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Review Article

Gel Dosimeters for Radiotherapy: An Introductory Review

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Abstract

A major challenge in radiotherapy treatment is to deliver precise dose of radiation to the tumor with minimum dose to the healthy normal tissues. Recently, gel dosimetry has emerged as a powerful tool to measure three-dimensional (3D) dose distribution for complex delivery verification and quality assurance. Dosimeters currently in use are inadequate for clinical use as they measure one-dimensional (e.g. ion chambers) or two-dimensional (e.g. Radiographic films) dose distribution. There are basically two types of gel dosimeters i.e. Fricke and polymer gels. Fricke gel dosimeters are easy to prepare and are tissue equivalent but their use is limited because of dependence on oxygen concentration. Polymer gels are also sensitive to oxygen contamination however different formulations are used to solve this problem. The review summarizes improvements in gel dosimeter models and different gel compositions that had been proposed. These dosimeters act both as a phantom and detector, thus confirming the versatility of dosimetry technique. In this review imaging techniques most widely used for gel dosimeters. Magnetic Resonance Imaging, X-ray and Optical Computed Tomography shall be evaluated along with their limitations and sensitivity of gels.
Key words: Gel dosimeter, 3D dose distribution, MRI, X-ray CT, optical CT.

Introduction

Radiotherapy treatment techniques, such as Stereotactic Radiotherapy (SRT) and Intensity Modulated Radiation Therapy (IMRT), require accurate measurement of three-dimensional radiation dose distribution to minimize radiation dose to healthy tissues and enhance target dose delivery to the affected tissues. Present clinical dosimeters, such as ionization chambers, Thermoluminescent Detectors (TLD) and radiographic films measure one or two dimensional dose distribution while gel dosimeters measure three-dimensional dose distribution to meet the growing challenges of advanced radiotherapy techniques.[1-3]

Gel dosimetry started with the use of gels containing Folin's phenol, in which color changes were observed when exposed to radiations. Later, agar gels were introduced for the measurement of photon and electron depth doses. Subsequently, Fricke gels were introduced which were later replaced by acrylic monomers and polymers.[4]

The most attractive quality of gel dosimeters is that they act both as a phantom and a detector.[5] Gel dosimeters enable physicists and radiologists to define planar dose distribution with high resolution. Gel dosimeters have been applied to proton beam,[6-7] neutron beam, electron beam,[8] and high energy carbon ion beam.[9] A number of studies have confirmed the versatility of measuring dose distribution in special applications of radiotherapy such as brachytherapy, IMRT and stereotactic radiosurgery.[10-11]

Gel dosimetry involves the use of emerging techniques in which absorbed dose is measured by the use of radiation sensitive gels. This review briefly discusses Fricke and polymer gel dosimeters including their manufacture, imaging, characteristics and limitations of these gels.

Evaluation of tissue in homogeneities

Research in gel dosimetry moves around water equivalence of gels. The water equivalence of gels was found by determining its atomic number, element composition, electron density and mass density.[12] For external beam radiotherapy involving megavoltage beams, it is desirable for the gel to have electron density as close as possible to water. Therefore, gels based on aqueous media are preferred because their radiological attenuation properties are similar to that of tissues. In clinical

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dosimetry, the depth dose response in gels should mimic the same response in patients who are subjected to cancer treatment; therefore, the criterion of a good gel is that its radiation absorption and scattering properties are similar to that of water.[13-15]

Previous studies have revealed electron densities of Fricke and polymer gels within 1% of soft tissues.[16] With growing research in the use of radio sensitive gels, dose distribution behind high atomic number heterogeneities have been estimated to imitate the presence of bones.[17] Recent studies indicated attempts to manufacture gel dosimeters to simulate lung tissues either by producing foam of gel or by introducing polystyrene beads into gel mixture.[18]

Gel Manufacturing and composition

For decades ferrous sulphate (Fricke) solutions have been used in radiation dosimetry. These gels are attractive for 3D dosimetry as they are relatively easy to prepare, yield reproducible results and are tissue equivalent over a wide range of photon energies.[19]

Dose distribution transformation of ferrous ions (Fe^{+2}) into ferric ions (Fe^{+3}) forms the basis of Fricke solutions, which is an acidic oxygenated solution of ferrous ions Fe^{+2}. The chemical reactions account for the conversion of ferrous ions into ferric ions. When this solution is irradiated, there is formation of hydroproxy radical by the reaction of oxygen with the hydrogen atom, which is formed by decomposition of water.

