

Reviewing three dimensional dosimetry: basics and utilization as presented over 17 Years of DosGel and IC3Ddose

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Abstract. For seventeen years a community of basic and clinical scientists and researchers has been meeting bi-annually to promote the clinical advance of techniques to measure radiation dose in three dimensions. The interest in this dosimetry was motivated by its promise as an effective methodology for 3D measurement of the complex conformal dose distributions achieved by modern techniques such as Intensity Modulated and Volumetric Arc Radiation Therapy. Each of the International Conferences on 3D Radiation Dosimetry resulted in the publication of informative proceedings [1-8], the majority openly available on the internet. The proceedings included papers that: i) reviewed the basic science of the radiation sensitive materials used to accumulate the dose information, ii) introduced the science and engineering of the imaging systems required to read the information out, iii) described the work flows and systems required for efficient dosimetry, iv) reported the protocols required for reproducible dosimetry, and v) showed examples of clinical use illustrating advantage and limitations of the dosimetry. This paper is intended to use the framework provided by these proceedings to review the current 3D chemical dosimeters available and to discuss the requirements for their use. The paper describes how 3D dosimetry can complement other dose delivery validation approaches available in the clinic. It closes with some personal reflections of how the motivation for, and practice of, 3D dosimetry have changed (or not) over the years.

1. Introduction

Since its early days when megavoltage radiation advances first enabled delivery conforming the shape of the beam to the tumour volume (as described by Trump [9, 10]), conformal therapy has progressed considerably with the development of advanced external beam techniques such as provided by Intensity Modulated Radiation Therapy (IMRT), Volumetric Modulated Arc Therapy (VMAT), Stereotactic Ablative Radiation Therapy (SABR), Fractionated Stereotactic Radiotherapy (FSRT), etc.; and through improved procedures for high-dose rate brachytherapy. The radiation delivery associated by these modern techniques is complex and results in shaped conformal dose distributions that must be correctly registered to the patient's anatomy to achieve the treatment intent. Associated with the increased complexity of the targeting of this radiation delivery is a heightened requirement for quality assurance (QA) for technical components of the delivery, including the treatment unit and planning systems, for validation of the dose delivery planned for individual patients and, perhaps, for end-to-end QA of the multi-staged process associated with the delivery over the full course of treatment [11]. Numerous approaches have been established in the clinic to provide this assurance including, for example, the use



of 2D and 3D arrays of detectors for patient specific dose delivery validation [12-14], and electronic portal imaging detector (EPID) based assessment [13, 15-18]. These approaches have their place and are clinically very useful [14]. But they typically provide sparse 3D data and only surrogate validation of 3D dose delivery. Full 3D dosimetry using volumetric chemical dosimeters probed by 3D imaging systems does provide for dose measurements an irradiated volume and hence gives a unique methodology for conformal delivery QA [19, 20] (see Fig. 1).



Figure 1. A recent illustration of the 3D dose information captured in three different gel dosimeters from the proceedings of IC3Ddose [21]. (left) The Fricke-xylenol-orange-gelatin dosimeter shows a colour change in the volume irradiated with a 12 MeV electron beams. (centre) The polyacrylamide polymer gel dosimeter shows increased scatter in the high dose areas radiated using a Cobalt-60 tomotherapy IMRT delivery. (right) The colour change of a Leuco-crystal-violet micelle gel dosimeter after a VMAT prostate plan irradiation.

The clinical applicability of 3D dosimetry has advanced considerably in the last decade by the development of improved dosimeters [21] (e.g., radiochromic plastics [22, 23], radiochromic gel dosimeters [24,25] and normoxic polymer gel systems [26]) and by improved readout protocols using optical computed tomography or magnetic resonance imaging.

