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Development, characterization and radiation dosimetry evaluation of Bovine gelatin crosslinked with Gum Arabic Aldehyde as brain phantom gel material in radiation therapy

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ABSTRACT

Brain phantom gel materials are of critical importance for accuracy of dosimetry, treatment planning and quality assurance in radiotherapy. Development of reliable and realistic phantoms enhances improved radiotherapy practices. Gel dosimeters have unique property to record radiation dose distribution in three dimensions. Polymer gels also have added advantages for brachytherapy dosimetry. Objective of the study was to develop an alternative polymeric gel material equivalent to human brain for conducting radiation dosimetry studies in radiotherapy. Hydrogel prepared from gelatin and gum arabic aldehyde was used to develop a brain phantom gel material for radiation dosimetry in radiotherapy. The results of comparative studies with G-GAAB gel strongly suggest, the gel can successfully be utilized as a brain equivalent material for radiation dosimetry in place of standard water phantom by measuring (a) CT number values (b) mass attenuation coefficient values at two X-ray energies used in radiation treatment (c) absorbed dose values at different depths for various setup conditions. The midrange CT number values inside gel material and that of human brain measured from CT images were 25.5HU and 25HU respectively with a variation of 2%. The mass attenuation coefficients for brain, water and gel material at 6MV photons were 0.0275cm^2/g, 0.0280cm^2/g,0.0270cm^2/g and for 15MV photons, the attenuation coefficients were 0.0192cm^2/g, 0.0190cm^2/g and 0.0180cm^2/g respectively. The percentage deviation of all measurements of absorbed dose values in gel phantom material, compared with the values of standard water phantom at various radiation dosimetry setup parameters, is less than 2%.

1. Introduction

Interaction of high energy gamma rays and X-rays with normal tissues of human body can cause harmful effects due to thermal and ionising properties, which may ultimately lead to cancer. Hence it is necessary to evaluate, measure and study the extent of dose distribution of radiation energy in the target tissues before actual treatment is delivered. For radiation dosimetry in radiotherapy, a suitable material is chosen as phantom to be considered as a tissue equivalent material. The phantom material should precisely simulate the interaction of radiation with the specific human tissues, providing reliable data for radiation dose measurements and treatment planning in radiation therapy.

Death rate due to brain tumours has been increased in last thirty years around the world (Irena Ilic and Ilic, 2023; Grech N et al., 2020). Since radiation risk will be high for increased radiation dose, proper dose measurements and quality assurance is highly essential for safe and efficient dose delivery before actual and precise radiation treatment (Ximenes.R.E et al., 2015). Interaction of radiation beam and dose absorbed per unit mass in phantoms must relatively be close to that of respective human tissues (Fisher and Hintenlang, 2006). Water is considered as a universal phantom ideal for dosimetry protocols for its similarity in physical and dosimetry properties with human soft tissues (Khan, F.M. and Gibbons, 2014; Kabir et al). Water is considered as the best substitute as brain equivalent material (Ferreira, C.C. et al., 2010). Tissue equivalent materials should have equivalency factors for radiation absorption and scattering properties similar to radiation interaction

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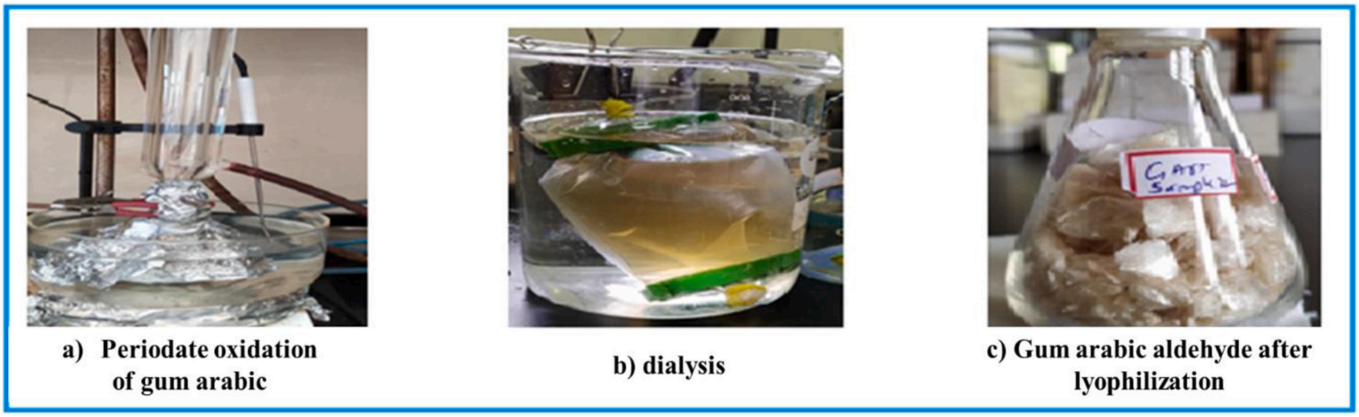

Fig. 1. Various stages of the preparation of gum arabic aldehyde.

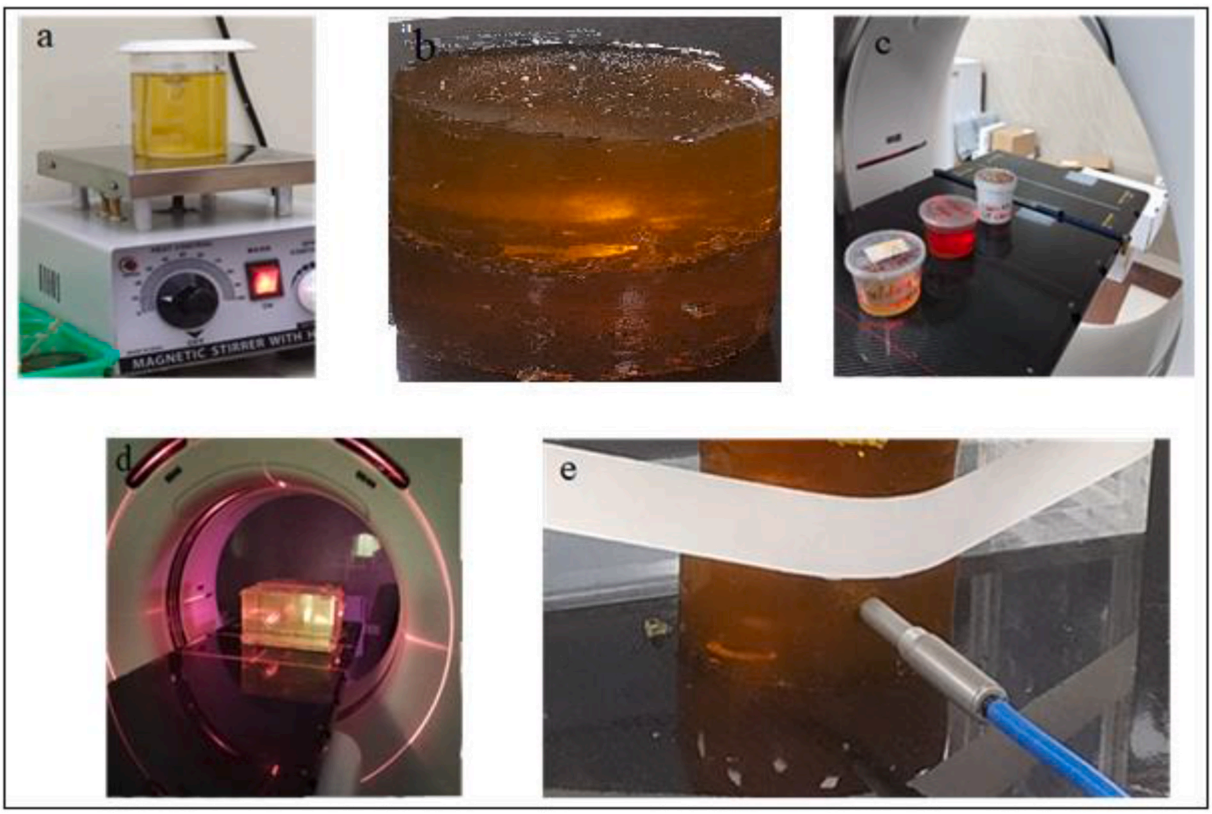

Fig. 2. Preparation and radiation dosimetry studies of G-GAAB gel. **(a)** preparation of gelatin solution, **(b)** G-GAAB gel, **(c)** & **(d)** Imaging of G-GAAB gel in CT sim, **(e)** ionization chamber inside G-GAAB gel.

with water (Valente et al., 2018). Hence, for a particular energy range, the developed material must also have physical and radiological properties similar to that of tissues (Yohannes et al., 2012). Brain tissue is more like a gel material than liquid and the HU value of brain is different than that of water. Thus, radiation attenuation properties inside brain can be evaluated accurately in a gel medium with similar HU values other than water.

