Applications of Gel Dosimetry

Geoffrey S. Ibbott, Ph.D.
Department of Radiation Physics
UT M.D. Anderson Cancer Center, Houston, Texas 77030, U.S.A.
Email: gibbott@mdanderson.org

Abstract
Gel dosimetry has been examined as a clinical dosimeter since the 1950s (Day 1950, Andrews 1957). During the last two decades, however, the number of investigators has increase rapidly, and the body of knowledge regarding gel dosimetry has expanded considerably (Gore 1984, Schreiner 1999). Gel dosimetry is still considered a research project, and the introduction of this tool into clinical use is proceeding slowly. This paper will review the characteristics of gel dosimetry that make it desirable for clinical use, the postulated and demonstrated applications of gel dosimetry, and some complications, setbacks, and failures that have contributed to the slow introduction into routine clinical use.

Introduction
Gel dosimetry was introduced by Gore who recognized that the ferrous sulfate Fricke dosimeter (Fricke 1927, 1966) could be examined with magnetic resonance rather than spectrophotometry (Gore 1984). Stabilizing the Fricke solution with gelatin or agarose allowed the capture of spatial dose information in three dimensions, and the use of MR imaging revealed the absorbed dose distribution. It was shown that the T1 relaxation parameter varied proportionally to dose. However, the ferric ions produced by absorption of radiation diffuse readily through the gel or agarose matrix, leading to a decrease in signal intensity, and a loss of spatial information (Baldock 2001). Imaging must be performed within about two hours of irradiation to avoid serious degradation of the dosimetric detail (Schreiner 2002). The diffusion has been reduced by replacing the gelatin matrix with a poly vinyl acohol (PVA) matrix, which is less porous to the ferric ions (Chu 2000). Other investigators have developed further methods to delay diffusion, although imaging  must still be performed quite soon after irradiation (Kelly 1998).
Gels that replaced the Fricke solution with acrylic monomers were introduced in 1993 (Maryanski 1993, 1996a). Early work was conducted using a poly-acrylamide gel based on the radiation-induced polymerization and cross-linking of bis and acrylamide. The formation of acrylic polymer chains resolved the problem of diffusion exhibited by Fricke gels, as the long polymer chains were too large to diffuse rapidly. The reciprocal of T2, or R2, the relaxation rate, was found to vary proportionally with dose, and MR imaging of polymer gels was shown to yield quantitative dose distributions (Maryanski 1993). Subsequently, alternate gel formulations have been developed in which the bis and acrylamide are replaced with acrylic acid or methacrylic acid, which has yielded increased sensitivity of the gels, and reduced toxicity (Baldock 1998a, Maryanski 1999). However, the polymer gels continued to show another disadvantage; their response was inhibited by the presence of oxygen. This effect was addressed through the recent introduction of a class of polymer gel dosimeters containing oxygen scavengers (Fong 2001). Several variations of these normoxic gel dosimeters (so called because they can be prepared under normoxic conditions) have been characterized (De Deene 2002).

For a number of gel compositions presently being evaluated, the fundamental chemistry and physics of response are well understood. Several gel compositions have been characterized in great detail (Maryanski 1994b, De Deene 2000, 2002, MacDougall 2002). In polymer gels, for example, it is understood that the interaction of radiation with water produces free radicals, which trigger the cross linking of monomers into polymer chains (Spinks 1964). The polymer chains bind water protons tightly causing a change in their paramagnetic properties that is detectable by magnetic resonance imaging. Some complications due to the distortion of MR imaging systems have been identified (Watanabe 2002).

In some compositions, polymerization changes the optical characteristics, and measurements of optical density can be related to absorbed dose (Gore 1996, Maryanski 1996b, Oldham 2001, 2003, Wolodzko 1999). The formation of polymer chains changes the physical density of the gel, and the resulting change in attenuation coefficient can be measured by measurements of x-ray transmission such as by computed tomography (Hilts 2000, Trapp 2001, 2002, Audet 2002, Brindha 2004). Polymerization leads to changes in elasticity of the medium, and the corresponding changes in ultrasound absorption can be exploited (Mather 2002, 2003). Finally, vibrational spectroscopy can be used to demonstrate the conversion of monomers to polymer chains (Baldock 1998b, Lepage 2001a, Rintoul 2003).

