Fabrication and Determination of Radiation Sensitive Features of Tissue Equivalent Gels in Radiation Dosimetry and Diagnostic Radiology

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Abstract
Various types of gel dosimeters have been developed so far, but two types, polyvinyl alcohol (PVAL) gel and MAGIC gel, have been abundantly applied in medical physics research. This work is divided into two parts. First, this study aims to analyze an ultrasonic imaging device for accurate patient positioning and organ motion detection during prostate radiotherapy. The images of gel were taken before and after the irradiation, using CT, ultrasound and MRI and dose profiles were plotted. This gel will be used as a prostate phantom for the applications in trans-rectal ultrasound imaging. Secondly, this work aims to develop a realistic artificial breast using PVAL gel. The gel was X-rayed on a digital mammography machine which has 3 different programs which will select 3 different beam energies. Results for 2 sample thicknesses were compared against Perspex. PVAL gel was confirmed to be a close match to the Perspex for three beam energies.

Keywords: Magic Gel, PolyVinyl Alcohol (PVAL) gel, Magnetic Resonance Imaging (MRI), Realistic Artificial Breast, Ultrasound Imaging Probe

1. Introduction
The treatment of cancer through radiation is possible by gamma rays, X-rays, electron beams, and proton beams; but the key issue in cancer treatment is imaging. It is never possible to achieve desired outcome unless the target volume is highlighted in a better contrast. The radiation therapy physics is advancing towards an optimal goal, that is to improve accuracy where necessary and to reduce uncertainty where possible. Currently, applied methods in radiation therapy can provide dose distribution to the target volume with great precision and accuracy (Novotny Jr, J., Spevacek, V., Dvorak, P., Novotny, J., & Cechak, T. (2001). It should be noted that any inaccuracy or miscalculation in radiation dose delivery may end up in either depleted dose to target volume or an excessive dose to surrounding normal tissues. Therefore, determining the 3D dose distribution in phantom prior to radiation therapy can reduce any possible inaccuracy (Abtahi, S. M., Zahmatkesh, M. H., & Khalafi, H. (2016), Farhood, B., Geraily, G., & Abtahi, S. M. M. (2019). Despite the fact that standard dosimeters like ion chamber, thermoluminescent dosimeter (TLD), and radiographic film dosimeters, calculate radiation dose in one or two dimensions only, a dosimeter is needed which can calculate three-dimensional dose distribution with high resolution to verify dose distributions of
modern radiation therapy techniques (Dhakal, R., Yosofvand, M., & Moussa, H. (2021). Gel dosimeters have superior characteristics, notably in conditions in which conventional dosimeters can’t be used (Dhakal, R., Yosofvand, M., & Moussa, H. (2021). Few of these properties include the potential of measuring complex three-dimensional dose distribution, integration of dose during the process of treatment, radiation direction independency, radiological tissue equivalence, and high spatial resolution, (Abtahi, S. M., Zahmatkesh, M. H., & Khalafi, H. (2016). Abtahi SM, Aghamiri SM, Khalafi H.). Additionally, gel dosimeters are comparatively safe to manufacture and handle, even though there are few toxic components, inclusive of acrylamide that need to be implemented with suitable protection (Dhakal, R., Yosofvand, M., & Moussa, H. (2021). These properties may be examined through magnetic resonance imaging (MRI), Optical scanning, computed tomography (CT), and ultrasonography (Maryanski, M. J., Gore, J. C., Kennan, R. P., & Schulz, R. J. (1993), Hils, M., Audet, C., Duzenli, C., & Jirasek, A. (2000), Gore, J. C., Ranade, M., Maryanski, M. J., & Schulz, R. J. (1996), Mather, M. L., Whittaker, A. K., & Baldock, C. (2002). Gel dosimeters are widely employed in fundamental dosimetry which include wedge dose profile, depth dose, penumbra etc. These dosimeters have gained widespread acceptance and implementation in measuring dose distribution from various radiotherapy techniques such as 3DCRT, IMRT, VMAT, dose distribution around different brachytherapy sources, dose distribution from imaging procedures, and computation of tissue heterogeneities such as air and bone (Kozicki, M., Berg, A., Maras, P., Jaszczyk, M., & Dudek, M. (2020), Atiq, M., Atiq, A., & Buzdar, S. A. (2017). The major aim was to address the issues regarding a better diagnostic physics using gel dosimetry which is a diversified get-together of physics, chemistry and medicine. It is never possible to measure the radiation absorbed dose in real patient, so the phantoms are used in this purpose to act as dummy patients. The intention of this work was to explore the various physical properties of tissue equivalent gels and to evaluate their diverse applications. This could resultantly lead to develop not only dosimetric phantoms but also artificial organs for better imaging and surgical advantages. This work is divided into two parts.

