Review of recent advances in non gel dosimeters

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1. Introduction
Radiation dosimetry is a diverse topic encompassing physics, chemistry and biology. This review highlights some of the developments in radiation dosimetry that are relevant to radiotherapy and have been reported since the previous DOSGEL meeting in 2004, excluding gel dosimetry. The results included in this presentation were obtained primarily from searches of the PubMed database.

Two advantages of gel dosimetry are the tissue or water equivalence of the dose response and the inherent 3D geometry of the gel phantoms. However, in practice ion chambers and film have been the most common dosimeters for clinical radiation dosimetry. Ion chambers have a history of precise and dependable dose measurement. Silver halide film is also one of the original technologies for radiation dosimetry. Both were used in the original discoveries of x-rays and radioactive decay. Detailed measurements of dosimeter performance continue to reveal insights that further improve the accuracy of radiation measurements with both film and ion chambers. As the complexity of delivered radiotherapy treatments increases verification at many distinct points becomes essential. Standard methods to validate agreement between calculated and measured complex dose distributions have yet to be agreed upon. But the more points compared the more accurate difference quantification becomes. The trend towards full 3D dosimetry for technique validation and multiple planar measurements for routine quality assurance (QA) measurements is evidenced in the literature.

Dosimeters can be categorized by their spatial character as point (0D), linear (1D), planar (2D) and volume (3D). Three dimensional measurements are often approximated by scanning with lower dimensional detectors. For example, 3D dose distributions can be measured by scanning a single (0D) ion chamber in a water phantom along 3 orthogonal directions, a linear array of ion chambers (1D) in two directions or a planar array of detectors (2D) in one direction. An alternate 3D approach is to fill a volume with 0D, 1D or 2D detectors. For example, a powder dosimeter could be arranged in a line, sheet or volume and then irradiated. Reading individual voxels of the powder generates a point dose measurement.

This review has been organized from the most general point dosimeters to the more specific 3D array dosimeters. Finally a brief section related to biological dosimetry with examples indicating the evolution from physical and chemical dosimeters to biological systems, such as small animals where dose response not physical dose will be the parameter of interest.
2. Point detectors

The evolution of external beam radiotherapy to intensity modulated radiotherapy (IMRT) is currently proceeding at a rapid rate because multi-leaf collimators and IMRT capable planning programs are now standard technologies for new equipment purchases. Key to IMRT commissioning is accurate dosimetry for small radiation fields or beamlets. Small, water equivalent dosimeters are ideal for these measurements.

2.1. Ion chambers

Ion chambers are the local standard dosimeter in nearly all radiotherapy centers. They are calibrated against a national standard. Ion chambers give precise measurements and their accuracy is tied to the dosimetry protocol employed. The accuracy of relative dosimeters is directly tied to the accuracy of the ion chamber calculated dose.

Buckley and Rogers have compared Monte Carlo calculations of wall correction factors, \( P_{\text{wall}} \), with recent measurements and found closer agreement than with values recommended in current protocols [1]. The magnitude of the discrepancies can be up to 0.6%. It was also determined that this effect is depth dependent for electron beams. Specifically, for a 6 MeV electron beam \( P_{\text{wall}} \) varied 2.5% from 0.5 cm to \( R_{50} \). They recommend updating the parameters in current protocols to reflect these more accurate values, which reduce variations between measurement and calculations.

Clearly trying to maintain a dosimetry accuracy of ~2% for clinical measurements is complicated by variation in the accepted standard measurements. Also, when the comparison between ion chamber and other dosimeter systems approach the 1% difference it becomes important to question which measure is more accurate. For example, plastic scintillator results may actually be more accurate than the standard ion chamber data in water.