**Characteristics of Gel Dosimeters**

Gel dosimeters have a number of characteristics that make them attractive for radiation dosimetry (McJury 2000). A novel comparison of gel dosimeters with conventional dosimetry systems has been presented in the form of a spider plot (see Figure 1, Oldham 2003).

This graphical presentation illustrates the relative performance of dosimeters such as ion chambers, film, TLDs and gels by considering such parameters as accuracy, volume measured, cost, three-dimensionality, resolution, energy dependence, and time required for the measurement. Oldham has shown that gels compare favorably with the other detectors in most
characteristics, including their relative accuracy, volumetric nature, inherent three-dimensional nature, high resolution and lack of energy dependence over much of the important energy range. Methods for characterizing the response of gels have been found, and in particular, a technique for characterizing the dose resolution has been described (Lepage 2001b, Baldock 2001, Trapp 2004a).

However, today gels are still time-consuming and relatively expensive. Several dosimetric aspects have not yet been realized, including the absolute accuracy of measurement, and the ability to render a 3-dimensional dose distribution as opposed to multiple planes of data, although progress is being made rapidly on both aspects.

Figure 1. A “spider plot”, illustrating the capabilities of several common dosimetry systems, as well as gels, and the potential capabilities of gels. Redrawn with permission from Oldham 2003.
Applications of Gel Dosimetry

Potential applications of gel dosimetry have been summarized on several occasions in the recent past (Day 1990, McJury 2000, Bonnet 2001, MacDougall 2002) although the field is developing rapidly. Today it is considered by many that gel dosimetry has useful characteristics that can facilitate radiation therapy dosimetry, especially in situations that are not handled well by conventional dosimeters. These characteristics include the ability to measure complex three-dimensional dose distributions; to integrate dose accurately without dependence on dose rate, at least over a fairly wide range; tissue-equivalence; high spatial resolution; and lack of energy dependence over most of the kilovoltage and megavoltage range. With most gels, data are stored permanently, making gels suitable for performance of dosimetry at remote locations (Ibbott 1995). They also are relatively safe to manufacture and handle, although some components such as acrylamide are toxic and must be handled with appropriate protection until mixed.

Demonstrated applications of gel dosimetry to date include basic dosimetry (depth dose, penumbra, wedge profiles) in photon, electron, neutron and proton beams; dose distributions from imaging procedures; conformal therapy, stereotactic radiosurgery, and intensity-modulated radiation therapy (IMRT); dose distributions around brachytherapy sources (low- and high-dose rate, and intravascular sources); internal dosimetry (iodine-131 doses); and evaluation of tissue heterogeneities. The advances made recently in these areas will be discussed.

Basic Dosimetry

Gel dosimeters have the capability to record and display the dose distribution throughout a three-dimensional volume. This ability affords advantages over conventional dosimeters, even for basic dosimetry parameters such as percent depth dose in photon and electron beams (Andrews 1957, Haraldsson 2000, Maryanski 1994b). Gel dosimetry has been shown to be useful to validate simple multiple-field arrangements (Oldham 1998) and more complex anatomical situations including tangential breast treatment (Baldock 1996, Love 2003) and scalp treatment with electron beams (Trapp 2004b). Dynamic functions, such as a programmable wedge filter are difficult to measure with ionization chambers or diodes, and film is often used to provide data in a single plane. Gels have proven useful for capturing the dose distributions from programmable wedge filters, and allow distributions in multiple planes to be demonstrated from a single exposure (Bengtsson 1996).