Gelatin is a protein made up of a certain amino acid sequence. There are two types of gelatin obtained based on the pre-treatment procedure. Hydrolysis of collagen with acid and alkali results in the formation of type A and type B gelatin respectively. Gelatin is used in medical applications for its negative antigenicity, bio-compatible nature (Sarika P R et al., 2014). Various studies using gelatin as hydrogels and nanoparticles were conducted in the field of medicine and tissue engineering (Saravanan and Rao, 2010; Ching-Li Tseng et al., 2008). Crosslinking process is achieved from the reaction between the functional groups in crosslinking agent and usually in amino groups of gelatin, forming a water-resistant network. In the case of gelatin, crosslinking process with glutaraldehyde, sucrose aldehyde is achieved by the reaction with amino (-NH_2) group of gelatin and aldehyde (-CHO) group of crosslinking agents thereby forming Schiff base (K.Jalaja and Nirmala R James. 2015). Gelatin hydrogels are used as wound dressings and scaffold for cell culture studies (Junpeng.Xu et al., 2019). Gum arabic is a highly branched and complex polysaccharide. It is a mixture of glycoproteins and polysaccharides, predominantly polymers of arabinose and galactose. Complex nature of gum arabic reflect the composition present in brain tissue, as brain tissues contain mainly amino acids, proteins and polysaccharides. In this study, we explored the possibility of utilizing a

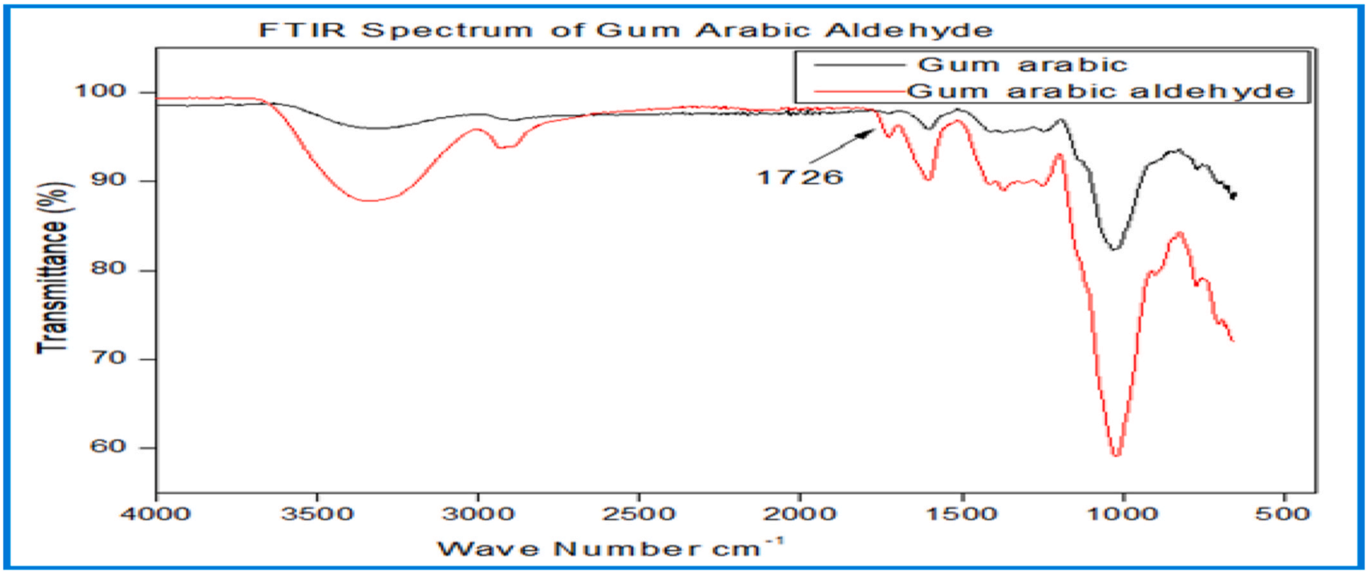

Fig. 3. FTIR spectra of gum arabic (GA) and gum arabic Aldehyde (GA Aldehyde).

Table 1
Properties of gum arabic Aldehyde (Mean ± Standard deviation are reported, n=3).

Test	Result
Degree of oxidation	14±0.38%
Aldehyde content	$2.35\pm0.14\times10^{-3}$mol/g

natural gum, namely gum arabic as cross linker for hydrogel on gelatin. Gum arabic is a biocompatible, nontoxic, water soluble natural gum obtained from acacia tree. Natural bio adhesive properties of gum arabic was utilized for Rhizophora spp. particleboard preparation and studies showed that, gum arabic bonded particleboards can be effectively considered as tissue equivalent phantom material for radiation dosimetry (Ali, 2014).

In this study, Bovine gelatin type-B crosslinked with gum arabic aldehyde in borax solution was developed as a hydrogel material which we named as 'G-GAAB gel'. Gelatin cross linked with various aldehydes is explored in the field of wound dressing, tissue engineering, drug delivery, etc. Since aldehyde group in gum arabic aldehyde create strong bond with gelatin leading to the formation of stable gel material, gum arabic aldehyde was chosen as a cross linking agent. Also, among other aldehyde sources, gum arabic aldehyde-based hydrogels have desirable properties like non-toxicity, water-solubility, eco-friendly, biodegradability, and pH sensitivity. Other aldehyde source like glutaraldehyde was used for cross linking with gelatin which also resulted in strong gel formation. But due to the toxic nature, hyperallergic forming skin and eye irritation, glutaraldehyde was not used for further study. Hence, gum arabic aldehyde was considered for this study. To the best of our knowledge, G-GAAB gel is the first time used for performing dosimetry

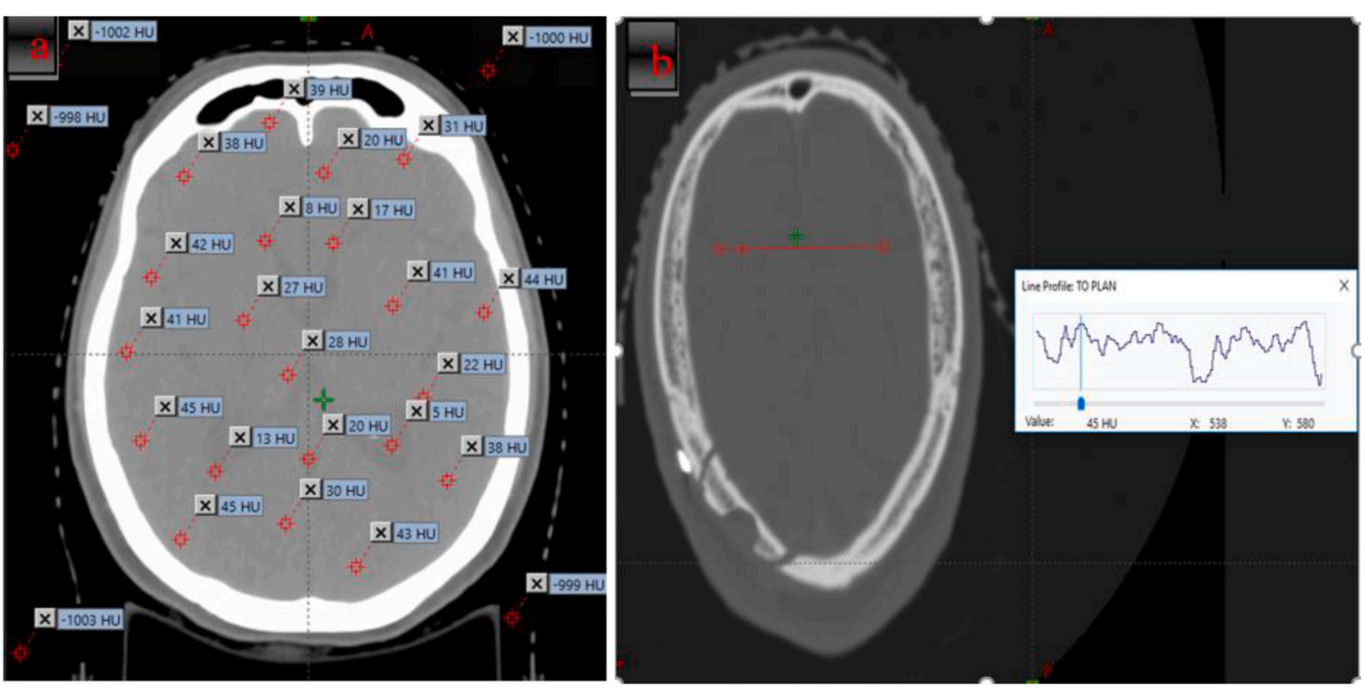

Fig. 4. (a) CT number of brain and air from CT image **(b)** HU line profile of brain from CT image.

