Review of gel dosimetry: a personal reflection

C Baldock
Faculty of Science, Engineering and Technology, University of Tasmania, Sandy Bay, Tasmania 7005, Australia
Email: clive.Baldock@utas.edu.au

Abstract. Gel dosimeters are manufactured from radiation sensitive chemicals which, upon irradiation, polymerize as a function of the absorbed radiation dose. These gel dosimeters have the capacity to record radiation dose distribution in three-dimensions (3D) compared to one and two-dimensional dosimeters. 3D dosimeters are radiologically soft-tissue equivalent and may be evaluated using magnetic resonance imaging (MRI), optical-computerized tomography (optical-CT), x-ray CT, ultrasound or vibrational spectroscopy.

1. Introduction
Radiation dosimetry is an important part of the radiation therapy quality assurance process in which measurements are undertaken in one, two or three dimensions to ensure that the absorbed dose, as prescribed by the radiation oncologist, is delivered correctly [1-8].

2. Fricke Gel Dosimeters
As long ago as 1950, the radiation-induced colour change in dyes was used to investigate radiation doses in gels [9]. Gel dosimetry today however, is founded mainly on the work of Gore et al who in 1984 [10] demonstrated that changes due to ionising radiation in Fricke dosimetry solutions [11] which were introduced in the 1920’s, could be measured using nuclear magnetic resonance (NMR).

The nuclear magnetic resonance (NMR) relaxation properties of irradiated Fricke or ferrous sulphate dosimetry solutions show that radiation-induced changes, in which ferrous (Fe2+) ions are converted to ferric (Fe3+) ions, can be quantified using NMR relaxation measurements [11]. Further, Fricke dosimetry solutions dispersed throughout a gel matrix could be used to obtain three-dimensional (3D) spatial dose information using magnetic resonance imaging (MRI) [12]. Fricke-type gel dosimeters however do not retain a spatially stable dose distribution due to ion diffusion within the irradiated dosimeters [13, 14]. Fricke solutions with various gelling agents such as gelatine, agarose, sephadex and polyvinyl alcohol (PVA) along with chelating agents such as xylenol orange (XO) do reduce diffusion [15-17]. The diffusion problem however is considered to be a significant one in gel dosimetry.

3. Polymer Gel Dosimeters
Polymer systems for the use of radiation dosimetry were first proposed as early as 1954, where Alexander [18] discussed the effects of ionising radiation on polymethylmethacrylate. Hoecker [19] in 1958 investigated the dosimetry of radiation-induced polymerisation in liquids, and in 1961 Boni [20] used polyacrylamide as a gamma dosimeter.

A new gel dosimetry formulation was subsequently proposed based on the polymerisation of acrylamide and N,N’-methylene-bis-acrylamide (bis) monomers infused in an aqueous agarose matrix
This type of gel dosimeter, known as PAG, did not have the associated diffusion problem of Fricke gels and was shown to have a relatively stable post-irradiation dose distribution with the polymerisation reaction occurring by cross-linking of the monomers induced by the free radical products of water radiolysis [22-24]. Subsequent work investigating different compositions and formulations of polymer gel dosimeters have been summarised [25].

Although polymer-type dosimeters do not have the diffusion limitations of Fricke-type gel dosimeters, there was another significant limitation in their use. Due to the nature of their free radical chemistry, polymer gel dosimeters were susceptible to atmospheric oxygen inhibition of the polymerisation processes and, as a result, had to be manufactured in an oxygen-free environment [26].

A number of studies have been undertaken to investigate these radiological tissue-equivalent [27-29] PAG-type polymer gel dosimeters. De Deene et al [30] undertook an investigation into the overall accuracy of an anthropomorphic polymer gel dosimetry phantom for the verification of conformal radiotherapy treatments. It was established that significant issues relating to the accuracy of this dosimetry technique were a result of oxygen inhibition in the polymer gel and MRI imaging artefacts [31]. Authors continued to investigate clinical aspects of polymer gel dosimetry using MRI [32] including conformal therapy, IMRT and IMAT [33], stereotactic radiosurgery [34], brachytherapy [35], low energy X-rays [36], high-LET and proton therapy [37], boron capture neutron therapy [38].