Dose from Imaging Procedures

More recently, the use of gels to demonstrate dose distributions from imaging procedures has been explored (Hill 2004a, 2004b). In a novel experiment, a high-sensitivity gel was used to determine the dose from CT imaging. The benefit of this measurement is that the dose distribution throughout a patient volume can be estimated without requiring the use of numerous point dosimeters (e.g., TLD) and without averaging the dose along a line or throughout a volume (e.g., a pencil ionization chamber). These benefits may be most apparent in evaluating the dose distribution from helical CT scanners.
**Dose Distributions in Complex External Beam Therapy**

Without question, this aspect of dosimetry has shown the greatest interest, and promise, for gel dosimetry. Other dosimetric techniques, such as ionization chambers, TLDs and film are notoriously inadequate for confirming the complicated distributions produced by techniques such as 3D conformal radiation therapy (3D CRT) and intensity modulated radiation therapy (IMRT). The significance of errors in IMRT delivery, for example, has been recognized, and the necessity of confirming patient treatment plans by measurement cannot be overstated (Webb 1997). Gels, more than any other dosimeter available today, offer the advantage of demonstrating both the dose and the dose distribution in three dimensions.

Gels have been used to demonstrate the dose distributions from stereotactic treatments both from dedicated multisource cobalt units and from linear accelerators (Olsson 1992, Schulz 1993, Ibbott 1993, 1996, 1997, Meeks 1999, Novotny 2002, Scheib 2002). A clear benefit of gel dosimeters is that they can display a dose distribution, especially a highly conformal one as is produced by stereotactic radiosurgery techniques, so that it can be appreciated qualitatively in three dimensions without need of imaging systems or processing (see Figure 2, Ibbott 1997). For comparison of measured doses and calculated distributions, a superposition method has been described (Meeks 1999). An example of a comparison between measurements and calculations is shown in Figure 3 (Ibbott 1997).

![Figure 2. A gel irradiated with a highly-conformal dose distribution produced by a Gammaknife treatment unit. The distribution can be appreciated qualitatively without the need of imaging systems or processing. Photograph by the author. See also Ibbott 1997.](image-url)
Figure 3. A comparison between the calculated dose distribution and that measured by the gel shown in Figure 2. A: Axial plane, B: Sagittal plane (Ibbott 1997).
Gels dosimeters have proven themselves to be valuable for evaluating and confirming IMRT dose distributions (Low 1999, Beach 2003, Ibbott 2002, 2003, Gustavsson 2003, Oldham 1998, Vergote 2003, 2004a). Most investigations have been conducted in simple geometric phantoms, but others have employed anthropomorphic phantoms in arrangements that allowed direct comparison with measurements using other techniques such as film and TLD (Beach 2003, Ibbott 2002, 2003). Vergote et. al. have compared the dose distribution measured with gels to the calculated distribution, for complex intensity-modulated arc therapy treatments (Vergote 2004a). They observed a reproducible difference between calculations and measurements in low-dose regions near steep dose gradients; a phenomenon also observed by Cadman et. al. and attributed to the failure of treatment planning systems to model the transmission of radiation through the rounded ends of multileaf collimator leaves (Cadman 2002).

**Dose Distributions from Brachytherapy Procedures**

The complex nature of dose distributions around brachytherapy sources has invited the use of gel dosimetry. Its ability to record and display dose distributions around a high-dose rate (HDR) source was first demonstrated over a decade ago (Schreiner 1994, Olsen 1994, Maryanski 1994b) and additional studies have been conducted more recently (Heard 2004). Difficulties associated with the high dose gradients found around brachytherapy sources have complicated these measurements. In some gel formulations, the formation of polymer particles can shrink the gel, distorting the dose distribution toward high-dose regions. Furthermore, there are suggestions that the high dose rates found near brachytherapy sources, particularly those of HDR afterloaders, can introduce temperature gradients which influences the polymerization of acrylamide monomer gels (De Deene 2002, Gelfi 1981, Maryanski 1997, Omidian 1998).

Efforts also have been made to characterize low-dose rate (LDR) sources such as prostate seeds (Ibbott 1999, Heard 2003), eye plaques (Chan) and intravascular sources (Wuu 2003). Studies have indicated that the diffusion of monomers (or ferrous and ferric ions in Fricke gels) across steep dose gradients can introduce errors in measurement (Vergote 2004b). As the use of gels to measure dose distributions from LDR sources requires long exposure times, diffusion of monomers or ions could introduce significant errors, and gels exhibiting high diffusion rates should be avoided for these measurements.