2.2. Diodes

Silicon diodes are the most sensitive dosimeter type available. They typically have lateral sensitive areas of much less than 1 mm\(^2\). And the relatively large currents generated by these detectors can be recorded with simple electrometers. Previously diodes have had limited use because of their over-response to low energy photons due to the photoelectric effect. Previously a metal shield has surrounded the small sensitive volume of silicon. This shield introduced errors due to excess scatter in electron fields. The performance of a new unshielded p-type silicon diode from PTW, model 60012 was reported by Griessbach et al [2]. Comparisons between a pinpoint ion chamber, shielded and unshielded diodes and a diamond detector are made. Excellent agreement between measured depth doses for electron and photon beams for the ion chamber and unshielded diode. Also, relative outputs for small fields agree with diamond detector results. This report represents a significant advance for small field dosimetry with diodes.

Rosenfeld et al have compared silicon metal oxide field effect transistors and silicon p-n junction detectors for in-vivo dosimetry [3].

2.3. Plastic fibre scintillators

Plastic scintillators are under investigation by several authors for tissue or water equivalent dosimetry. The physical characteristics of plastics can be precisely tuned for physical and electronic density providing near ideal agreement with tissue or water dose responses. Plastics are inexpensive, chemically inert and can be formed into arbitrary shapes and volumes. Light emitted by the host plastic is usually absorbed by a dopant such as an organic dye molecule and re-emitted at longer wavelengths. For radiation dosimetry, scintillators which emit visible light are of primary importance because the long coupling optical fibers are more efficient at transmitting the longer wavelength light. The optical fiber allows remote light detection to occur in a low noise environment. The main impediment to plastic fiber dosimetry is the stray light generated in the length of coupling fiber in the radiation beam. Several approaches have been demonstrated to account for the light not generated by absorbed dose in the scintillator detector. The primary source of light in the coupling fiber is due to
the Cerenkov effect. The spectrum of Cerenkov light is inversely proportional to the wavelength cubed.

Archambault et al investigated commercially available plastic scintillators and plastic fibre scintillators that emitted blue and green light [4]. Scintillators which emitted at longer wavelengths with narrower emission peaks were optimal, because of less overlap of Cerenkov and scintillator light. As the length of 1 mm diameter detectors decreased from 10 mm the advantages of the fiber cladding diminished. It is anticipated that 1 mm long x 1 mm diameter plastic scintillators and plastic scintillator fibre detector would be essentially equivalent in performance. The authors suggested detectors of green plastic scintillator fibre 3 mm length x 2 mm diameter may be optimal considering SNR. However, 2 mm coupling fiber would generate significantly more stray light. Archambault et al investigated three approaches to stray light rejection with a red-green-blue colour CCD camera [5]. The methods included background subtraction from a second fibre not connected to a scintillator, simple filtering of the green or blue channels and chromatic removal using the ratio of green and blue channels. All methods were effective with chromatic removal generating the best overall performance. For, this data the blue scintillator generated the best results. However, other factors such as yellowing of the coupling fiber may have lead to different conclusions for higher doses. The authors predicted this system could be adapted to read 150 independent detectors simultaneously. Such a system may be ideal for accurate real-time water equivalent 3D dosimetry.

Frelin et al also investigated spectral filtering as a means of essentially eliminating the Cerenkov light background signal [6]. They demonstrated less than 1% difference between spectrally corrected plastic scintillator signals (1 mm long x 1 mm diameter) and ion chamber doses for MV photon and electron beams. They used a Bicron BCF-60 scintillator with emission peak at 550 nm. The calibration procedure involved irradiating both a short and long length of coupling fibre and scintillator. These two irradiation geometries had similar scintillator signals but small and large Cerenkov stray light contributions. Solving two linear equations for the blue and green signals in the irradiation geometries allowed accurate determination of dose from scintillator. The data suggest that corrected scintillator data may be more accurate that ion chamber data.

Plastic fibre scintillator detectors are valuable for dosimetry with low-energy x-ray sources for brachytherapy since the absorption coefficients are similar to tissue or water and can be tuned to agree for specific energies. Cerenkov radiation is not present for these sources and fluorescence from the coupling fibre is a minor issue because of the high dose gradient. The detector is always closer than the coupling fibre to the source. This geometry effectively minimizes radiation induced stray light in the coupling fibre. Results of a system for brachytherapy are reported by Sliski et al [7].