4. Normoxic Polymer Gel Dosimeters
A significant development in the field of gel dosimetry occurred using an alternative polymer gel dosimeter formulation [39]. This new type of polymer gel dosimeter, known as MAGIC gel, bound atmospheric oxygen in a metallo-organic complex thus removing the problem of oxygen inhibition and enabling polymer gels to be manufactured on the bench-top in the laboratory. This created what was to be known as a normoxic gel dosimeter, compared with the previous PAG formulation which subsequently became known as a hypoxic gel dosimeter. The MAGIC polymer gel formulation consisted of methacrylic acid, ascorbic acid, gelatine and copper. The principal behind the MAGIC gel is in the ascorbic acid oxygen scavenger. Ascorbic acid binds free oxygen contained within the aqueous gelatine matrix into metallo-organic complexes and this process is initiated by copper sulphate. It was subsequently shown that other antioxidants could be used in the manufacture of normoxic gels [40, 41] including tetrakis (hydroxymethyl) phosphonium chloride [42]. Work has also included the development new formulations of normoxic gels [43-45] and of less toxic polymer gels [46].

With the introduction of normoxic gel dosimeters, MRI studies were undertaken to investigate their usefulness for IMRT [47], and radionuclide therapy [48].

5. Evaluation of Gel Dosimeters
Since the work of Gore et al in 1984 [10], the majority of evaluations of gel dosimeters have been undertaken with MRI. However, in 1996 the potential of optical-CT as an alternative imaging technique to MRI [49] for PAG-type polymer gel dosimeters was demonstrated [50] and further investigated [51, 52]. Subsequently, the use of X-ray CT [53-55] to image PAG-type gels was demonstrated [56]. In 1998 the use of variational spectroscopy was demonstrated to evaluate PAG-type polymer gel dosimeters [57, 58]. In 2002 the use of ultrasound to image polymer gel dosimeters was demonstrated [59-61].

6. PRESAGE^TM^ Dosimeters
A new class of polymer dosimeter, PRESAGE^TM^ (Heuris Pharma, Skillman, NJ) [62] was proposed in 2003 and based on clear polyurethane combined with leuco-dye leucomalachite green, an alkyl diisocyanate prepolymer and a hydroxyl reactive polyol along with a catalyst, which polymerises into optically clear polyurethane. Although not suitable for MRI evaluation, this radiation tissue-equivalent dosimeter [29, 63, 64] contains leuco dyes which have a maximum absorbance at a wavelength of 633 nm and are therefore suitable for evaluation with a He-Ne laser-based optical scanning system [65-67].
7. Other Non-radiotherapy Developments
A non-radiotherapy development in gel dosimetry was reported by Gore et al in 1997 using polymer gel
dosimeters to develop an image quality test tool for MRI [68]. Hill reported the use of polymer gel
dosimeters in measuring the CTDI (Computer Tomography Dose Index) on diagnostic x-ray CT
scanners [69, 70] indicating the potential of using polymer gel dosimeters for diagnostic dose levels.
The use of polymer gel dosimeters to measure absorbed dose from Tc-99m, the radionuclide used in
nuclear medicine imaging [71].

8. Discussion and Conclusions
This paper is based on reviews on gel dosimetry previously published by the author [72-74].

