Review of recent advances in non 3D dosimeters

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Abstract. This review covers papers from the previous two years not being represented at this conference. Optically stimulated luminescence detectors, diamond detectors and radiochromic film are the major topics. An effort to link these papers to 3D dosimetry is included in this brief report. An overall theme of linear, water equivalent response is seen throughout the topics included.

1. Introduction
This review has a limited scope of reporting papers concerning dosimeters for radiotherapy that were published since the IC3DDose10 conference. It also attempts to complement research being presented at this meeting by highlighting dosimetry results that are not included at this meeting. The selection is intended to assist dosimeter researchers by providing a short list of papers outside their current focus. The review is broadly organized into point (0D) and planar (2D) dosimeters. Point detectors can be packaged as 1, 2, 3 and 4D dosimeters. Papers were selected from searches of PubMed, Web of Science and Summons databases with the keywords; dosimeter, ionizing radiation and radiation therapy. Papers dealing with doses greater than 50 Gy were excluded to limit material.

2. Miscellaneous
Valuable information related to radiotherapy dosimetry was published in recent review papers and more general data analysis papers. They are reported here for the benefit of readers interested in starting with a selected list of publications from the broad literature available.

2.1. Review papers
Small field dosimetry is challenging and provides an opportunity to learn the basic physical principles of dosimeter measurements. This information also provides the input to modeling with Monte Carlo calculations. The Institute of Physics and Engineering in Medicine report number 103, entitled Small field MV photon dosimetry, provides a wealth of information on this topic [1]. Dosimeter materials for 3D dosimetry can be evaluated using this report as a template. Often small field dosimetry is used to test the performance of an entire 3D dosimetry system. An even more challenging problem is accurate dosimetry for microbeam radiation therapy with x-ray beams generated by synchrotron sources where spatial resolution of tens of micrometers is required. A review of relevant high resolution dosimeters has been recently prepared, Bräuer-Krish et al [2].
2.2. Analysis

Methods for comparison of large 3D dose distribution data sets have been limited since few ‘bench mark’ data sets are available. Many researchers are still quantifying performance of readout scanners and the dosimeter materials. However, experimental progress indicates that efforts to develop analysis methods are needed and dedicated sessions are now part of this conference program, see previous proceedings. It is anticipated that new analysis methods will stimulate design of 3D measurements and provide guidance on required characteristics of 3D dosimetry systems, for example, spatial and dose resolutions.

A standard comparison method involves spatially aligning a data set to the corresponding reference set and subtracting element by element. These dose difference arrays are easy to interpret and quantify. However, dose distributions are often normalized before comparison, eliminating absolute differences that may be important. For clinical comparisons, the ‘gamma analysis’ approach combines dose differences and distances to agreement is a practical method of deciding pass-fail treatment QA. Bak et al have developed a modified dose difference analysis which provides a weighting factor proportional to the local dose gradient. Results are similar to gamma analysis with the advantages of providing the sign and magnitude of the dose difference [3]. Measurement theory likely holds many useful solutions that could be adapted to 3D dosimetry. Comparison of data sets is a generic problem. Interaction with researchers in other disciplines will generate new ideas for analyzing results. An example of this cross discipline thinking is contained in a report examining Bland-Altman analysis for comparison of different radiation dosimeter performances as standards [4]. They compared different ion chambers for kV energy depth doses. Graphical analysis involves plotting dose differences against the mean dose and determining dependences. This analysis should generate ideas for comparisons of different 3D dosimetry systems.

Watanabe and Hayashi provide an excellent discussion of errors related to scaling doses for relative dosimetry [5]. This issue is very important when comparing data sets. In general, comparison of independently measured doses is much more useful. When differences are found outside the anticipated limits then investigations will reveal the causes of the discrepancies. Only after evaluating the dose differences should normalizations be performed. They have provided a practical example of errors introduced for dose analyses with radiochromic film and BANG3 polymer gel. The results emphasize that linear response in dosimeters is a valuable parameter for subsequent analysis.