Additional reactions are required for conversion of ferrous ions into ferric ions. Ferric ion concentration is related to energy absorbed by the solution. Constituents needed for typical Fricke gel are ferrous ions, usually obtained from ferrous ammonium sulphate, deionized water, sulphuric acid, gel and oxygen. The gel is required for spatial stability of the radiation induced changes. Chemical probe for the dosimeter is provided by ferrous ion concentration. The sensitivity of gel also depends on oxygen concentration. To prevent the spontaneous conversion of ferrous to ferric ions, Fricke gel solutions should be kept in cool and dark place.[20]

Fricke gel dosimeters are easy to form and can be modelled into different shapes. The dosimetrist properties of Fricke gel are strongly dependent on the gel composition, temperature and measurement conditions like time of measurement and Nuclear Magnetic Resonance (NMR) frequency.[21] Unfortunately Fricke gel dosimeters are limited by poor spatial resolution due to diffusion of Ferric ions after irradiation of solution and consequently dose distribution is blurred. Attempts to reduce diffusion rates can be achieved by adding various gelling agents or chelating agents. The addition of these agents increases the permissible time between irradiation and measurement of dose distribution.[22]

Diffusion problem of Fricke gels was resolved by the introduction of polymer gels which refers to 3D polymer network in a liquid medium. The network of the polymer is cross linked by strong (covalent) or weak (hydrogen) bonds. Preliminary work was conducted using varying concentration of polyacrylamide gel. The principle of operation is radiation induced polymerization and cross linking of N, N′-Methylene bis(acrylamide) and acrylamide.[23] Upon irradiation, acrylic monomers polymerize and their degree of polymerization is dose dependent. A polymer gel contains water and gelatin along with cross linkers and monomers.[24] The gelling agents such as agarose or gelatin are found advantageous as they provide mechanical stability. Spatial dosimetric information is preserved in polymer gels through gelling agents which keeps polymers in their point of formation.[25] As the irradiation properties depend to a large extent on the amount of water so typically 90% of gel constitutes water. When irradiated, highly reactive radicals and ions are formed in the process called "radiolysis".[26]

Oxygen sensitivity is an important issue in polymer gel dosimeters, therefore many attempts were made to remove oxygen. Normoxic Polymer gels were manufactured to solve the problem of oxygen contamination by adding oxygen scavenger.[27] Subsequently, many new formulas were investigated such as MAGAT, MAGAS, PAGAT and PAGAS.[28] Further improvement in gel dosimeter, which can be easily prepared under normal levels of oxygen at room temperature, has been explored by many investigators. The acronym MAGIC has been used for these gels. This formulation consists of methacrylic acid, ascorbic acid (oxygen scavenger), gelatin and copper sulphate.[29]

Composition of 1000g of 9 % MAGIC gels.

Component	*Amount (g)*
Gelatin (300 bloom)	80
Methacrylic acid	90
Ascorbic acid	0.352
$CuSO_4.5H_2O$	0.02
Hydroquinone	2.0
Water (HPLC grade)	828

Recent work includes the development of new class of dosimeters called PRESAGE. This three-dimensional dosimeter consists of optically clear polyurethane matrix, containing a leuco dye and halogen containing free radical indicators. PRESAGE has optical attenuation coefficient that changes linearly with absorbed dose.[30,31]

These gels are more advantageous than Fricke gels because of their stability and non-diffusion properties. On a positive note, these gels are not energy dependent over a large range of photon energies and are also tissue equivalent. Although much advances have been made in this field still Fricke gels are preferred in clinical applications because of the complicated fabrication process and greater cost of polymer gels.[32-33]

Irradiation of gels

With the improvements in radiation therapy, many treatment planning softwares are introduced which compute absorbed dose in 3D space. These sophisticated computational tools reduce the error in intended dose distribution which otherwise could result in incorrect dose to target cells as well as to normal healthy tissue.[34] The monotonous variation in the properties of the gel, when radiation dose is applied, can be calculated using various imaging techniques such as X-rays, optical Computed Tomography (optical CT), ultrasound and Magnetic Resonance Imaging (MRI).[35] To verify complex radiation doses such as in intensity modulated radiotherapy 3D techniques are preferable for systematic analysis rather than 2D techniques such as radiographic films. In gel dosimetry, gels can be designed into humanoid form thus making all anatomical measurements possible. Therefore, gel dosimetry is referred to as a basic tool to measure 3D dose distribution which can be computed by advanced computing softwares.[36]