9. References
[1] Hill R F et al 2005 Phys. Med. Biol. 50 N331-44
[2] Hill R et al 2008 Radiat. Meas. 43 1258-64
[3] Vial P et al 2008 Med. Phys. 35 1267-77
[4] Greer P B et al 2007 Med. Phys. 34 4389-98
[5] Hill R et al 2010 Med. Phys. 37 4355-63
[6] Hill R et al 2009 Med. Phys. 36 3971-81
[7] Vial P et al 2008 Med. Phys. 35 4362-74
[8] Hill R et al 2014 Phys. Med. Biol. 59 R183-231
[9] Day M J and Stein G 1950 Nature 166 146-7
[10] Gore J C et al 1984 Phys. Med. Biol. 29 1189-97
[11] Fricke H and Morse S 1927 Am. J. Roentgenol. Radium Therapy Nucl. Med. 18 430-2
[12] Appleby A et al 1986 Med. Phys. 14 382-4
[13] Baldock C et al 2001 Australas. Phys. Eng. Sci. Med. 24 19-30
[14] Harris P J et al 1996 Phys. Med. Biol. 41 1745-53
[15] Hill B et al 2002 Phys. Med. Biol. 47 4233-46
[16] Davies J and Baldock C 2008 Radiat. Phys. Chem. 77 690-96
[17] Healy B J et al 2003 Med. Phys. 30 2282-91
[18] Alexander P et al 1954 Proceedings of the Royal Society A223 392
[19] Hoecker F E and Watkins I W 1958 Int. J. Appl. Rad. Isotop. 3 31-5
[20] Boni A L 1961 Radiation Research 14 374-80
[21] Maryanski M J et al 1994 Phys. Med. Biol. 39 1437-55
[22] Lepage M et al 2001 J. App. Poly. Sci. 79 1572-81
[23] Lepage M et al 2001 Phys. Med. Biol. 46 1061–1074
[24] Lepage M et al 2001 Phys. Med. Biol. 46 2827-39
[25] Lepage M et al 2001 Phys. Med. Biol. 46 2665-80
[26] Baldock C et al 1998 Phys. Med. Biol. 43 695-702
[27] Keall P and Baldock C 1999 Australas. Phys. Eng. Sci. Med. 22 85-91
[28] Venning A J et al 2005 Med. Phys. 32 1047-53
[29] Brown S et al 2008 Appl. Radiat. Isot. 66 1970-4
[30] De Deene Y et al 2000 Magn. Reson. Med. 43 116-25
[31] Gustavsson H et al 2004 Phys. Med. Biol. 49 227-41
[32] Murry P J and Baldock C 2000 Australas. Phys. Eng. Sci. Med. 23 44-51
[33] Vergote K et al 2004 Phys. Med. Biol. 49 287-305
[34] Watanabe Y et al 2002 Med. Phys. 29 797-802
[35] Hurley C et al 2006 Nuclear Inst. and Methods in Physics Research, A 565 801-11
[36] Boudou C et al 2004 Phys. Med. Biol. 49 5135-44
[37] Gustavsson H et al 2004 Phys. Med. Biol. 49 3847-55
[38] Gambarini G et al 2004 Appl. Radiat. Isot. 61 759-63
[39] Fong P M et al 2001 Phys. Med. Biol. 46 3105-13
[40] De Deene Y et al 2002 Phys. Med. Biol. 47 3441-63
[41] De Deene Y et al 2002. Phys. Med. Biol. 47 2459-70
[42] Venning A J et al 2004 J. Phys.: Conf. Ser. 3 155-8
[43] Hurley C et al 2005 Appl. Appl. Rad. Isotop. 63 443-56
[44] Venning A J et al 2005 Phys. Med. Biol. 50 3875-88
[45] Venning A J et al 2005 Nuclear Inst. and Methods in Physics Research, A 555 396-402
[46] Senden R J et al 2006 Phys. Med. Biol. 51 3301-14
[47] Gustavsson H et al 2003 Med. Phys. 30 1264-71
[48] Gear J I et al 2006 Phys. Med. Biol. 51 3503-16
[49] Lepage M et al 2002 Phys. Med. Biol. 47 1881-90
[50] Gore J C et al 1996 Phys. Med. Biol. 41 2695-704
[51] Oldham M et al 2001 Med. Phys. 28 1436-45
[52] Bosi S G et al 2009 Phys. Med. Biol. 54 275-83
[53] Baldock C et al 1994 J. R. Soc. Med. 87 806-08
[54] Trapp J V et al 2004 Phys. Med. Biol. 49 N139-46
[55] Hill B et al 2005 Brit. J. Radiol. 78 623-30
[56] Audet C et al 2002 J. Appl. Clin. Med. Phys. 3 110-8
[57] Baldock C et al 1998 Phys. Med. Biol. 43 3617-27
[58] Rintoul L et al 2003 Appl. Spectroscopy 57 51-7
[59] Mather M L et al 2002 Phys. Med. Biol. 47 4397-409
[60] Mather M L et al 2003. Ultrasonics 41 551-59
[61] Mather M L et al 2003. Phys. Med. Biol. 48 N269-75
[62] Adamovics J and Maryanski M 2003. Med. Phys. 30 1349
[63] Gorjiara T et al 2011. Med. Phys. 38 2265-74
[64] Gorjiara T et al 2012 Med. Phys. 39 7071-9
[65] Guo P et al 2006 Med. Phys. 33 1338-45
[66] Guo P et al 2006 Med. Phys. 33 3962-72
[67] Oldham M et al 2008 Med. Phys. 35 2072-80
[68] Gore J C et al 1997 Med. Phys. 34 1405-8
[69] Hill B et al 2005 Med. Phys. 32 1589-97
[70] Hill B et al 2008 Physica Medica 24 149-58
[71] Braun K et al 2009 J. Phys.: Conf. Ser. 164 012050
[72] Baldock C et al 2010 Phys. Med. Biol. 55 R1-63
[73] Baldock C 2006 J. Phys.: Conf. Ser. 56 14-22
[74] Baldock C 2009 J. Phys.: Conf. Ser. 164 012002