Prostate cancer is the most common cancer among men in western countries. Patients in which the cancer is restricted to the prostate and are classified as low risk of spreading are considered suitable for external beam radiotherapy. However, there are chances of radiation exposure to healthy tissues i.e. bladder and rectum. The risk can be minimized by accurately locating the target volume. Presently surgical implant markers are used for this purpose but this is an invasive and uncomfortable procedure which carries a risk of infection, adds cost, and can be susceptible to errors due to marker migration and gland deformation. This project aims to build a novel ultrasound imaging probe for that purpose. The probe will be inserted into the rectum during treatment to position it adjacent to the prostate for accurate localization and a detailed view. In this part of the project, it is aimed to investigate the effects of IMRT planning with transrectal ultrasound (TRUS) scan placed in the rectum. It is aimed to design a gel phantom which will be used to measure the radiation dose distribution, so that the effect of probe material in the interaction of different TRUS probe design with IMRT beam will be investigated. The phantom will also be helpful to explore the incorporation of the prostate motion tracked by TRUS probe.

Secondly, diagnosis of breast cancer using x-rays is complicated task and x-ray guided issue sampling procedures require high levels of training to ensure that patients and staff
are kept safe, each patient's dignity is preserved, and accurate diagnoses are consistently established. Some artificial breasts are available in the market to aid the training of these procedures, but none accurately mimics the whole spectrum of challenges encountered during a single procedure. Using a recently developed material which closely resembles breast tissue, we aim to construct an artificial breast which is similar to a real breast both in terms of how it compresses during x-ray mammography and in the x-ray images it produces. The breast is to be molded into an authentic shape, covered in a realistic rubber skin and mounted onto the chest of a mannequin to allow the demonstration of patient positioning. It will be possible to sample the artificial breast with specialized needles as we do with real breast lesions. The artificial breast will contain a selection of items which resemble genuine breast abnormalities on x-rays and can be sampled. Successful sampling of these items will then be confirmed using further x-rays, as we do in practice.

2. Methods and Materials
2.1 Preparation of MAGIC Gel
The phantom needed for dosimetry should have a number of distinct characteristics, both in its mechanical behavior and in its imaging compatibility. The Normoxic MAGIC gel was prepared with the method as shown in Table-1, described by Fang et al (Fang, P. M., Keil, D. C., Does, M. D., & Gore, J. C. (2001). It should show significant potential as radiation dosimeter. Ideally the X-ray attenuation, optical, and mechanical properties of the gel are needed to be tested to closely match with the target tissue characteristics. The dose response can be varied by altering the precise composition of the gels.

| COMPONENT            | AMOUNT (G) |
|----------------------|------------|
| GELATIN (300 BLOOM)  | 80         |
| METHACRYLIC ACID     | 90         |
| ASCORBIC ACID        | 0.352      |
| CuSO$_4$.5H$_2$O     | 0.02       |
| HYDROQUINONE         | 2.0        |
| WATER (HPLC GRADE)   | 828        |

For a one litre batch of 9% MAGIC gel, the process begins by placing 700 ml of water and a magnetic stir-bar in a glass flask and next adding 80 b of gelatin. After the gelatin was swelled from soaking, the flask is heated to 50°C to ensure that the gelatin is completely dissolved. At this point 2.0 g of hydroquinone in 48 ml of HPLC grade distilled water was added and the solution is allowed to cool. When the solution was cooled to 37 °C, the appropriate amounts of ascorbic acid (0.352 g in 50 ml of water), CuSO$_4$.5H$_2$O (0.2 g in 30 ml of water) and 90 g of methacrylic acid were added to the flask. The solution was allowed to stir until the mixture was homogenously dissolved. The 3 % and 6 % MAGIC gels were made in the same fashion.

