contains all the elements in both materials except aluminium (Al) and titanium (Ti) (figure 1).

The decreasing μ_m values of all the materials at higher photon energies indicated reduced attenuation at higher photon energies [21]. From the XCOM attenuation data of these materials, contributions from the interaction processes to the total attenuation coefficient (mass attenuation coefficient) between 6 – 15MV were mainly from Compton scatter and pair production processes. The closer μ_m values of the test materials to that of CRC tissue at lower photon energies indicated good matching [6] and maybe due to Compton scatter. The decreasing trend of Compton scatter with the increasing effect of pair production processes could have accounted for the deviation of the μ_m values of the test materials from that of CRC tissue with increasing photon energy as verified from the attenuation data of these materials. The ratio of the test materials μ_m values to that of CRC tissue revealed bewaclay with the closest degree of match to the CRC tissue between 6 – 9MV and at 6MV for the theoretical and experimental methods respectively. Bewaclay showed a better match compared to gelarice which was the closest to CRC tissue in terms of the elemental composition. This suggests that the elemental composition of these materials was not accountable for the degrees of match of their μ_m values but their radiation interaction parameters confirming that the formulation of tissue substitutes were usually based on their radiation interaction properties rather than their elemental composition [1]. The closer degree of match of μ_m values may have been due majorly to the Compton scatter and the nuclear field values of the pair production process of bewaclay being closer to that of CRC tissue as verified from the XCOM attenuation data of these materials. This implies that bewaclay can be used as a tissue substitute for CRC tissue between the energies of 6 – 9MV with respect to μ_m as the parameter for matching. Beyond 9MV, there was marked deviation from the CRC tissue due to the increasing pair production processes suggesting that none of the test materials could be used as a tissue substitute for CRC tissue at energies higher than 9MV.

Mass energy absorption coefficient (μ_{en}/ρ) accounts for the amount of dose deposited in biological materials [22]. The μ_{en}/ρ values showed similar energy dependence as μ_m at higher photon energies for all the materials confirming that reduction in dose deposition in materials occurs at higher photon energies [23]. The μ_{en}/ρ values of bewaclay also showed the closest degree of match of all the locally sourced materials to the CRC tissue like their μ_m values. This behavior of bewaclay may be due to the dependence of mass energy absorption coefficient on the mass attenuation coefficient. The percentage difference in the μ_m and μ_{en}/ρ values between bewaclay and CRC tissue was about 3% between 6 – 15MV for both the theoretical and experimental methods. This percentage difference is less than that recommended for radiotherapy applications. However, the mixture - bewaclay can be made to achieve better matching with CRC tissue beyond 9MV with improved production methods [6]. Also, a Probability value of $p = 0.542$ and $p = 0.633$ for theoretical values and $p = 0.999$ for the experimental values reveals that the differences between the mean of CRC tissue and the test materials are not significant. This suggests that the radiation interaction properties of these test materials are not different from that of the CRC tissue. With better treatment methods, these test materials can be made to simulate the CRC tissue within the energy range of 6 – 15MV with respect to μ_m and μ_{en}/ρ as parameters for matching.

Conclusion

Gelarice showed the closest degree of match to the CRC tissue based on the elemental composition while bewaclay with the closest degree of match with respect to the μ_m and μ_{en}/ρ values can be used as tissue substitute for the CRC tissue between 6 – 9MV. The utilization of this locally sourced material – bewaclay for the construction of the human CRC tissue phantom would be a cost-effective option considering the cost of imported tissue substitutes and phantoms.

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