A further problem with gel dosimetry for LDR brachytherapy has been demonstrated by recent studies indicating energy dependence at lower energies. Data show that a polymer gel dosimeter under-responds to radiation in the 20 keV – 60 keV range (Pantelis 2004). Others have shown differences in gel response from one formulation to another, and suggest that the MAGAT gel is most water-equivalent over a wide range of energies (Venning 2004). Changes in mass attenuation coefficient of polymer gels during irradiation can also introduce errors in the dose distributions measured around low-energy sources.
**Internal Dosimetry**

Gel dosimetry has shown promise in the determination of dose distributions from administrations of unsealed radioactive sources. (Courbon 1999). The authors embedded a vial of iodine-131 into a flask of polymer gel and observed a distance-dependent change in the T2 signal. They also mixed iodine-131 into the gel and demonstrated a change in T2 signal that was dependent on distance from the concentration of activity. No more-recent investigations have been located.

**Measurement of Neutron Dose Distributions**

Some developments have been reported in characterizing fast and epithermal neutron beams with gel dosimetry (Gambarini 1999, 2001, 2002). Thin layers of Fricke-xylenol orange gels have been irradiated in phantoms composed of insensitive gel. Adding $^{10}$B or other nuclides with large cross-sections has increased the sensitivity of the gel dosimeter to neutrons. This technique has been used to determine the profiles of neutron beams used for boron neutron capture therapy. Some benefits of the use of gel dosimetry are the tissue-equivalence of the dosimeter to these energies, and the ability to separate the components of dose.

**Measurement of Particle Dose Distributions**

Several investigators have demonstrated the use of polymer gel dosimeters to record the dose distributions produced by proton beams (Bäck 1996, Maryanski 1994a, Gustavsson 2004). However, several authors have noticed disagreements between measurements with gels and conventional dosimeters such as diodes in the peak region of the distribution. Gustavsson has suggested that the response of gels, as they are based on the formation of free radicals, is dependent on the LET of the radiation (Gustavsson 2004). As the LET of the beam increases in the peak region, the local ionization density increases. As the distance between the radicals formed in the gel decreases, the likelihood of recombination of radicals increases. A decrease in the production of radicals with increasing LET has been described previously (Swallow 1973). Consequently, significant differences appear between depth dose measurements with gels and those with detectors such as diodes (see Figure 4, Gustavsson 2004).

Gels have been used also to demonstrate the dose distribution produced by $^{12}$C ions (Ramm 2000). Similar effects associated with decreased radical formation at high LET were observed in the carbon beam.
Evaluation of Tissue Heterogeneities

A valuable feature of gel dosimeters is that they are very nearly tissue-equivalent. Previous investigations have shown that the BANG™ gel, the MAGIC and MAGAS normoxic gels, as well as gels based on Fricke or vinyl solutions have electron densities within 1% of soft tissue, and effective atomic numbers in the range of 7.4 (Pantelis 2004). However, several investigators have attempted to measure the effects of non-unit density tissues on external beam dose distributions. Early measurements were performed to estimate the dose distribution behind high atomic number heterogeneities, to simulate the presence of bone (Vergote, Hepworth 1999, Gum 2002). More recently, measurements have been made behind or adjacent to cavities filled with air or with lung-equivalent plastic (Vergote 2003). To attempt a measurement in lung-equivalent gel, Olberg produced a foam of gel with the approximate density of lung tissue (Olberg 2000). Other investigators have evaluated the promise of gel dosimeters to simulate lung tissue, by introducing polystyrene foam beads into a gel mixture (Borges 2003). While these measurements have shown promise, there are several sources of error. First, the introduction of air, or air-containing polystyrene beads introduces the possibility of oxygen contamination. This has been addressed by purging the polystyrene beads with nitrogen, or using nitrogen rather than air to foam the gel. The introduction of air or polystyrene eliminates the possibility of evaluating the measured dose distribution by optical scanning, and MR imaging must be used. The presence of air may lead to partial volume imaging effects that could introduce errors into the measurement.

Complications to be Addressed

As has been suggested earlier in this paper, there are a number of complications associated with gel dosimetry that remain to be addressed, and that are inhibiting the routine use of gels in the clinic. Some of these are listed below, with short descriptions of the causes of the problems, and possibilities for correcting them.