However, we intended to measure the dose distribution in gel, not only by MRI and Optical CT, but also interested to evaluate whether qualitative electrographic methods offer potential for imaging dose in radiation sensitive gels based on radiation-induced stiffness contrast. Tissue equivalence of the gel was determined by measuring the
physical density of the gel at room temperature. Gel was kept in a container (Nalgene LabWare Styrene-Acrylonitrile Utility Boxes 5700-0750) of size 129x75x105 mm³.

2.2 Irradiation
The gels were stable in the absence of radiation. Once the gel sample temperature had equilibrated to room temperature, it can be irradiated, for particular prostate plan. The phantom will be taken through the entire treatment planning procedure as though it were an actual patient. An IMRT treatment plan is designed to conform to the desired dose constraints.

2.3 Imaging
Phantoms that are visible in multiple imaging modalities are valuable, because they do not restrict their use to just a single type of image-guided procedure (Hungr, N., Long, J. A., Beix, V., & Troccaz, J. (2012). However, we extend our investigation to image the radiation dose distribution in phantom which was recorded due to polymerization of gel. In 1993, a polymer gel dosimeter was developed that maintained spatial information following irradiation and could be visualized with the use of MRI (Maryanski, M. J., Gore, J. C., Kennan, R. P., & Schulz, R. J. (1993). The MR or alternate imaging modality will give information about the dose, and this measured dose will be compared with the calculated dose (Eclipse). The techniques suggested by Low DA et.al (Low, D. A., Harms, W. B., Mutic, S., & Purdy, J. A. (1998). can be used for quantitative evaluation of dose distribution by comparing gamma maps and dose profiles.

2.4 Preparation of PVAL Gel
For the preparation of PVAL based gel, the method of Price et.al was followed (Price, B. D., Gibson, A. P., Tan, L. T., & Royle, G. J. (2010). Ethanol-based gels were made by dissolving PVAL, in a solvent made from equal parts by volume of ethanol and water. Gels with PVAL concentration of 10 % w/v (weight-volume) were produced using a 50 % v/v (volume — volume) ethanol solvent. Forty gram of PVAL (Sigma-Aldrich, catalogue 363146) in 400 ml of solvent (50 % v/v ethanol- water) for each gel. Quick fit apparatus was used to prevent evaporation of ethanol during the prolonged heating and stirring of mixture. The reaction vessel was placed on a heating mantle, and covered by a lid containing three access holes. The first of these was fitted with a water cooled condenser. The second was sealed with a thermometer to monitor the temperature of the mixture. The third was fitted with a bung through which the shaft of a stirring rod was placed. Initially the water (200 ml) and ethanol (200 ml) were added to the vessel and stirrer started as shown in Figure 1. The PVAL (40 g) was then added through the access point reserved for thermometer. The heating process started then, and continuously monitored. The mixture was allowed to reach the boiling point, and then the heat was reduced such that the solution remained at this temperature (approximately 83 ° C) but did not boil too robustly. The mixture was heated for almost 90 minutes after boiling point was achieved so that PVAL dissolved completely. After this period, the solution was transferred to the molds of breast shape and solution was allowed to cool for 1 h before being placed in the freezer, at -35 °C, to solidify. After 5 hours, the gel was removed from the freezer and submerged in a 1:1 mixture of ethanol and distilled water for storage.
3. Results and Discussion

Magic gel characteristics

The dose profiles of MAGIC gel were determined using different imaging techniques. The images of gel were taken before and after the irradiation, using CT, ultrasound and M.R. The dose profiles were plotted using IMAGEJ software. A few figures are presented below to highlight the radiation effects and the significance of imaging techniques. Figure 2 and Figure 3 represent the dose profile of central slice, as there were 112 CT slices taken for the evaluation.

Figure 2: Post Irradiation (central slice) Beam Profile for MAGIC gel by CT image
Figure 3: Pre Irradiation (central slice) Beam Profile for MAGIC gel by CT image

The ultrasound image profiles are represented below in Figure 4 and Figure 5

Figure 4: Post Irradiation (central slice) Beam Profile for MAGIC gel by Ultrasound Image
The different batches of MAGIC gel prepared, were stored in rectangular boxes as shown below in figure 6. The physical density of the gel were measured and found to be matched closely with tissue.
The most significant imaging modality to quantify the radiation absorbed dose was Magnetic Resonance Imaging. The polymerization process starts when the gel is irradiated and that process can be mapped with MR images. The images can quantify the dose and also can differentiate between different absorbed doses. The pre and post irradiation MR images of MAGIC gel are presented below in figure 7. The gel was irradiated with 6 MV photon beam, for a field size of 3.5 x 7 —cm.