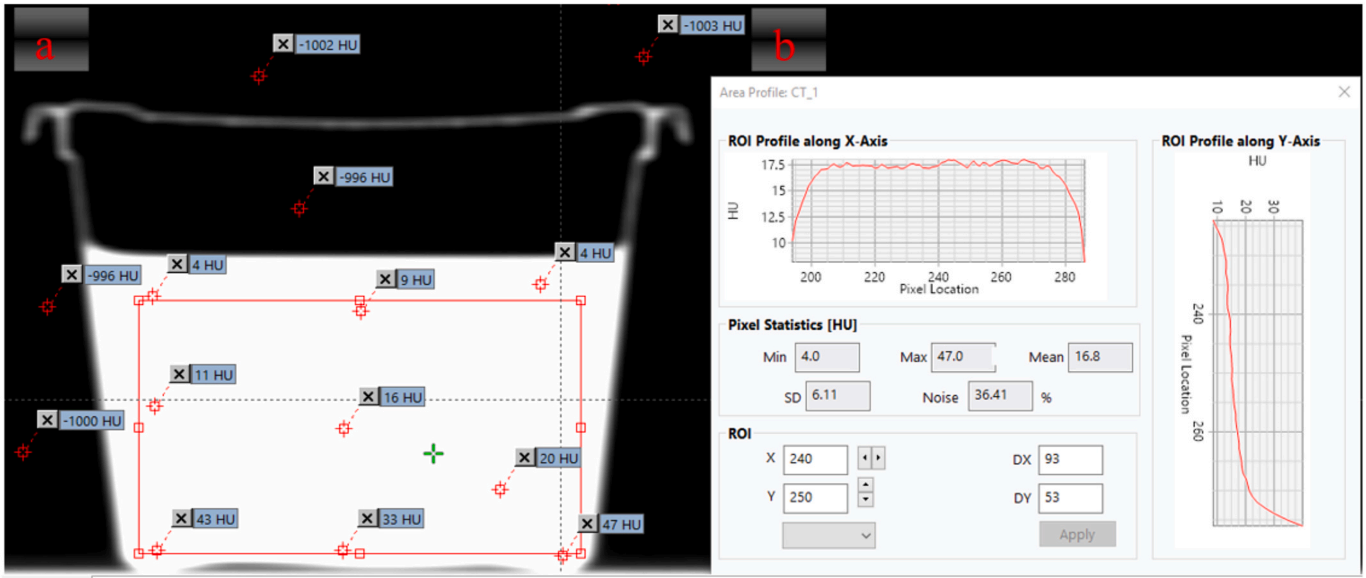

Fig. 5. (a) CT number of G-GAAB gel and air **(b)** HU Area profile of G-GAAB gel.

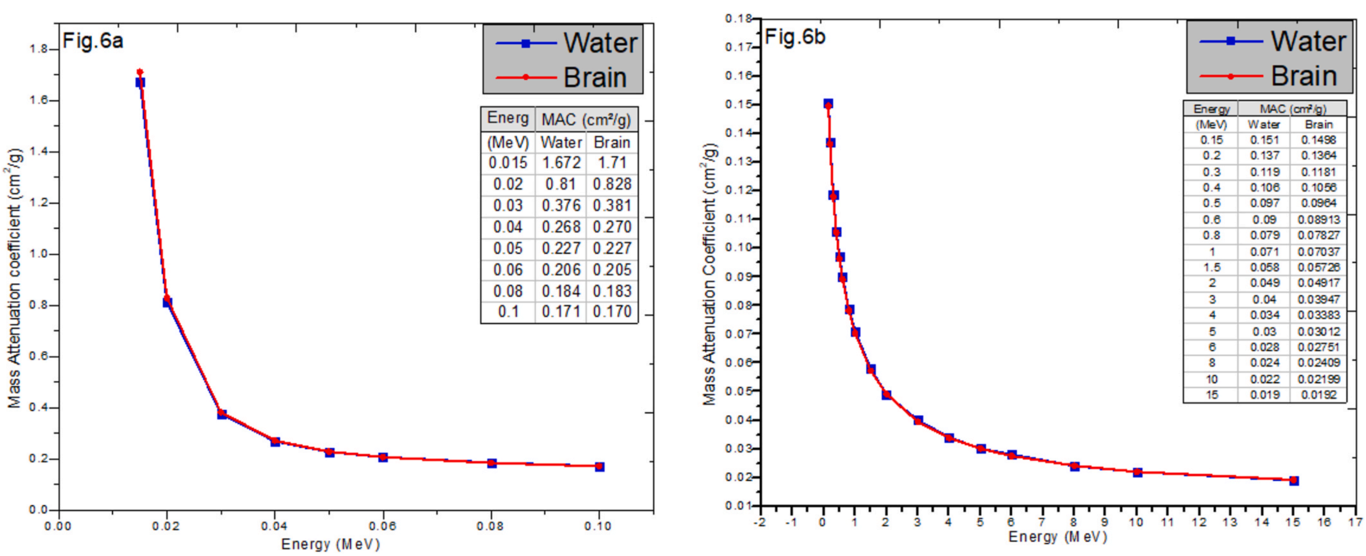

Fig. 6. MAC vs Photon energy, **(a)** for water and human brain in low energy range, **(b)** for water and human brain in therapeutic energy range.

studies as brain phantom material in the field of radiation therapy.

2. Materials and methods

For the preparation of the gel, superior quality analytic grade chemicals were used. Bovine gelatin (Type B), acetic acid and gum Acacia were procured from Sisco Research Laboratories, India, Sigma Aldrich and ISOCHEM, Canada, Dialysis Membrane (MWCO 6000–8000 KD). Periodate oxidation of gum arabic yielded gum arabic Aldehyde (Sarika P R et al., 2014). Gum arabic aldehyde was synthesized using Gum arabic (10g, 0.058mol) and sodium periodate (2.48g, 0.011mol) in water by maintaining a temperature of 20°C for 6h in darkness to achieve 20% oxidation. After the reaction, the mixture was purified by dialysis against distilled water for three days using dialysis membrane. The dialysate was freeze dried after purification to obtain gum arabic Aldehyde. Different stages of the preparation, namely periodate oxidation of gum arabic, dialysis and formation of gum arabic aldehyde are shown in Fig. 1.

Using classical titration, quantity of aldehyde group in oxidized gum arabic was determined (Sarika P R et al., 2014). To a solution of 0.25N hydroxyl ammonium chloride, 0.1g of gum arabic (GA) Aldehyde was added. Hydrochloric acid was released during the reaction between Aldehyde group in GA Aldehyde and hydroxyl ammonium chloride which was titrated using 0.1N NaOH. The end point was determined for colour change using a drop of methyl orange. The amount of sodium hydroxide consumed in the neutralization is equal to the amount of aldehyde in the titration sample. Procedure was repeated with duplicate samples of gum arabic aldehyde prepared. Gelatin solution was prepared by dissolving gelatin in water (25% w/v) at 40°C with constant stirring (Fig. 2a). As the Bovine gelatin dissolved completely the mixture was allowed to cool. For crosslinking gelatin with gum arabic aldehydes, 0.1M borax was used to prepare 10% GA Aldehyde solution to which aqueous gelatin was added with constant stirring. Then the mixture was kept aside without disturbing for the gelation to form. On the onset of gel point, there is a sudden increase in viscosity leading to highly cross-linked gel (Fig. 2b).

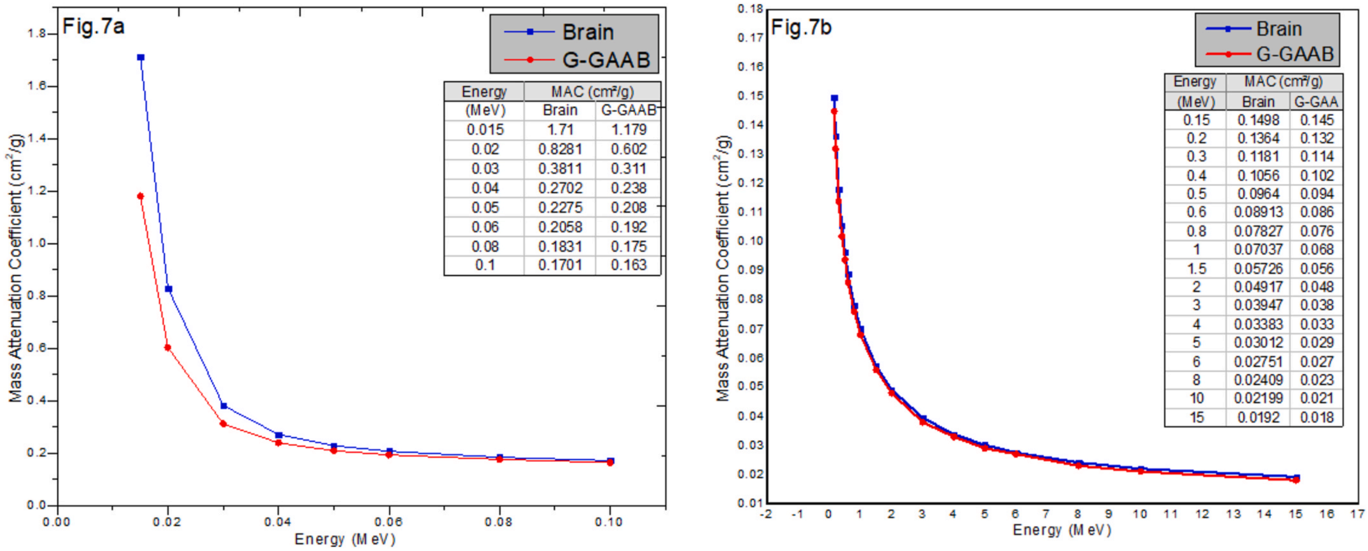

Fig. 7. MAC vs Photon energy, **(a)** for G-GAAB gel and human brain in low energy range, **(b)** for G-GAAB gel and human brain in therapeutic energy range.