2.4. Glass fibre scintillators
Small glass radiation detectors are currently under investigation for radiation dosimetry. They are rugged and simple devices. The optical properties allow several mechanisms for readout of the dose. Copper doped glass has a millisecond decay time when excited with ionizing radiation. This fact allows time delayed gating as an effective method to reject fluorescence and Cerenkov light generated in coupling fiber from detector signal with pulsed radiation sources, see Justus et al [8]. Detector sizes of less than 1 mm allow dose measurements that were accurate for all field sizes.

2.5. Optically stimulated luminescent glass
Optically stimulate luminescence (OSL) is also an effective method to read dose absorbed in glassy or crystalline materials. One of the most studied materials is carbon doped aluminum oxide. The submillimeter detector is coupled to an optical fibre. Following irradiation, an infrared laser stimulates the detector to emit visible light proportional to the absorbed dose. These systems have been demonstrated to be precise and accurate to less than 1% for absorbed dose [9]. Gaza et al have also demonstrated that by simultaneously irradiating and stimulating the detector and near real time readout of the dose can be achieved [10]. This furthers the versatility of this dosimetry system.
Another OSL material is magnesium oxide doped with terbium. Bos et al have reported this material to be 1.7 times more sensitive than Al₂O₃:C and has a 2.4 faster decay time [11]. Dose response is linear from 10⁻⁴ to 10 Gy.

2.6. Liquids
Chemical dosimetry with liquids has had little reported activity during recent years. However, Ilijas et al have shown a personal dosimetry system that has a useful dose range of 0.2-15 Gy with a chlorobenzene-ethanol-trimethylpentane solution (CET) [12]. The readout device consists of a dual wavelength transmission measurement with LED sources and a photodiode detector. Differential absorption measurements with a spectrometer show a linear response. But a nonlinear response is observed with the optoelectronic readout device. They discuss the implications of spectral bandwidth on the transmission measurements. This is a common problem for optical absorption measurements and is again addressed with radiochromic film dosimetry, see below Lee.

2.7. Solids (powders, TLD crystals)
Powders and crystalline materials can act as dosimeters by generating metastable species such as molecular radicals and populating excitation traps. Quantitative detection can involve microwave photon absorption with electron paramagnetic resonance spectrometers and thermal luminescence. Alanine / EPR dosimetry is one of the most thoroughly investigated powder dosimeters. Post irradiation visible and UV illumination produce measurable changes in signal from a 1 kGy irradiation [13]. The energy independence for clinical electron beams from 8-22 MeV was experimentally verified and compared with Monte Carlo calculations. Also, the ratio of absorbed dose-to-alanine and absorbed dose-to-water was reduced 1.3% when comparing ⁶⁰Co beam to electron beams [14].

A less common method for dosimetry with organic materials involves optical absorption spectrometry. Nilekani and Gupta reported a comprehensive examination of the L-threonine powder dosimeter with the ferrous xylenol orange (FX) solution for readout [18]. The irradiated threonine contains peroxy radicals that generate a colour change proportional to the absorbed dose when dissolved in a FX solution. They reported a linear dose response from 1-50 Gray with 10 cm cuvettes and solutions containing 4% by mass dissolved threonine. The amount of threonine per measurement was 0.8 g and this corresponds to a spatial resolution of less than 1 cm³. Lowering the threonine content to 0.5% extended the useful dose range to 10 kGy. A reproducibility of 2% was achieved with this system. The flexibility of FX solution for dosimetry was extended to glycine by Shinde and Mukherjee [19]. In principle any material that is soluble in the FX solution is a potential dosimeter. This may become one of the most versatile approaches to tissue equivalent dosimetry since powders can be placed into phantoms to record, point, linear, planar and three dimensional dose distributions.

Sucrose is also a versatile tissue equivalent material for radiation dosimetry. ESR absorption measurements have demonstrated dose resolution to 10 cGy. Post irradiation variations in signal have been minimized by employing ruby as an independent reference [20]. ESR of sucrose radicals has also been able to record the dose and linear energy transfer (LET) from heavy ion irradiation [21].