Before the inception of application of MRI for scanning gel dosimeters in 1984, post irradiation of color changes in dyes was used to measure absorbed dose in gels. A number of researchers has investigated clinical aspects of Fricke gels using MRI and they found that conversion of ferrous ions into ferric ions changes the paramagnetic properties of the gel which can be measured using NMR relaxation measurements. This results in a reduction of spin relaxation times (T1 and T2) of hydrogen nuclei in the aqueous gel. Changes in spin relaxation times are computed using NMR techniques.[37] Dose sensitivity of the gel depends on ferrous sulphate concentration.[38] Diffusion of ferric ions into the gel limits the use of MRI technique for Fricke dosimeters.[39] MRI is used to obtain precise 3D dose distribution of polymer gel dosimeters with high spatial resolution. When polymer gels are irradiated there is a variation in mobility of surrounding water molecules which results in alteration of spin lattice relaxation rate R1 (=1/T1) and spin relaxation rate R2 (=1/ T2). R2 is more sensitive to dose response then R1. Later it was proved that besides relaxation rates R1 and R2, chemical shift and Magnetic Resonance contrast are also used as imaging parameters.[40]

Three dimensional images were obtained using X-ray CT. However, in 1996, Gore et al acquired images using visible light, thus introducing the idea of Optical CT. It works on the principle that when the gel is irradiated, it no longer remains optically transparent to visible light rather it becomes opaque due to polymerization.[41] Evaluation of gels using optical CT is a promising tool for 3D dose verification. Principle on which dose distribution in gels is imaged by CT depends on linear attenuation coefficient of polymer gels after irradiation. Varying intensity results in changes in linear attenuation coefficient. Dose distribution is secured from 3D reconstruction of attenuation coefficient of gel dosimeter. The CT number rises with the increase in absorbed dose. Additionally, by increasing monomer concentration, sensitivity of gel increases. Studies indicated that x-ray CT serve as evaluation tool for measuring dose response of polymer gels and have advantages, which are the availability of economical CT scanners for imaging in-phantom dose measurements in radiotherapy treatments and short imaging times. It is emerging as a good alternative to MRI which is gold standard imaging modality.[42-44] To read out the dosimeters, other imaging techniques besides MRI and CT have also been explored.

Characteristics of gel dosimeters

Many studies have suggested the criteria for reliable dosimeters. Gel dosimeters must have stable and well defined dose response with time, should be tissue equivalent and should be operated in available radiation units. Moreover, a good dosimeter should be independent from environmental factors and changes in spectral range during gel irradiation.[26] Gel dosimeters are affected by factors such as light and oxygen contamination, temperature, concentration of cross linkers, gel pH and gel toxicity. Oxygen contamination degrades the performance of gels by removing free radicals produced by irradiation. Free oxygen must be removed from gels to solve this problem. For many years an appropriate amount of nitrogen was bubbled through gel solution. However problem of oxygen contamination was completely removed by formulation of new gel known as MAGIC gel.[45]

The sensitivity of polymer gels is also affected by changes in temperature.[46] It is therefore important that before irradiation and imaging by MRI, gels equilibrate to a uniform temperature. It has been reported that relaxation rate R2 of the gel increases with pH. Poor reproducibility of dose responses is associated with acidic pH. Besides many other explanations, multi-equilibria proton exchange model was used to indicate the dependence of relaxation rate on pH. It is noted that reproducible pH response is achieved using gel with neutral pH.[47] In spite of enhanced dosimetric capabilities of polymer gels, its use requires careful handling as acrylamide used in polymer gels is neurotoxic and carcinogenic in humans. Some of these concerns have been reduced by replacing acrylamide with other monomers such as Di-Acetone Acrylamide (DAA), N-Vinyl Formamide (NVF) and Niso-Propyl Acrylamide (NIPAM). These alternatives are highly water soluble and less toxic than acrylamide.[48]

Conclusion

Gel dosimetry offers the promise of precise and appropriate 3D dose measurement over conventional dosimeters. A lot of work has been done to make these gels less toxic and user friendly. These gels offer advantages such as tissue equivalence, measurement of

precise dose and high spatial resolution. Analyzing the body of published data on Fricke gel dosimeter indicated that they have an important role in radiotherapy because they are simple, reproducible and can be modeled in different shapes. However, their use is limited due to diffusion problem. Diffusion problem of Fricke gels is resolved by the introduction of polymer gels which accurately measure three-dimensional dose distribution with good spatial resolution. Polymer gels are more advantageous then Fricke gels because of their stability and non-diffusion property. However, polymer gels are effected by oxygen contamination and concentration of cross linkers. It is necessary to remove free oxygen from gels. To extract accurate dose information imaging modalities of choice are MRI, X-ray CT and Optical CT. CT scanning emerged as an alternative to MRI for imaging in-phantom dose measurements in radiotherapy treatment because of their availability and cost effectiveness. Although much advances have been made in this field, but because of perceived inconvenience it finds little acceptance in clinic. It is incumbent for the key members working in this field to encourage wider use of gels.