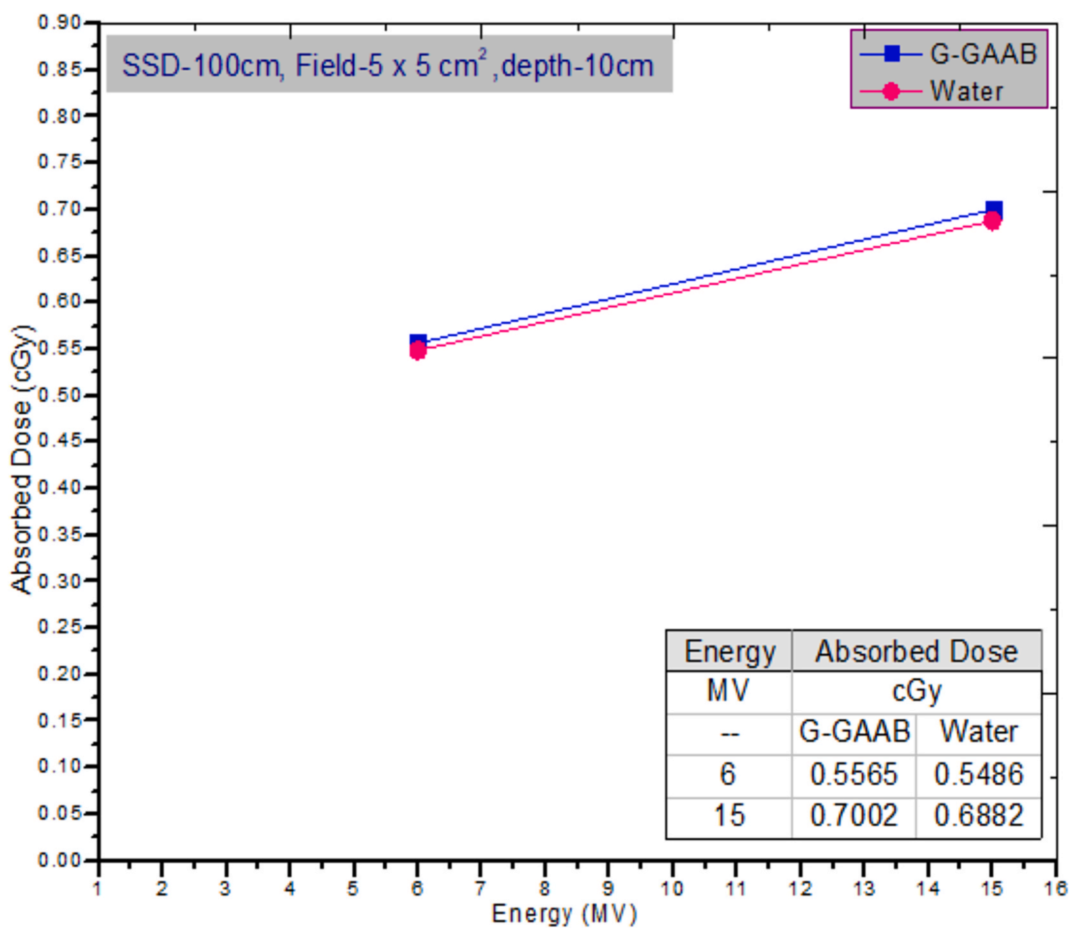

Fig. 8. Absorbed dose vs X-ray Energy for SSD-100cm, FS-5 x 5cm^2, depth-10cm for G-GAAB gel and water at 6MV and 15MV.

2.1. Characterisation and analysis

The characterization of prepared G-GAAB gel was performed extensively for its vital properties. FTIR studies were carried out to confirm the formation of Aldehyde group in Gum Arabic. The FTIR (PerkinElmer, USA) spectrum was obtained with universal attenuated total reflectance accessory (UATR). For each spectrum 35 scans were taken at 4cm^{-1} resolution, in a scanning range of 4000 - 400cm^{-1}. Density of G-GAAB gel was measured using Gas Pycnometer (Microtrac, BELPYCNO L). Radiation dosimetry studies were carried out with calibrated Farmer ionization chamber (PTW, Germany) and electrometer (PTW)with the help of X-rays generated from Linear Accelerator

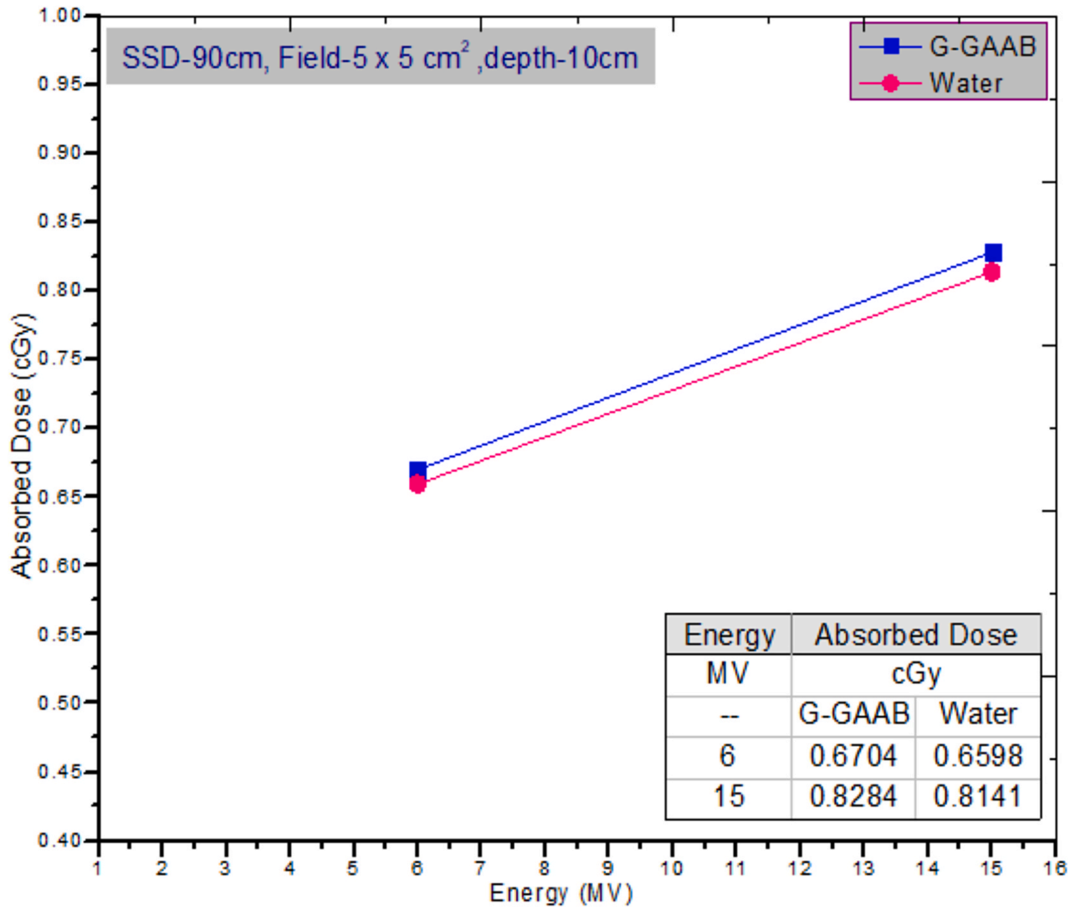

Fig. 9. Absorbed dose vs X-ray Energy for SSD-90cm, FS-5 x 5cm^2, depth-10cm for G-GAAB gel and water at 6MV and 15MV.

(Varian-Clinac-iX, UK). CT number verification was performed using CT simulator (GE-Discovery RT, USA) and treatment planning system (Varian-Eclipse 16.1). Mass attenuation coefficient calculations were carried out with Phy-X software.

2.2. Verification of CT number

CT number or Hounsfield Unit is a normalized value of measured absorption coefficient of X-ray beam in a computed tomogram and a quantitative scale for describing radiodensity (Richard Bibb et al., 2015). CT number is determined using equation (1) and is the relative intensity of the transmitted X-ray beam expressed in Hounsfield Units (HU):

$$HU = \left(\frac{\mu_{material} - \mu_{water}}{\mu_{water}} \right) \times 1000 \quad (1)$$

Where, μ is the X-ray beam attenuation coefficient in the specified media.