3. Two dimensional detectors
Films optical density is measured with several types of densitometers. These instruments need to be independently calibrated for accurate dosimetry. Handling and processing of films can also be
significant variables for dose accuracy. Depending on the specific film type and scanner design and processor maintenance any or all could be the major limitations for accurate measurements.

Film is commonly used for verification of IMRT delivery. Since treatment is delivered in a series of small field segments the dose delivery history per voxel may be considerably different. This leads to important questions of dose history and dose rate effects for tissue response in patients. Similar questions concerning dose rate and fractionated response of chemical detectors such as films and gels are currently under investigation, see below.

3.1. Silver halide film
Silver halide film is a high performance technology that has continued to evolve due to recent advances in nanoparticle manufacturing. However, this technology is disappearing from medical facilities as digital imaging is implemented. Dosimetry will need to develop alternatives to this standard radiation detection material.

Kodak EDR2 film contains significantly less silver halides compared to older film types such as XV2. Several groups have reported on its performance in relation to IMRT QA. Childress et al have performed an extensive study concerning its dosimetric accuracy [22]. They examined 547 film calibrations over an 18 month period and found dose uncertainties of 2% at the 3 Gy level for 6 or 18 MV photon beams. Film optical densities varied between 7-15% of the mean values. Dose rate effects were examined with a series of small dose irradiations similar to an IMRT treatment. They measured a 2% decrease in optical density for 3 Gy delivered in 4 to 14 min relative to a continuous 0.75 minute delivery. They also compared ion chamber and film doses for full patient verifications and found film to be systematically 2% lower. Sites that required more fields and longer overall delivery times had even larger differences between film and ion chamber. They also noted the film orientation relative to the beam has a measurable effect with films perpendicular to beam giving better agreement. Djouguela et al also reported on the dose rate effect (Schwarzschild effect or failure of the reciprocity law) for EDR2 film and found a 5% decrease in optical density for a 12 fold decrease in dose rate [23]. They cautioned that dose rate corrections need to be applied for target regions that are irradiated at largely different dose rates relative to the dose rate at the calibration point.

Van Battum and Huizenga examined the curvature of sensitometric curves for Kodak XV-2 film obtained over a 10 year period and were able to determine that the sensitometric curvature is related to the sensitometric slope [24]. The relationship is dependent on the particular type of densitometer used. Employing the relationship between curvature and slope increases the accuracy of measured dose. A single dose point and a densitometer dependent factor are predicted to be sufficient to determine the relation between optical density and dose. They presented a specific example of 1.7% measurement uncertainty at 0.1 Gy and 1.1% uncertainty at 0.7 Gy. While the experimental conditions were carefully recorded it is difficult to assess the film area sample in order to reach these low uncertainties. This calibration analysis may be generalized to other forms of densitometry, such as optical CT of gels.

Palm and LoSasso investigated Kodak XV film response as a function of phantom size and material relative to water [25]. Comparisons were made with Monte Carlo calculations. Measurements and calculations agreed to within 4% for field sizes smaller that 10 x 10 cm² and depths less than 10 cm. Indicating phantom materials (water, plastic water, PMMA or polystyrene) were nearly equivalent. For larger field sizes and depths much larger differences were observed. They were able to correlate variations in film response for published data with the size and type of phantom employed for the measurements, and to improve consistency in film dosimetry.