3. Point dosimeters

Point detectors are common in radiotherapy dosimetry. They are often translated through water phantoms to generate dose profiles from ionizing radiation beams. Their sensitive volumes dictate the spatial resolution achievable. If their absorption and scatter coefficients are similar to water, they are more valuable since knowledge of the local beam energy is not required to obtain accurate dose to water measurements. OSL films can be considered as 0, 1 or 2D depending on the readout geometry. Bending the films allows dose on a non-planar surface to be recorded. This is sometimes considered a form of 3D dosimetry.

3.1. Optically stimulated luminescence dosimeters (OSL)

OSL dosimeters have been reviewed since DOSGEL06 for this meeting. Since then Al2O3:C packaged by Landauer Inc. as the NanoDot™ with the MicroStar reader has become the replacement technology for thermal luminescence dosimetry (TLD) systems. The ease of use, physical size and lower cost led to quick adaptation into radiotherapy clinics. This dosimeter also has the benefit of detailed studies over many decades of TLD and other OSL materials.

A pair of papers from the same authors have re-examined the angular dependence of the nanoDot dosimeter and found a 4% lower response when irradiated parallel to a 6 MV photon beam compared to normal incidence [6, 7]. The dosimeter was also modeled with Monte Carlo calculations and the effect was attributed to partial volume effects. The thin air pocket within the nanoDot cassette was found to lower the angular dependence. The authors concluded that angular dependence should not be
ignored when using these dosimeters for irradiation geometries that involve multiple beam angles. The second paper examines the response of the OSL’s for measurements at beam locations away from the central axis where calibrations were performed. Generally, dosimeters are calibrated at or near central axis and at depths of charge particle equilibrium. In practice, these dosimeters are often used to measure dose just outside the beam edge or several centimeters from the beam edge where the energy spectrum is lower. In the case of patient treatment QA the OSL’s may be at a location in a phantom that is sometimes in the beam and others outside with a range of incident angles. This inconsistency may lead to errors in measured dose. In the second paper, the authors examined out of field response and found doses up 30% lower than with ion chambers. This paper highlights the complexity of dosimetry and provides a clear example of how incorrect calibration procedures can lead to errors in measured dose. It can be cited when considering the overall importance of using energy independent dosimeters for complex 3D dosimetry.

OSL’s can be further characterized following optical erasure of the previous signal. By this method dosimeters can be individually characterized when higher precision is required. In practice, the dosimeters can be grouped by sensitivity and then average group sensitivity is used for clinical dosimetry. There are now a few papers examining optical annealing effects, but there is no consensus on best protocol and or spectrum. Mrčela et al used both tungsten and UV filtered metal halide lamps, and found increased reproducibility in readings with optical annealing [8]. They found a reproducibility of 1% with annealing for repeated 1 Gy irradiations. My own experiments indicated blue light was more effective than green or yellow light. If the light source contains UV then higher readings are present following annealing. With LED’s that peak near 450 nm we obtain background readings of 200-300 counts post annealing, compared to initial readings of a new dosimeter of ~50 counts. More results characterizing OSL’s at diagnostic energy range have been reported [9]. The authors recommend optical bleaching to improve reproducibility, corrections for angular dependence and beam energy.

Many different materials have been reported for TLD dosimetry and the same process is likely to be repeated for OSL dosimeters. Dhabekar et al reported on the OSL performance of LiMgPo4:Tb,B phosphor [10]. The main advantage of this material is the large linear range from 10^-3 to 10^3 Gy. It has a dose sensitivity similar to Al2O3:C but a greater energy dependence below 100 keV. This report may stimulate development of similar phosphors. Jahn et al developed a 2D OSL reader with sub millimeter resolution for BeO films [11]. BeO has been studied as a dosimeter for several decades and its effective atomic number of 7.14 is close to tissue equivalence. A linear dose response from 10^-3 to 10^3 Gy was presented. Commercially available films with dimensions of 52x52x1 mm were used to record a dosimetric image. Further development of this technology should provide a very useful 2D dosimeter system.

### 3.2. Alanine powders

Alanine, lithium formate and lithium fluoride were compared for water equivalent energy response using Monte Carlo simulations [12]. Lithium formate with ESR readout provides the closest approximation to water response and exhibits sensitivity 5 times that of alanine and has a linear response from 0.2 to 1,000 Gy. These attributes make lithium formate an alternative dosimeter when accuracy is required from a small integrating dosimeter.