Figure 4. The variation in LET as a function of depth for a monoenergetic proton beam (dashed curve, left-hand scale) and the measured relative sensitivity for the gel dosimeter (full curve, right-hand scale). Also shown is the depth dose curve for the proton beam (dotted curve), normalized to 100% at the Bragg peak. Reproduced with permission from Gustavsson 2004.
**Imaging Artifacts**

This paper has discussed several methods of generating images of dose distributions using gels. Principal methods are magnetic resonance imaging (MRI), optical computed tomography (OCT), and x-ray computed tomography (CT). Each of these imaging methods is prone to imaging artifacts. In MRI, for example, susceptibility artifacts can result from variations in the conductivity of the volume being imaged, and interference is likely when multiplanar imaging of adjacent planes is attempted. The presence of air or low density structures can lead to partial volume effects or susceptibility artifacts.

In OCT, any structure that blocks the light beam is likely to cause a streak artifact, similar to those produced by high densities in x-ray CT images. In addition, the refraction of the light at interfaces between the gel and other materials can cause ring artifacts or distortion of the image.

When x-ray CT is used, artifacts can result from the low signal to noise ratio that occurs because of the very small density differences present in the gel.

**Temperature Dependence**

The existence of a dependence on temperature during irradiation of polymer gels was not recognized immediately, but it has since been shown that this dependence exists. Furthermore, the temperature dependence can be more pronounced for some polymer gel formulations than others. The polymerization that occurs as a result of irradiation of the gel is exothermic, and consequently can lead to a temperature rise that influences further polymerization of gel in response to continuing exposure. In extreme cases, this temperature rise can exceed several degrees C (reference here).

**Oxygen Sensitivity**

The sensitivity of polymer gels to oxygen has been discussed extensively, and several investigators have responded by developing gels that contain oxygen scavengers, such as the MAGIC gel. The oxygen scavenger removes oxygen present in the gel at the time of manufacture, even if this is done in normoxic conditions. It can remove additional small amounts of oxygen, but ultimately will be overwhelmed if exposure to normal atmosphere is ongoing. While this problem has been addressed, it still creates minor inconvenience that might limit the successful introduction of gels into routine clinical use.

**Tissue Equivalence and Energy Dependence**

Gels, both Fricke and polymer types, compete well when compared to other dosimeters in terms of their tissue equivalence and energy dependence. In comparison to thermoluminescence dosimeters (TLD), radiographic film, and even ionization chambers, for example, gels are considerably less energy dependent and are much more tissue equivalent. However, under extreme conditions of photon energies below 60 keV, and LET values greater than about 2.5 keV/micron, gels show a dependence that remains to be fully characterized.
Simulation of Non-Unit Densities

The benefits of gels discussed in the previous paragraph lead to the inability of gels to easily simulate non-unit density tissues. To date, limited efforts have been described to create low-density gel mixtures, to simulate lung tissue. No attempts have been described to date to create high-density mixtures and are unlikely to be with today’s emphasis on the use of gelatin-based formulations.

Diffusion of Monomer in Steep Gradients

The diffusion of monomer, and the shrinkage of gel proportional to the creation of long polymer chains, can be addressed through the development of better gel mixtures. Avoiding small monomers such as acrylamide can reduce the rate of diffusion in regions of steep dose gradient, such as the penumbra of radiation beams. Employing different concentrations of gelatin might reduce or eliminate problems associated with shrinkage of gels in high-dose regions.

Summary

Gel dosimetry offers the promise of accurate and convenient dosimetry under a variety of circumstances. In most of the examples discussed above, gel dosimeters offer a number of advantages over conventional dosimeters. Chief among these is the ability to measure a complex dose distribution throughout a volume with a single radiation exposure. Additional advantages include tissue-equivalence, high spatial accuracy, good dose precision, and reasonable convenience.

However, gel dosimetry continues to experience little acceptance in the clinic, largely because some aspects of promise have not been achieved, and because of a perceived lack of convenience. Members of the radiation physics community are apparently not convinced that the benefits of gels sufficiently outweigh conventional dosimeters such as film and TLD. It is incumbent on those of us working with gels to encourage more widespread use, by taking every opportunity to display the results of measurements with gels.

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