3.2. Radiochromic film
Radiochromic films from International Speciality Products known as GafChromic films have been widely used as the commercial tissue equivalent 2D dosimeter. The early products had low dose sensitivity and were limited to higher dose applications such as brachytherapy and radiosurgery. A more recent product Gafchromic HS (high sensitivity) is suitable for the 0.5 - 40 Gy range.
prototype product Gafchromic EBT (external beam therapy) is the most sensitive film to date and is suitable for measurements in the 0.1 to 8 Gy range. Type B EBT was investigated by Todorovic et al with a flat-bed document scanner for readout [26]. They determined the film to be homogeneous within 2%, the dose response to be independent of calibration field size from 10 x 10 to 2 x 2 cm, independent of photon beam energy between 4 and 15 MV. Application of rapid color stabilization technique improved colour stability but was not essential for accurate readout 3 hours post irradiation. This report forms the standard measurement protocol for type B EBT film within the European Society for Therapeutic Radiology and Oncology. The film contains two active layers for a total thickness of 0.229 mm and 0.3 % Li and 0.3% Cl appear to be the key sensitizing additives. Cheung et al have also investigated the post-irradiation darkening of EBT film and recommended that quantitative measurements include a wait time of at least 6 hours [27]. Otherwise a calibration film with the same post-irradiation time should be referenced.

Another radiochromic film product is Gafchromic XR-QA for patient dosimetry in both radiotherapy and radiology. This film was investigated in the energy range of 28-145 kVp for the dose range 0-100 mGy. At 28 kVp and 10 mGy the total uncertainty was 10% [28]. Short exposures to visible light did not influence the measurements. Fractionated dose effects with MD-55 film were investigated by Ali et al and they found transient over responses up to 20% that were minimized by wait times of 24 hours prior to reading the films [29]. Fractionated dose effects in the range 0.5-5 Gy for Gafchromic HS film were examined by Hirata et al [30]. They determined a low-dose nonlinearity similar to the MD-55 film was present and that TG-55 would be insufficient to minimize errors associated with fractionated low dose irradiations.

Gafchromic RTQA film with a Microtek flatbed scanner in reflective mode was investigated by Thomas and Warrington [31]. This film is being considered as a replacement for silver-halide film as film processors are eliminated from radiotherapy clinics. RTQA film has an opaque white backing. The film has a dose range of 0.02-8 Gy and is recommended for ‘qualitative dosimetry’. The authors determined the film and scanner readout had a variation of 5-10% at the 2 Gy range that precluded its use for dosimetry. They also recommended that improvements to the scanner sensitivity with time and position be developed and software development for film QA be further developed by manufacturers.

The higher sensitivity radiochromic films have high-energy absorption spectra and film scanners optimized for the older films will be of limited value in reading the newer film types. To further improve quantitative measurement of dose with radiochromic film multiple wavelength measurements are required. Lee et al have reported the development of a dual peak spectral densitometer which uses the output from a monochromator as the tunable light source and a cooled CCD camera for detection of transmitted light [32]. Fitting the transmission at both the higher and lower sensitivity peaks provides a more effective method of determining measured dose. Performance of the system found a maximum discrepancy between measured and expected dose of less than 1%.

A competitor to Gafchromic film is SIFID (self-developing, instant film for imaging and dosimetry) film that was developed by JP Laboratories. This uses symmetrical diacylenes versus asymmetrical diacylenes which may result in less expensive and more reproducible films. Watanabe et al reported SIFID film to be less sensitive to light and has a dose sensitive range of 5 to 1000 cGy [33]. Post irradiation increases in optical density suggest 12 hour wait times for quantitative readings. Dose response is slightly nonlinear and saturates at 180 cGy.

A comparison of silver-halide films (Kodak XV2 and EDR2) and radiochromic films (Gafchromic MD55-2 and HS) for small photon field dosimetry showed equivalence for depth doses, profiles and isodose distributions for the 1 x 1 cm² beamlets [34].

3.3. Plastic scintillator sheet
Plastic scintillator sheets can be adapted for two-dimensional water equivalent dosimetry. Petric et al have incorporated a plastic scintillator sheet as one face of a plastic water-filled box containing a diagonally mounted mirror [35]. The plastic scintillator sheet faces the incident radiation beam and
the emitted light from back side of sheet is imaged with a CCD camera. The mirror redirects the emitted light so that the camera is outside of the radiation beam in a low noise region. The images correspond to 2D dose distributions. Stacking water equivalent layers on top of the scintillator sheet allows slices through a 3D dose distribution to be recorded. Optical photon spread was reduced using a microlouvre optical collimator sheet and internal glare was accounted for with a deconvolution procedure. The systems effective voxel size was $5 \times 0.5 \times 0.5$ mm$^3$. The $15 \times 15 \times 0.5$ cm$^3$ scintillator sheet limited the maximum field size that could be imaged. Agreement with film dosimetry was less than 8% inside field edges. The system performance was reproducible to less than 2% over a six month study. The data suggest this approach may become a sufficiently rugged device for routine clinical dosimetry.