For determination of CT number, G-GAAB gel was scanned in the CT simulator (Fig. 2c and d) using standard brain simulation protocol. The gel was aligned with external moving lasers and irradiated with 120kVp tube voltage (Mahur et al., 2017), and scan parameters of 331mA tube current, 0.0625mm slice thickness, FOV 50cm, Pitch of 0.938:1 and 1.8 Noise index were used. The image series was exported to treatment planning work station. Reconstructed image was studied using the CT number values. Measurements were taken at various positions of gel material. CT number, line profile and area profile for CT images of gel material and brain was measured using Eclipse treatment planning system for comparison and analysis. To verify the accuracy in the measurements using software, CT number of air was also measured at various positions around the gel material and brain in the corresponding CT images. Standard CT number of air is −1000HU (Sharma et al., 2006). Contrast medium injected while imaging could affect the accuracy in CT number measurement (Chuang et al., 2020). Hence plain CT images (without contrast medium) of brain were taken for this study. For better CT analysis, CT electron density phantom of Gammex (Tissue Characterization Phantom-Model 467 of diameter 33cm and height 5cm) was used to scan G-GAAB gel which was positioned into one of the spacings of the phantom and exposed with 120kVp. The phantom was scanned and measured the average CT number of G-GAAB gel, brain and water from different slices of CT images.

2.3. Mass attenuation coefficient

Mass attenuation coefficient (MAC) of tissue equivalent material can be derived linearly from its chemical structure. The MAC depends on the energy of photons (Dhammajyot et al., 2017; A. Akar et al., 2006) and its values for brain was first compared with that of water for the energy range 0.015MeV – 15MeV and MAC values of the G-GAAB gel was calculated and compared with that of brain and water. Measurement of MAC was carried out from the Phy-X software (Sakar, E et al., 2019). The Mass Attenuation Coefficient of G-GAAB gel material was compared with water to evaluate its effectiveness as a tissue-equivalent material in dosimetry studies and to determine how well the gel material simulates human tissue in terms of radiation attenuation. This comparison helps in assessing the accuracy and reliability of the gel material for use in dosimetry and treatment planning in radiotherapy.

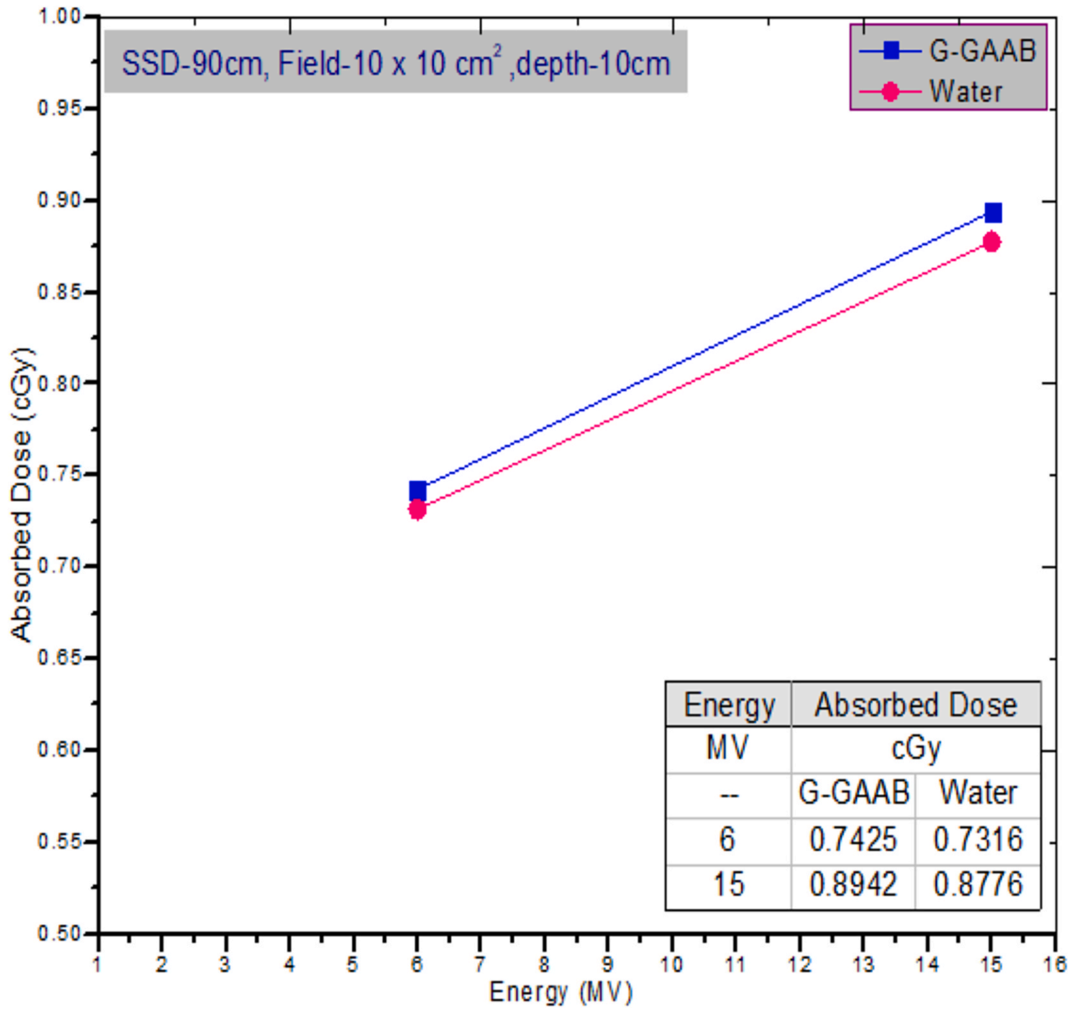

Fig. 10. Absorbed dose vs X-ray Energy for SSD-90cm, FS-10 × 10cm^2, depth-10cm for G-GAAB gel and water at 6MV and 15MV.

2.4. Dosimetry studies on G-GAAB gel

The radiation dosimetry study was carried out in G-GAAB gel kept on carbon fibre couch in Linear accelerator unit (Varian Clinac-iX) using 6MV and 15MV for field sizes 5×5 cm^2 and 10×10 cm^2 at 80cm, 90cm and 100cm SSD in different setup. The 0.6cc Farmer type Ionization chamber (PTW) without build up cap was inserted directly at the depth of study from the surface (Fig. 2e), in the beam central axis and aligned with external lasers. The charge was collected using an Electrometer (PTW Unidose E). Calibration factor for the ionization chamber was 5.393×10^{7}Gy/C. Mode of the electrometer kept at medium and polarizing voltage at +400V. Initial Zeroing was performed and the camber was irradiated with 500MU for warm up before actual charge measurements. X-rays of energy 6MV and 15MV were irradiated to the G-GAAB gel and with the measured charge in nC, absorbed dose was measured for different conditions. Different clinical treatments require different SSDs and field sizes to replicate the actual conditions as closely as possible. As the percentage depth dose depends on depth, field size, SSD and beam energy, different combinations of these four parameters were studied.

For 6MV energy, charge collection was first recorded for 5×5 cm^2, 100MU, 100cm SSD, 300MU/min, time 0.4min and chamber at 10cm depth. Repeated measurements were carried out with this setup. Readings were taken by changing the SSD to 90cm with the same setup. Further. field size was changed to 10×10 cm^2 and readings were taken at SSD 100cm and 90cm by delivering 100MU with dose rate 300MU/min for 0.4min. With the same setup as above, charge measurements were also obtained for 15MV X-ray energy.

Radiation Field Analyzer with distilled water was kept for irradiation and 0.6cc Farmer type Ionization chamber (PTW) inserted into the holder and readings were taken at similar setup as in the case of G-GAAB gel. The values obtained were analyzed and compared.

A beam quality index verification phantom was filled with gel solution and after 4h of gelation time to become G-GAAB gel, ionization charges were measured using farmer chamber under different setup conditions of field size, depths, SSDs and energies in Linear Accelerator and the absorbed dose was measured (IAEA TRS 398).

3. Results and discussion

In the present study, crosslinking agents were synthesized from gum arabic. Different chemical crosslinking agents have been used to achieve cross linking between the polymer chains in a protein. The GA Aldehyde was prepared by periodate oxidation of gum arabic. Sodium periodate is a highly oxidising agent that cleaves the vicinal diols by breaking C2–C3 linkage in polysaccharide with the formation of di-Aldehyde groups (Hongbo et al., 2016). The vicinal hydroxyl groups in the polysaccharide were converted to di-aldehyde. This method is of great importance and advantageous because, percentage of oxidation can be varied by the amount of periodate used.