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References

1. Venning AJ, Nitschke KN, Keall PJ, Baldock C. Radiological properties of normoxic polymer gel dosimeters. Med Phys 2005;32(4):1047–53.
2. Gambarani G, Brusa D, Carrara M, Castellano G, Mariani M, Tommatis S, et al. Dose imaging in radiotherapy photon fields with Fricke and Normoxic-polymer gels. J phys Conf Ser 2006;41:466-74.
3. Baldock C, Deene Y, Doran S, Ibott G, Jirasek A, Lepage M, et al. Topical review: Polymer gel dosimetry. Phys Med Biol 2010;11;55(5):R1–R63.
4. Aljamal MA. Magic polymer gel dosimetry using x-ray computed tomography: A feasibility study [Thesis]. Malaysia: Universiti Saina Malaysia; 2008.
5. Kumar DS, Samuel EJ. Cone beam optical CT investigation on tissue equivalent normoxic polymer gel dosimeter. J Phys Conf Ser 2010;250:012041.
6. Jirasek A, Duzenli C. Relative effectiveness of polyacrylamide gel dosimeters applied to proton beams: Fourier transform Raman observations and track structure calculations. Med Phys 2002;29:569–77.
7. Heufelder J, Stiefel S, Pfaender M, Ludemann L, Grebe G, Heese J. Use of BANG polymer gel for dose measurements in a 68 MeV proton beam. Med Phys 2003;30:1235–40.
8. Andrews HL, Murphy RE, LeBrun EJ. Gel dosimeters for depth dose measurements. Rev Sci Instrum 1957;28:329.
9. Ramm U, Weber U, Bock M, Kramer M, Bankamp A, Damrau M, et al. Three-dimensional BANGTM gel dosimetry in conformal carbon ion radiotherapy. Phys Med Biol 2000;45:N95–N102.
10. McJury M, Oldham M, Cosgrove VP, Murphy PS, Doran S, Leach MO, et al. Radiation dosimetry using polymer gels: methods and applications. Br J Radiol 2014;73:873.
11. Senkesen O, Tezcanli E, Buyuksarac B, Ozbay I. Comparison of 3D dose distributions for HDR 192Ir brachytherapy sources with normoxic polymer gel dosimetry and treatment planning system. Med Dosim 2014;39:266-71.
12. Aljamal M, Zakaria A, Shamsuddin S. Radiological properties of MAGIC normoxic polymer gel dosimetry. J Phys Conf Ser 2013;423:012016.
13. Keall P, Baldock C. A theoretical study of the radiological properties and water equivalence of Fricke and polymer gels used for radiation dosimetry. Australas Phys Eng Sci Med1999;22(3):85-91.
14. Bosi SG, Naseri P, Baldock C. Light-scattering-induced artifacts in a complex polymer gel dosimetry phantom. Appl Opt 2009;48(13):2427-34.
15. Khan FM. Physics of Radiation Therapy. Lippincott, Williams & Wilkins, USA, 2003.
16. Pantelis E, Karlis AK, Kozicki M, Papagiannis P, Sakelliou L, Rosiak JM. Polymer gel water equivalence and relative energy response with emphasis on low photon energy dosimetry in brachytherapy. Phys Med Biol 2004;49:3495–514.
17. Ibbott GS. Clinical applications of gel dosimeters. J phy Conf Ser 2006;56: 08–31.
18. Olberg S, Skretting A, Bruland O, Olsen DR. Dose distribution measurements by MRI of a phantom containing lung tissue equivalent compartments made of ferrous sulphate gel, Phys Med Biol 2000;45:2761–70.
19. McAuley KB. Fundamentals of Polymer Gel Dosimeters. J Phys Conf Ser 2006;56:35-44.
20. Schreiner LJ. Review of Fricke gel dosimeters. J Phys Conf Ser 2004; Conference Series. 3:9-21.
21. Nazir A, Afzal M, Aleem F, Bano S, Buzdar SA. MRI Dose Response of Ferrous Benzoic Xylenol Orange Gel. Eur J Sci Res 2014;120(1):80-8.
22. Pearce JAD, Crossley DC. Gel dosimetry for direct measurement of dose distributions: Progress report. National Physical Laboratory; 2007.
23. Ibbott GS. Applications of gel dosimetry. J Phys Conf Ser 2004; 3:58.
24. Panagiotis E, Antoniou, Kaladoudi E. MR imaged polymer gel radiation dosimetry: disclosed yet unpatented. Recent Pat Biomed Eng (discontinued) 2008;1(3):203-12.
25. Maryanski MJ, Gore JC, Kennan RP, Schulz RJ. NMR relaxation enhancement in gels polymerized and cross-linked by ionizing radiation: A new approach to 3D dosimeters by MRI. Magn Reson Imaging 1993;11: 253-58.
26. Deene YD. Essential characteristics of polymer gel dosimeters. J Physonfer 2004;3:34-57.
27. Deene YD, Vergote K, Claeys C, Wagter CD. The fundamental radiation properties of normoxic polymer gel dosimeters: a comparison between a methacrylic acid based gel and acrylamide based gels. Phys Med Biol 2006;51:653.
28. Sobotka P, Kozicki M, Maras P, Boniecki L, Kacperski K, Domanski AW. Optical Scanner for 3D Radiotherapy Polymer Gel Dosimetry. Acta Physica Polonica 2012; 122:969-74.