3.4. Radiophotoluminescent glass plate
Aaki et al have investigated small photon field (2 to 20 mm diameter) dosimetry using a silver activated meta-phosphate glass sheet detector [36]. Irradiated plates are images with a CCD camera as a UV light depopulates the photostimulable phosphor traps emitting visible light. Profiles and output factors were compared to Monte Carlo calculations, radiochromic film, ion chambers, diodes and diamond detectors. Good agreement is attributed to low energy dependence of small fields.

4. Three dimensional detectors
There are very few reports of 3D dosimeters other than the radiation sensitive gels which are the focus of this DOSGEL meeting. Kirov et al have shown that 3D dosimetry can be accomplished with scintillator solutions [37]. They irradiated a scintillator solution volume with a $^{106}$Ru eye plaque applicator and recorded fluorescence images at several orientations. An iterative reconstruction algorithm allowed a 3D dose map to be calculated. Agreement with radiochromic film was within 25% and most distance to agreement was generally less than 2 mm. With improvements this approach may be useful for brachytherapy type dose distributions.

5. Biological dosimetry
As dosimetry evolves measurements will biological dosimetry will become essentially the individual’s local and overall response to the dose and dose rate. This area is likely to be dominated by the sensitive functional imaging modalities as they become more quantitative. Early patient results can be observed from treatment response studies with positron emission studies, MRI, and x-ray CT. New targeted contrast agents will result in sensitive evaluations of tissue response. Likely the meaning of tissue equivalent dosimetry will change as well. Optical imaging of small animals is an early example of the potential for biological dosimetry within the patient. Walls et al have developed optical projection tomography which uses a diffuse light source for transillumination of small animals and low resolution microscope and CCD camera for detection [38]. Tomographic reconstruction results in 3D optical images of intact specimen with a voxel size of approximately 5 microns for a 1 cm field of view. The optics of this system is very similar to the cone beam CT geometry previously described by Wolodzko [39]. The key to obtaining high resolution images in biological specimens is the dramatic reduction in scattering obtained by replacing water with a higher refractive index material throughout the sample. This technique is referred to as optical clearing. The resulting images are essentially a low resolution 3D image. Oldham et al have extended this work to show a 3D image of mouse lung that was stained in vivo [40]. They show the potential to directly image microvasculature structure and follow the effects of radiation and anti-angiogenic agents in tissue.

6. Summary
Arrays of point detectors can be configured for linear, planar and 3D measurements. This approach has been commonly used for producing commercially available clinical dosimetry products. The performance of these devices is ultimately limited by the performance of the individual detectors. Which systems are most useful will depend on accuracy of the dosimetry. Spatial resolution is not a
significant factor since lower resolution systems could be scanned. Higher resolution can be achieved using a step and shoot approach.

Several of the issues being discussed at this meeting with respect to gel dosimetry such as accuracy, dose rate and fractionation effects are common issues for other chemical dosimeters such as films. Techniques for improving densitometric accuracy can be adapted to improving optical CT accuracy as well. Since the root physical issues are the same. For example, spectral analysis becomes important when more than one chemical species is formed. In the push to reach a goal of 1 mm isotropic spatial resolution and 3% dose accuracy for 3D gel dosimetry other techniques such as ion chambers and films have been used for comparison. As the quality of gel data approaches these target levels the question of the most appropriate measurements to compare with need to be addressed since recent reports have shown that errors of 2% with film and 1% with ion chambers are easily possible. Dosimetry may be approaching the stage where calculations are more accurate than measurements for low doses, low dose rates, small fields, low energy radiation (less than 100 keV) and regions of high gradients.

7. References

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