3.1. FTIR studies

FTIR spectra of gum arabic and GA Aldehyde are given in Fig. 3. Gum

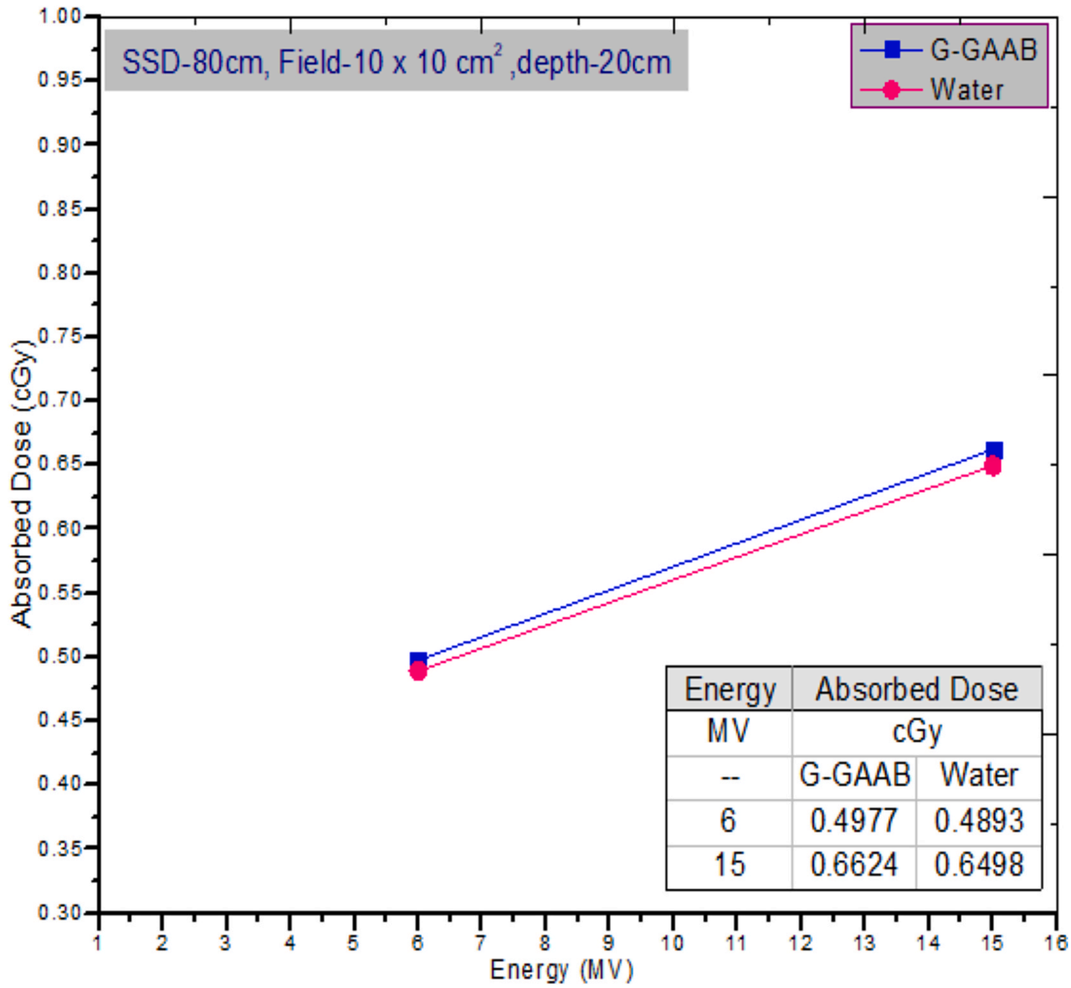

Fig. 11. Absorbed dose vs X-ray Energy for SSD-80cm FS-10 × 10cm^2, depth-20cm for G-GAAB gel and water at 6MV and 15MV.

arabic Aldehyde has all the characteristic peaks of gum arabic and an additional new peak at 1726cm^{-1} which reveals the presence of carbonyl group(C=O) of Aldehyde introduced by the periodate oxidation (Ali et al., 2018).

Percentage degree of oxidation and quantity of Aldehyde were estimated using hydroxylamine hydrochloride test. The Aldehyde content and degree of oxidation were calculated from the amount of HCl released. At the end point, number of moles of NaOH reacted were estimated and was equivalent to the number of moles of aldehyde group and from this, percentage degree of oxidation was obtained. The degree of oxidation of the prepared GA Aldehyde was found to be 14%. The aldehyde content of the sample was found to be $2.35 \pm 0.14 \times 10^{-3}$mol/g. The results are presented in Table 1.

Gelation occurred and smooth hydrogel was formed after 4h. Hydrogels were formed as a result of Schiff's base reaction occurring between Aldehyde groups of GA Aldehyde and free amino groups of gelatin. The prepared gelatin crosslinked with gum Arabic Aldehyde in borax solution (G-GAAB) was used as head phantom gel material for further studies. The same procedure was repeated to prepare a greater number of stable hydrogels. G-GAAB gel was formed due to the Schiff's base cross-linking reaction. The cross-linking reaction is due to the amino groups present in gelatin that reacts with the aldehyde group of oxidized gum arabic, to form C=N which is the Schiff base reaction. To improve the cross-linking reaction, pH of the solution was maintained at 9.1 in presence of 0.1M borax solution (B. BalakrishnanB and Banerjee, 2013). In the present study, crosslinked G-GAAB gel material was prepared by using 10% w/v gum arabic aldehyde in 0.1M borax with aqueous solution of 25% w/v gelatin. Since borax shows complexation ability which will highly enable crosslinking reaction resulting in forming stable gel. During the initial phase of trials, gel with 5% and 10% of aldehyde content were also prepared. But challenges were faced for obtaining stable gel. The gel formed with these concentrations of aldehyde content degraded within 24 – 48h. Hence to improve the stability, degree of oxidation was increased to 20% and concentration of gum arabic aldehyde was also increased to 10% w/v. This resulted in the formation of stable gel.

Density of the synthesized G-GAAB gel, measured in gas pycnometer was 1.034g/cm^3 which closely matches with that of human brain which is 1.04g/cm^3 (International Commission on Radiation Units and Measurements, 1989 Report 44). To verify and analyze the radiation absorption, scattering and dosimetry properties for G-GAAB gel, following studies were performed. CT number of gel material was measured to calculate radiation absorption coefficient in CT image, MAC value was evaluated to understand radiation attenuation characteristics. Charge produced due to ionization was used to calculate the absorbed dose inside the gel phantom material to study the depth dose distribution in gel material.

3.2. CT number

The G-GAAB gel was irradiated in the CT simulator with 120kVp (Mahur et al., 2017), 0.0625mm slice thickness and the image series were exported to treatment planning system through the server of Linear Accelerator. The CT number and area profile for CT images captured for

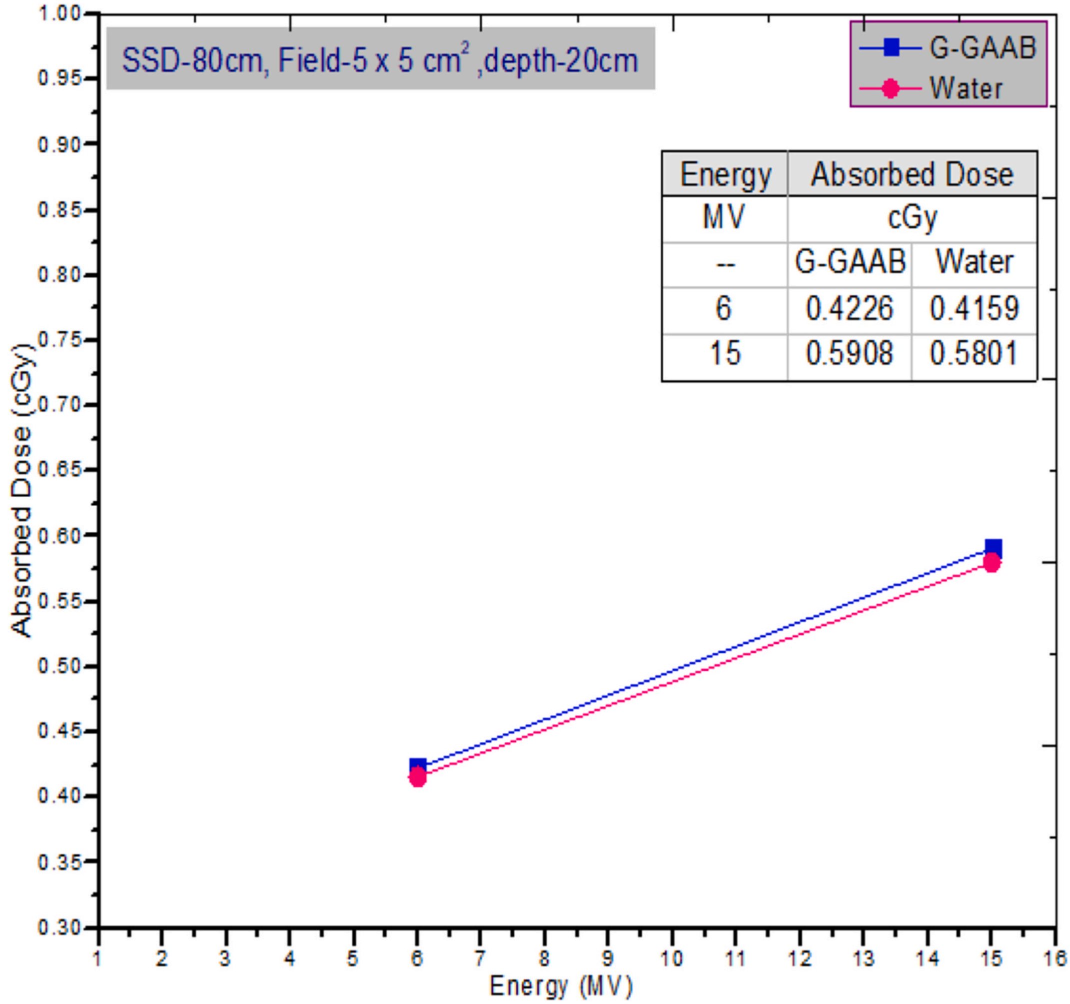

Fig. 12. Absorbed dose vs X-ray Energy for SSD-80cm, FS-5 x 5cm^2, depth-20cm for G- GAAB gel and water at 6MV and 15MV.