29. Gustavsson H, Karlsson A, Back SA, Olsson LE, Haraldsson P, Engstrom P, et al. MAGIC-type polymer gel for three-dimensional dosimetry: Intensity-modulated radiation therapy verification. Med Phys 2003;30:1264.
30. Guo PY, Adamovics JA, Oldham M. Characterization of a new radiochromic three-dimensional dosimeter. Med Phys 2006;33:1338.
31. Iqbal K, Gifford KA, Ibbott G, Grant RL, Buzdar SA .Comparison of an anthropomorphic PRESAGE® dosimeter and radiochromic film with a commercial radiation treatment planning system for breast IMRT: a feasibility study. J Appl Clin Med Phys 2014;15(1):4531.
32. Saur S, Strickert T, Wasboe E, Frengen J. Fricke gel as a tool for dose distribution verification: optimization and characterization. Phys Med Biol- 2005;50(22):5251-61.
33. Back SA. Implementation of MRI gel dosimetry in radiation therapy [Thesis]. Malmo: Lund University Malmo, Sweden; 1998.
34. Buzdar SA, Afzal M, Nazir A, Gadhi MA. Accuracy requirements in radiotherapy treatment planning. J Coll Physicians Surg Pak 2013;23(6):418-23.
35. Baldock C. X-ray computer tomography, ultrasound and vibrational spectroscopic evaluation techniques of polymer gel dosimeters. J Phys Conf Ser 2004;3:136–41.
36. Deene YD. Gel dosimetry for the dose verification of intensity modulated radiotherapy treatment. Med Phys 2002;12:77-88.
37. Gore JC, Kang YS. Measurement of radiation dose distributions by nuclear magnetic resonance (NMR) imaging. Phys Med Biol 1984;29:1189.
38. Nazir A, Afzal M, Buzdar SA. Effects of variation of MRI parameters on signal homogeneity: A Qualitative analysis for Ferrous Benzoic Xylenon Orange gel. J Pak Med Assoc 2010;60:470-73.
39. Harris PJ, Piercy A, Baldock C. A method for determining the diffusion coefficient in Fe (II/III) radiation dosimetry gels using finite elements. Phys Med Biol 1996;41:1745.
40. Deene YD. Fundamentals of MRI measurements for gel dosimetry. J Phys Conf Ser 2004;3:87–114.
41. Ding X. High Field Magnetic Resonance Imaging-based gel dosimetry for small radiation fields [Thesis]. Winston-Salem: Wake forest University graduate school of arts and sciences, North Carolina; 2012.
42. Florescu L, Ambartsoumian G, Wuu C-S. Effect of refraction on dose reconstruction in optical-CT gel dosimetry. J Phys Conf Ser 2013;444:12063.
43. Brindha, S, Venning AJ, Hill B, Baldock C. Experimental study of attenuation properties of normoxic polymer gel dosimeters. Phys Med Biol 2004;49:N353.
44. Schreiner LJ, Olding T, McAuley KB. Polymer gel dosimetry. J PhysConf Ser 2010;250:012014.
45. Baldock C. Historical overview of gel dosimetry. J Phys Conf Ser 2004;3:1-3.
46. Salomons GJ, Park SP, McAuley KB and Schreiner LJ. Temperature increases associated with polymerization of irradiated PAG dosimeters. Phys Med Biol 2002; 47:1435-48.
47. Antoniou PE, Kaldoudi E. MR Imaged Polymer Gel Radiation Dosimetry: Disclosed yet Unpatented. Recent Pat Biomed Eng (discontinued) 2008;1(3):203-12.
48. McAuley KB. Fundamentals of polymer gel dosimeters. J Phys Conf Ser. 2006;56: 5-44.