![Magnetic Resonance Images of MAGIC gel before and after radiation Tl map. Pre (left) and post (right) irradiation](image)

**Figure 7: Magnetic Resonance Images of MAGIC gel before and after radiation Tl map. Pre (left) and post (right) irradiation**

**PVAL gel characteristics**
PVAL gel was prepared exclusively to prepare an artificial breast having physical properties equivalent to tissue. Further it was desired to have the same shape and compressibility to be used as a mammographic phantom.

**Physical Density and coherent scattering**
The physical density of each batch of gel was measured at room temperature. Figure 8 represents artificial breast which is similar to a real breast both in terms of how it compresses during x-ray mammography and in the x-ray images it produces. The attenuation coefficients of the gels were calculated using XCOM and compared with that of water. The ingredients, their percentages in the gel fabrication as well as chemical formula are listed in Table 2 and Table 3, with which the coherent scattering was calculated.
Figure 8: Artificial breast phantom prepared using PVAL gel

Table 2: Composition of 10 % PVAL gel

| COMPONENT      | AMOUNT | CHEMICAL FORMULA | AMOUNT (%) |
|----------------|--------|------------------|------------|
| DISTILLED WATER| 220 ml | H2O              | 0.45       |
| ETHANOL        | 220 ml | CH3CH2OH         | 0.45       |
| PVAL           | 44 g   | C2H4O            | 0.1        |

Table 3: Composition of 15 % PVAL gel

| COMPONENT   | AMOUNT | CHEMICAL FORMULA | AMOUNT (%) |
|-------------|--------|------------------|------------|
| Distilled Water | 220 ml | 1420             | 0.425      |
| Ethanol     | 220 ml | CH3CH2OH         | 0.425      |
| "VAL        | 66 g   | C2H4O            | 0.15       |

Figure 9 compares coherent scattering for 10 % PVAL gel, 15 % PVAL gel and water.
Effect of Heating
A piece of 10 % PVAL gel was heated using a small beaker, placed on a heating mantle. On increasing the heat, gel tapered first and then it started to melt. It was again in gel form almost at 83 °C, which was the boiling point (noted during fabrication).

Covering the Gel
The different piece of gels were wrapped with latex, and silicon rubber, to select a better material which can keep the gel safe, and tolerate the compression well and have least effect of attenuation for radiation.

Effect of Compression
The gel was X-rayed on a digital mammography machine which has 3 different programs which will select 3 different beam energies. Results for 2 sample thicknesses were compared against perspex (converted to tissue equivalent thickness). The PVAL gel was confirmed to be a close match to both the perspex for all 3 beam energies. A couple of other observations like, rough surfaces and variations in gel thickness from the molding pot were clearly visible on the images, even with compression. The 10% PVAL gel reduces in thickness a lot under mid-level compression to half its thickness. After compression was released it remained partially squashed for quite a long time though it seems to have returned to full thickness after putting it in storage pot.

4. Conclusion
The MAGIC gel can be used as a dosimetric phantom and it can quantify the dose accurately. The three-dimensional dose distribution can be measured and dose profiles can be plotted for accurate absorbed dose determination. This normoxic gel will be used as a prostate phantom for the applications in trans-rectal ultrasound imaging during prostate radiation therapy. Further, a breast phantom was developed using PVAL gel for this purpose. The gel was X-rayed on a digital mammography machine which has 3
different programs which will select 3 different beam energies. Results for 2 sample thicknesses were compared against Perspex (converted to tissue equivalent thickness). The PVAL gel was confirmed to be a close match to Perspex for all three beam energies. Rough surfaces and variations in gel thickness from the molding pot were visible on the images, even with compression. The gel reduces in thickness a lot under mid-level compression (to half its thickness). After compression was released it remained partially squashed for quite a long time though it seems to have returned to full thickness after putting in storage pot.

5. References

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