G-GAAB gel was measured using Eclipse 16.1 treatment planning system software. To understand the radiation dosimetry characteristics of the developed gel material, study was conducted using CT numbers. CT images of 25 human brains from TPS were taken and CT number at different positions for each image was measured. Similarly, line profile of CT numbers inside brain was also studied for these images. It was observed that, the CT number value for human brains ranges from 5HU to 45HU (Fig. 4a) and line profile of CT number ranges from 11HU to 42HU (Fig. 4b) (McGarry, C. K et al., 2020; Leandrou, 2010; Boris P et al., 1987). These results were compared with G-GAAB gel which showed HU values in the range of 4HU to 47HU (Fig. 5a) and the values obtained for area profile using horizontal, vertical and diagonal positions matched the values ranging from 5HU to 41HU (Fig. 5b). To verify the authenticity of readings, CT number of air was measured around the G-GAAB gel and also around brain images. HU value for air around brain ranges from −998 to −1003 and that around G-GAAB gel was −996 to −1001 (J.A. Bryant et al., 2012) which was very much close to the actual CT number of air −1000HU. (Sharma D S et al., 2006). From the area profile, we measured the flatness of the profile to verify the density uniformity. The mean CT number from the profile was 16.8HU with 6.11 as standard deviation value. Hence the flatness of the profile measured was 0.6363. From the line profile of G-GAAB gel, maximum and minimum CT number measured is 47HU and 33HU. Uniformity index calculated was 0.825. Further the study was extended to measure and compare the midrange value of CT number for G-GAAB gel and human brain and evaluated the amount of percentage variation obtained on using developed G-GAAB gel as brain phantom material. The midrange CT number value obtained for G-GAAB gel was 25.5HU which closely matched with that of human brain having midrange value of 25HU with percentage variation of only 2%. The G-GAAB gel was scanned in Gammex Tissue characterization phantom. As per the specification chart of Gammex phantom, brain material has physical density of 1.051g/cm^3 and electron density relative to water was 1.047. The scanned image of the phantom, with G-GAAB gel as one of the inserts, was analyzed with constant area of measurement for all the tissue inserts and found that, average CT number obtained from different slices of the image for G-GAAB gel and brain phantom insert was 37.44 HU $\pm$ 12.09(SD) and 31.32 $\pm$ 17.59(SD) respectively. The CT number of water plug was observed as 7.15HU $\pm$ 16.91(SD). Above results prove that the developed G-GAAB gel material can be efficiently utilized as an alternate brain equivalent phantom material for radiation dosimetry.

3.3. Mass attenuation

MAC values of G-GAAB gel and that of water and brain are plotted with MAC in Y axis versus X-Ray energies in the range 0.015MeV – 15MeV in X-axis. Measurement of MAC was carried out from the Phy-X software program (Sakar et al., 2019). The Mac values of brain was first compared with that of water and found that, for energy range 0.015MeV – 15MeV, MAC ranges from 1.7100cm^2/g to 0.0192cm^2/g for brain and 1.6720cm^2/g to 0.0190cm^2/g for water respectively. It is evident that, the MAC values of brain and water have insignificant variation at very low X-Ray energies (Fig. 6a) and for high energies, both values in the graph coincide from 3MeV – 15MeV (Fig. 6b). MAC of Gel material when

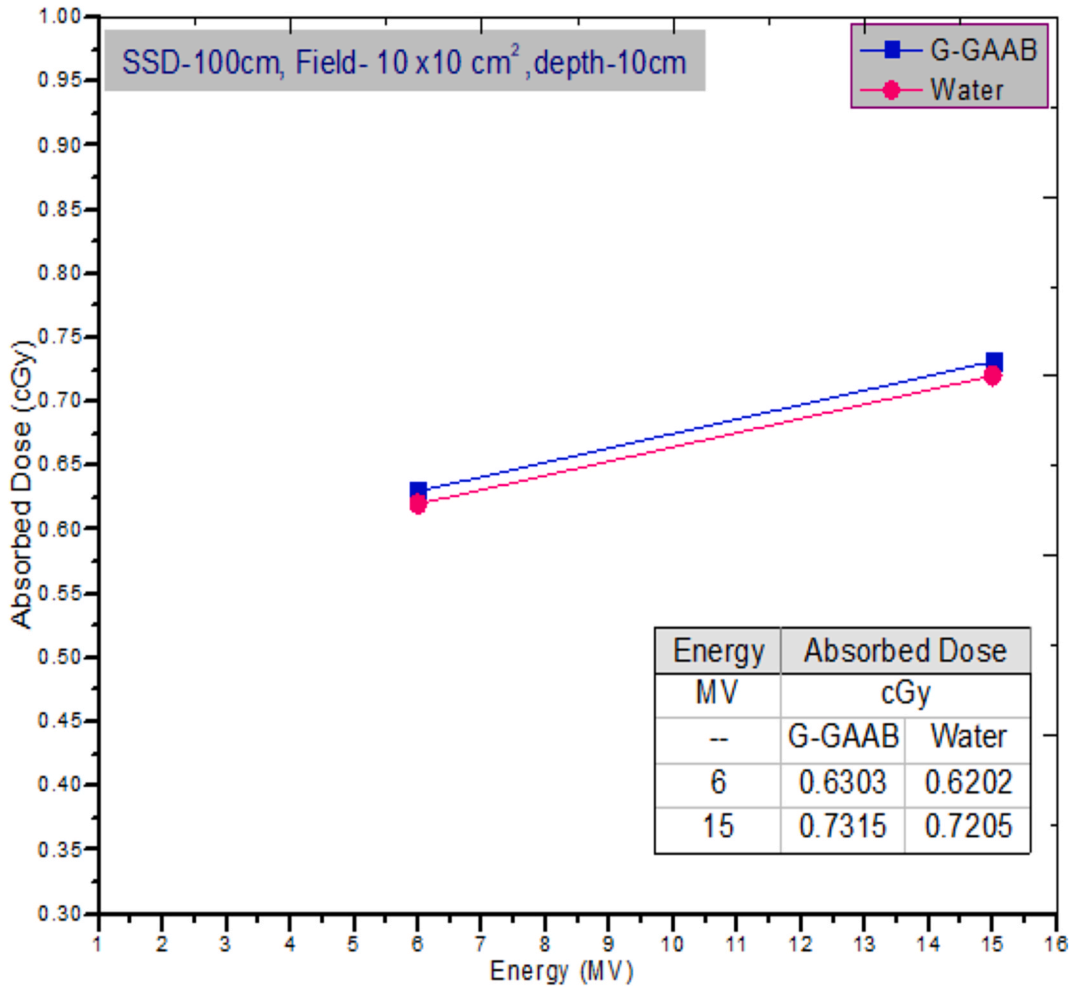

Fig. 13. Absorbed dose vs X-ray Energy for SSD-100cm, FS-10 × 10cm^2, depth-10cm for G-GAAB gel and water at 6MV and 15MV.

Table 2
Comparison of absorbed dose measurements in G-GAAB gel with that of water at various practical therapeutic setup conditions (Mean ± Standard deviation are reported, n=5).