A study examining the feasibility of using alanine dosimeters in combination with Monte Carlo calculations for mixed neutron photon dosimetry indicates the method can provide consistent results for proposed boron neutron capture therapy [13].

### 3.3. Diamond diodes

Diamond detectors are of interest for water equivalent dosimetry since the atomic number is closer to water than silicon. Recently chemical vapour deposition has allowed commercial production of synthetic diamond with sizes suitable for radiation dosimetry. Lansley et al have compared samples of synthetic diamond films, 3x3x0.5 mm against a commercially available diamond detector from PTW.
Overall performance was comparable. Spadaro et al examined response of detector and standard grade diamond films with two types of metal electrodes [15]. Synthetic diamond films have also been evaluated as thermal luminescence dosimeters and the performance is promising [16]. Agreement between 12 MeV electron depth dose and ionization chamber measured dose demonstrates these materials can be employed for accurate dosimetry. Repeatability of 4% maximum was reported. Single crystal synthetic diamond detectors have been compared against ion chambers and planning calculations for IMRT type dose distributions [17]. The results are comparable, indicating that diamond detectors may be useful for small field dosimetry. Independent studies are also reporting that commercial samples of CVC diamond films are suitable for radiotherapy dosimetry [18]. Larger crystals from other sources are also demonstrating acceptable performance [19]. Deposition of carbon nickel thin films by laser sputtering provided enhanced performance over both carbon and platinum electrodes, demonstrating importance of electrode quality on device performance [20].

3.4. Silicon diodes

Silicon diodes are commonly used in radiotherapy dosimetry because of their high sensitivity and potential sub millimeter spatial resolution. Drifts associated with accumulated dose and non-water equivalent energy response can be addressed by annealing with large doses and correct packaging of the detectors for specific applications. Silicon based dosimeters may become obsolete if synthetic diamond dosimeters become popular. However, silicon dosimeters have a large research literature to support continued development and are likely to be a less expensive technology for the near future. A thin 2D array of thin epitaxially grown diodes was characterized by Wong et al [21]. This technology could be used either in transmission mode or sandwiched into a water equivalent phantom. The sensitive volumes were 0.5x0.5x0.05 mm³. Dose rate dependence, energy response and angular response were reported. Based on the reported data, thin diodes appear to be an improvement over current commercial diode dosimeters. Eklund and Ahnesjo have modeled silicon diode response with Monte Carlo simulations and have concluded, that thin active layers sandwiched between thicker inactive layers is a preferred geometry for dosimeters [22]. Cranmer-Sargison et al have evaluated the small field performance of the commercially available diode dosimeters and reported the reproducibility to be within 1.25% [23].

4. Planar dosimeters

Two dimensional sub millimeter resolution continues to be the strength of film dosimeters. Silver halide film is now obsolete as a commercial product due to replacement by CCD and CMOS diode arrays in digital imaging systems. However, high resolution, water-equivalent detector arrays with fast readout have yet to be commercialized. Currently the only commercial film dosimeter is the radiochromic product from Ashland Chemicals referred to as external beam therapy (EBT) film. Nearly all other types of dosimetry are compared with film dosimetry either for validation within a plane or as a cross reference at selected points. For example, 2D film dosimetry is commonly used to validate Monte Carlo simulations and selected planes within a 3D dose distribution measured or calculated. For this reason, the film dosimetry papers continue to dominate the literature in numbers. In fact, 50% of the papers in this review are related specifically to EBT film dosimetry. The EBT product continues to evolve. EBT is now obsolete, replaced by EBT2 and EBT3 films. Scanner technology continues to evolve as well. Commercial radiochromic film scanners have yet to be marketed and much work is involved in developing calibration protocols for flatbed document scanners. It is interesting that many of the issues associated with quantitative optical CT scanning are the same for radiochromic film scanning. Stray light is generally the limiting feature in obtaining the maximum information recorded in 2D and 3D dosimeter materials.

4.1. Radiochromic film

A review of radiochromic film dosimetry was recently prepared by Devic [24]. This paper serves as an efficient introduction to the field. The range of calibration strategies is summarized and provides a
template for design of protocols for 3D dosimeters. The analogies between film and 3D dosimetry are useful to follow. Energy dependence and film uniformity are identified as current issues, but both can be solved with additional product development. A tremendous advantage of EBT2 film over silver halide films is that it can be directly immersed in water for several minutes without measurable impact on dose response. This feature is documented in a paper by Arjomandy et al in which film strips are mounted in a water tank, collinear with photon, electron and proton beams and measured depth doses are compared with calibrated ion chamber results [25]. When high resolution is required, EBT2 film provides a “excellent secondary dosimeter”. Stray light with flatbed document scanners is model dependent and requires careful evaluation to minimize impact of measured dose accuracy. Buston et al documented improvements that can be achieved for the Epson V700 model by placing additional white sheets of paper behind the film [26]. Generally, increasing the amount of scatter in an optical system degrades spatial resolution and dynamic range. A 1% uniformity was achieved over the entire scanning area.

Film uniformity has been reported by several authors as a problem with EBT2 film. While it is anticipated this is not a fundamental problem and improved manufacturing methods will make the uniformity within acceptable levels, users are left evaluating each film and developing protocols to minimize effect on measured dose. If each film is unique, then in principle, each pixel needs to be calibrated individually. Roozen et al have examined this issue and developed a pixel based calibration protocol that addresses the non-linear dose response of EBT2 film [27]. In this method a pre-irradiation is used to correct for non-uniformity film sensitivity (thickness) and record pixel sensitivity. Following irradiation and scanning of the dose distribution of interest, a second calibration irradiation is performed and used to correct the non-linear response of that pixel. This paper provides a clear example of the complexity of working with non-uniform, non-linear dosimeters and should be a warning to researchers working with 3D dosimeters. Mizuno et al evaluated EBT2 film homogeneity from different lots with an Epson GT-X970 scanner and recommended the each lot be evaluated before clinical use and the calibration curve be developed using net optical density of red channel only [28]. Another study by Aland et al reached the same conclusion with an Epson V700 scanner that incorporating the blue channel increased uncertainty [29]. EBT film dosimetry is actively being researched also by the staff of the manufacturer, Ashland Chemicals. Micke et al have developed several innovations in calibration protocols to maximize the accuracy of their product [30, 31]. They demonstrated an analysis method that uses the red, green and blue channels to correct for film non-uniformity pixel by pixel and maximize the dynamic range by merging dose responses for the three channels. They have also demonstrated calibration strategies using a ‘master response’ and individual sample responses to minimize the number of calibration points required to characterize a given film. With this approach accurate dosimetry within an hour of irradiation is demonstrated. This represents a significant achievement for making EBT2 practical for patient QA. The technique includes development of a formalism using a linear response function for the film-scanner system. A detailed comparison of different uniformity correction methods using the RGB channels demonstrated both improvements and degradations relative to the red channel netOD method [32]. Another detailed investigation found the RGB method proposed was equivalent to the single red channel approach with the advantage of not requiring a pre-irradiation film scan [33]. Mayer et al proposed another method involving ratios of the RGB images as an alternative to the “registered correction matrices” in the current analysis method of the manufacturer [34]. They concluded this method was simpler.

In order to achieve a high dynamic range in measuring a photon beam profile, Van den Heuvel et al, used three films and three central axis doses in order to use the scanner and film within optimum optical densities [35]. This technique, while useful for film dosimetry, may have less value in 3D dosimetry where the 3D stray light distribution is directly coupled the 3D dose image. However, the paper provides a clear demonstration of how to achieve the highest quality measurement possible within the limitations of the equipment available. EBT2 film with 40 Gy dose per fraction was demonstrated to have accuracy to less than 3% for 4 and 12 mm targets [36]. A very detailed film
dosimetry protocol that achieves 2% accuracy was documented by Huet [37] and could provide technical insights for novice and experienced users of film and Epson scanners to review.