Energy	6MV						15MV					
SSD (cm)	80		90		100		80		90		100	
FS (cm^2)	5 x 5	10 x 10	5 x 5	10 x 10	5 x 5	10 x 10	5 x 5	10 x 10	5 x 5	10 x 10	5 x 5	10 x 10
Depth (cm)	20	20	10	10	10	10	20	20	10	10	10	10
Avg. charge (nC) at+400V	7.621± 0.007	9.130± 0.007	12.438± 0.008	13.646 ± 0.015	10.316 ± 0.005	11.456 ± 0.019	10.919 ± 0.001	12.314 ± 0.008	15.589 ± 0.014	16.691 ± 0.004	12.971± 0.003	13.591 ± 0.007
Avg. charge (nC) at +200V	7.388± 0.013	9.002± 0.016	12.389± 0.007	13.448 ± 0.008	10.268 ± 0.004	11.198 ± 0.008	10.655 ± 0.005	12.086 ± 0.055	15.486 ± 0.029	16.446 ± 0.02	12.76± 0.012	13.38± 0.007
Avg. charge (nC) at −400V	7.602± 0.008	9.09± 0.001	12.412± 0.016	13.652 ± 0.017	10.29± 0.005	11.401 ± 0.19	10.916 ± 0.003	12.302 ± 0.016	15.572 ± 0.019	6.678± 0.004	12.810± 0.007	13.480 ± 0.001
K_{TP}	1.0036	1.0036	1.0036	1.0036	1.0036	1.0036	1.0036	1.0036	1.0036	1.0036	1.0036	1.0036
K_s	1.0326	1.0141	1.0038	1.0146	1.0045	1.0233	1.0252	1.0189	1.0065	1.0148	1.016	1.0157
K_{pol}	1.0012	0.992	1.001	0.9997	0.9998	1.0024	1.0001	1.0004	1.0005	1.0004	1.006	1.0041
K_{elec}	1	1	1	1	1	1	1	1	1	1	1	1
K_{QQ0}	0.992	0.992	0.992	0.992	0.992	0.992	0.975	0.975	0.975	0.975	0.975	0.975
Absorbed dose(cGy/MU) G-GAAB	0.4226 ± 0.0012	0.4977 ± 0.001	0.6704 ± 0.0011	0.7425 ± 0.002	0.5565 ± 0.0007	0.6303 ± 0.0027	0.5908 ± 0.0002	0.6624 ± 0.0011	0.8284 ± 0.0019	0.8942 ± 0.0007	0.7002 ± 0.0005	0.7315 ± 0.0006
Absorbed dose(cGy/MU)Water	0.4159± 0.0003	0.4893 ± 0.0002	0.6598± 0.0002	0.7316 ± 0.0002	0.5486 ± 0.0001	0.6202 ± 0.0003	0.5801 ± 0.0013	0.6498 ± 0.0003	0.8141 ± 0.0008	0.8776 ± 0.0004	0.6882± 0.0002	0.7205 ± 0.0006
Percentage deviation (%)	1.61	1.71	1.6	1.48	1.44	1.62	1.84	1.93	1.7	1.89	1.74	1.52

compared with that of brain has showed variation at very low energies 0.015MeV – 0.1MeV (Fig. 7a). It was observed that, MAC values for G-GAAB gel and brain in energy range of 0.015MeV – 0.1MeV were 1.1790cm^2/g to 0.1630cm^2/g and 1.7100cm^2/g to 0.1701cm^2/g respectively. Nevertheless, in clinical therapeutic range of 4MeV – 15MeV, G-GAAB gel exhibited similar radiation property of attenuation as that of brain (Fig. 7b).

At 6MV X-ray energy, the MAC values for water, brain and G-GAAB gel were 0.0280cm^2/g, 0.0275cm^2/g and 0.0270cm^2/g respectively and for 15MV photons, the corresponding values were 0.0190cm^2/g, 0.0192cm^2/g and 0.0180cm^2/g.

MAC of G-GAAB gel was also compared to brain equivalent material Perspex. MAC value of G-GAAB gel for 6MV was 0.0270cm^2/g and that of Perspex is 0.0265cm^2/g. For 15MV, corresponding MAC values for G-GAAB gel and Perspex is 0.0180cm^2/g and 0.0181cm^2/g respectively. From the comparison of MAC values of G-GAAB gel with that of perspex in two different X-ray energies of 6MV and 15MV, it was observed that, the values were closely matching with percentage variation of 1.88% and 0.55% respectively.

Therefore, from the comparative study, it was inferred that, the developed gel material exhibited similar radiation attenuation property like that of brain and water in the clinical therapeutic energies, thereby confirming the brain and water equivalency for the G-GAAB gel as brain phantom material.

3.4. Depth dose measurements

The parameters were set for irradiation with two different X-ray energies (6MV and 15MV) at three different Source to Surface Distances (SSD = 80, 90 and 100cm) with two sets of field size (FS = 5 × 5 and 10 × 10 cm^2) for two different depths (d = 10 and 20cm) and measured absorbed dose (cGy/MU in G-GAAB gel and water) using 0.6cc farmer ionization chamber and electrometer. X-Ray energies were delivered using Linear Accelerator machine. The material was held at the temperature of 21°C and station pressure on the day of measurement was 1013mbar. Average of five readings in each was taken with 12 different combinations of above parameters in G-GAAB gel and standard Radiation Field Analyzer water phantom. The graph plotted with absorbed dose versus X-ray photon energy for above mentioned measured parameters are shown in Figs. 8–13 and the results are tabulated in Table 2.

From the results obtained for absorbed dose in G-GAAB gel and standard water phantom it can be affirmed that the depth dose measurements are highly comparable and found that there is a linear correlation between the developed and standard material with variation less than 2%. Hence, the G-GAAB gel can be considered as a pertinent alternative for brain phantom material.

To summarize, Bovine Type B gelatin crosslinked with Gum Arabic Aldehyde in borax solution (G-GAAB gel) was prepared and was subjected to characterization studies for analyzing the presence of aldehyde group, chemical structure by FTIR and gelation time. For understanding the tissue and water equivalency of G-GAAB gel, radiation attenuation and dosimetry studies was conducted using verification of CT number, mass attenuation coefficient and absorbed dose distribution at different depths, field sizes and SSDs, by delivering high energy X-ray photons of 6MV and 15MVusing Linear accelerator. From the chemical analysis, it was clear that, there was sufficient aldehyde group formed in gum arabic aldehyde by periodate oxidation of gum arabic, which was further confirmed by FTIR spectrum. Gelation time also clearly indicated a strong Schiff base bond formed between aldehyde group of gum arabic aldehyde and amino group of gelatin, by forming stable gel within 4h. Further, it was observed that, even after irradiation with high energy X-rays for a period of 5h for three consecutive days, the stability and integrity of gel material was retained and no degradation in cross linking occurred for the prepared G-GAAB gel.

4. Conclusion

The CT number values, CT number area profile measured inside G-GAAB gel material using latest software of treatment planning system (Eclipse 16.1) ranges from 4HU to 47HU with midrange value of 25.5HU which closely matches with the CT number values inside human brain ranging from 5HU to 45HU with midrange of 25HU. The percentage variation obtained in the CT number values of gel material with that of brain is 2%. From the CT analysis using CT electron density phantom, the average CT number obtained from different slices of the image for G-GAAB gel and brain phantom insert was 37.44HU ± 12.09(SD) and 31.32 ± 17.59(SD) respectively.

The calculated mass attenuation coefficient of G-GAAB gel material in the two energy ranges of 6MV and 15MV was highly comparable with that of water and brain. MAC value of gel material for 6MV was 0.0270cm^2/g and that of water and brain is 0.0280cm^2/g and 0.0275cm^2/g. For 15MV, corresponding MAC values for gel material, water and brain were 0.0180cm^2/g, 0.0190cm^2/g and 0.0192cm^2/g respectively.

MAC of G-GAAB gel for 6MV was 0.0270cm^2/g and that of Perspex is 0.0265cm^2/g. For 15MV, corresponding MAC values for G-GAAB gel and Perspex is 0.0180cm^2/g and 0.0181cm^2/g respectively. From the comparison of MAC values of G-GAAB gel with that of perspex in two different X-ray energies of 6MV and 15MV, it was observed that, the values are closely matching with percentage variation of 1.88% and 0.55% respectively.

Hence the radiation attenuation property in G-GAAB gel is similar to that in brain and water in the clinical radiation therapeutic energies. The comparison of MAC values with brain and water helps in better understanding the similarity in attenuation properties of G-GAAB gel as a tissue equivalent phantom material.

Since the CT number studies of G-GAAB gel have similar range compared with that of brain using CT electron density phantom and CT number area profile, G-GAAB gel can be effectively considered as a brain phantom gel material in place of water for dosimetry studies in radiation therapy.

The measured charge due to ionization and calculated absorbed dose for each measurement at various factors inside the G-GAAB gel phantom material was measured for verification of depth dose in gel material and the results shown a linear correlation with that of the values obtained from standard Radiation Field Analyzer water phantom for reference dosimetry and the measurements in beam quality index verification phantom used for radiotherapy QA. The absorbed dose values measured in G-GAAB gel and in water phantom showed an insignificant deviation less than 2%. Hence from the above-mentioned results, the gel material in this study, Bovine gelatin crosslinked with Gum Arabic aldehyde in borax solution (G-GAAB gel), can be prepared commercially as it is cost effective and can be used as a new brain phantom material for dosimetry studies in radiotherapy as it will be useful and necessary to evaluate the dose deposition and distribution in brain before the actual radiation is delivered for treatment. As next phase of this study, variation of dose and comparison of different dosimeter responses to verify the dose characteristics in the fabricated G-GAAB gel will be conducted.

The initial concentrations (5% and 10% aldehyde) resulted in poor gel formation with less physical stability. Hence, dosimetric studies could not be performed with the gel in these concentrations. Hence, as future perspective, the rigidity function of gel material to withstand high energy radiation will also be carried out by increasing the degree of oxidation to obtain highly stable crosslinked gel.

CRediT authorship contribution statement

T. Niju Thankachan: Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Nirmala R. James:** Writing – review & editing, Visualization, Validation, Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Jojo P. John:** Writing – review & editing, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Conceptualization. **B.R. Bijini:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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