EBT film has been used to validate Monte Carlo calculations for 4-20 mm diameter, 6 MV photon beams [37], and identify dosimetric differences related to inter-leaf leakage, helical field junctioning and small field segments in IMRT deliveries [38]. Epson scanner comparisons reported similar dosimetry performance for 10000XL and V700 with V330 producing acceptable results [40]. An alternative to flatbed document scanners are devices specifically designed to digitize color film. Recently, immersion of film in refractive index matching fluid for scanning has been reported. This is completely analogous to the use of liquids for optical CT scanning of 3D dosimeters. Interference fringes, called Newton’s rings, can be observed when scanning film in partial contact with a glass plate. EBT3 film was engineered to eliminate these fringes by placing small beads that the film face to increase air space and eliminate the optical interference. An alternative method involves suspending the film in air during transmission imaging. The performance of the Nikon Coolscan 9000 ED film scanner with EBT2 film is reported demonstrating high quality images for film sizes less than 6 x 20 cm² [41]. The spectral dependence of HS radiochromic film was re-evaluated and provides a useful reminder that both stray light and spectral effects contribute to the overall shape of dose response curves and that narrower spectral sources provide more linear responses [42]. Such information is directly applicable to design of 3D optical CT scanners and 2D film scanners optimized for readout of radiochromic films.

A recent paper by Devic et al describes fitting dose response curves to a linear function [43]. Results are presented using the green channel of EBT2 film irradiated to a maximum dose of 10 Gy. This approach allows accurate relative dosimetry to be performed without developing a multiple point calibration curve and first determining absolute dose. This innovation may have considerable value for analysis of 3D dosimeters with non-linear responses.

4.1.1. EBT2 versus Presage
Synchroton machines can generate high resolution dose distributions and are invaluable for studying the effects of microbeam radiotherapy. High resolution 3D dose distributions are being presented at this meeting using optical CT readout of Presage. An alternative approach involves sampling with a confocal microscope operating in fluorescence mode. Data reveals that Presage can record higher spatial resolution than EBT2 film due to diffusion within the latter [44]. This is also a reminder that luminescence signals need to be eliminated when measuring absorption from strongly attenuating samples, whether the samples are 2D films or 3D dosimeters. Inference from this data suggests films of Presage may be very useful 2D dosimeters.

Many formulations of Presage have been reported and exploration continues to provide enhanced sensitivities [45].

5. Scintillation dosimeters
Plastic fiber scintillators have been reviewed in previous DOSGEL reviews. The key advantages are water-equivalent response and typical volumes of 1 mm³. They provide accurate dosimetry for small fields and with appropriate calibration protocols the coupling fiber ‘stem effect’ is minimized. In this program there is a review talk and several original presentations related to these dosimeters. For this reason, only other types of scintillation papers are reported in this review.

Analogous to larger 3D gel dosimeters, volumes of liquid scintillators can be used as both phantom and dosimeters. Imaging the visible scintillation light generated by dose deposition provides a real-time 3D (4D) dosimetry system. In principle, this process could also be performed with scintillation from appropriate gel materials, but liquids are likely better because of lower optical scatter and fewer chemicals to consider. The shapes are limited to the vessel that contains the liquid. By imaging at video frame rates, Archambault et al have demonstrated that spot scanned proton beamlets for intensity-modulated proton therapy can be verified [46]. Proton range, position and intensity were recorded with a 20x20x20 cm³ liquid scintillator system with sub millimeter resolution.
Many studies have been devoted to developing methods to quantify the amount of light originating in the optical fiber connected to the plastic fiber dosimeter. This light is analogous to the stem effect with ion chambers. There have been a few reports in which time resolved detection has been employed to isolate the light originating in the dosimeter from the extraneous light from the coupling fiber. Many of the commercially available plastic scintillators emit light on the nanosecond time scale. The light from the fiber is due to several mechanisms and spans the range from picosecond to millisecond. By finding an appropriate combination of scintillator material and coupling fiber, it should be possible to effectively discriminate signals using time. Most medical linear accelerators have pulse trains that last several microseconds and a repetition rate of less than a kilohertz. This window between pulses can be used for accurate dosimetry provided dosimeters with suitable decay rates can be developed. Organic scintillators with lifetimes of 20 microseconds have been evaluated and the data indicates even longer lifetimes are required [47]. This approach may lead to new high performance dosimeter materials with applications spanning 0 to 4D dosimetry.

6. Conclusion
Radiotherapy dosimetry remains an active area of research as witnessed by the many topics listed here and those being presented at this meeting. Three-dimensional dosimetry [48-50] builds on the knowledge developed for point dosimeters and 2D films. Overall, the dosimetry trend continues to evolve towards energy-independent (water equivalent), linear dosimetry systems.

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