In the discussion above the definition of a 3D dosimeter has been set by elements of the RTAP criteria [27, 28]. Under RTAP an ideal true 3D dosimetry system (dosimeter and associated readout) should be able to deliver dose measurements in a 3D volume with 1 mm isotropic spatial resolution in less than one hour with 3% accuracy and a precision of 1%. As noted in the past [21], criteria for the resolution, accuracy and precision may be relaxed in clinic practice, depending on the specific validation being performed (for example, the criteria in external dose delivery audit under IROC is relaxed considerable for a number of practical reasons [29, 30]). But to date the criterion for high resolution isotropic measurement limits ‘true’ 3D radiation dosimetry to chemical radiation dosimetry based on quantifying the effects of radiation-induced chemical changes occurring within some volume of material [21, 27, 31]. And this is the condition used in this review to set the “true 3D” designation.

While true 3D dosimetry is, despite its promise, still not widely practiced in the community, clinical adoption beyond research laboratories is now well indicated. In fact, a comprehensive account of how 3D dosimetry has developed and can be used has been presented in 17 years of DosGel and IC3Ddose proceedings of the International Conferences on 3D Radiation Dosimetry [1-8]. The 101 invited review papers and 469 submitted proffered papers therein outline the history of field, report technical improvements and developments as the dosimetry advanced, and describe various roles 3D dosimetry can play in the clinic. They present clear evidence for improvements over time that eliminated the constraints that moderated past clinical acceptance (such as loss of spatial integrity of dose information in Fricke gels [32], response inhibition in oxygen contaminated polymer gels [33], reproducibility and stability challenges as preparation protocols change [34], etc.). And the proceedings

have pointed to the benefits which 3D dose measurement could provide for specific clinical problems, often in conjunction with other dosimetry systems.

This paper presents a citation review of 3D dosimetry as collected in these conference proceedings, citing select literature from the proceedings to provide a reader new to 3D dosimetry a convenient and readily accessible introduction to, and presentation of, the field.

2. The Road to IC3Ddose

The International Conferences on 3D Radiation Dosimetry have, from the very first paper [35], presented a strong motivation for the use of true 3D dosimetry. Initially the main applications were thought to be best directed to patient specific dose delivery validation as had been indicated by Hiraoka *et al* in their visionary work using anthropomorphic phantoms and MRI [36, 37]. This promise was quickly supported in proffered reports of clinical applications such as Scheib *et al*'s [38] in-house measurement and analysis system for patient specific dose validation in radiosurgery using polyacrylamide gels, and many more papers that followed.

However, the conference reports over the years have also made clear that the requirements in the clinic [11, 14, 19, 27, 29, 30, 39, 40] do not limit useful dosimetry to the 'true' 3D dosimeters described above [11, 20, 39, 41]; rather it has been noted in the proceedings that other dosimetry techniques may be more efficient and effective in certain roles (see Table 1). For example, patient specific IMRT and VMAT dose delivery validation prior to, or during, treatment is often more efficiently and effectively performed with 2D EPID based techniques [13, 15-18]. The fact that various dosimetry techniques supplement each other and are important in the clinic was acknowledged explicitly in the history of the conferences when they were renamed in 2010 from the series of '*DosGel*' sessions to the '*IC3Ddose*' meetings, establishing a more widespread focus in order to encourage attendance by researchers and clinicians working with point, planar and pseudo 3D dosimetry techniques. This extension to the wider community with expertise in film, EPID based [13, 15-18], scintillation [42, 43] and point array measurements [12, 44-46] enabled a more critical assessment of the role of the different systems and facilitated an improved discussion of how these various dosimetry systems can complement each other [45, 47, 48]. Therefore, the literature reported in the conference proceedings to date provides a broader content not limited only to volumetric chemical 3D dosimeters.

3. The Themes of IC3Ddose as Presented in Invited Papers

There are a number of common themes in each of the proceedings of the previous 8 International Conferences on 3D Radiation Dosimetry (see Table 2). Each conference has included a strong didactic component with invited papers providing attendees the fundamental science and basic mechanisms that guided the development and response of various dosimetry systems. Initial papers in the first conference proceedings review the history and development of 3D dosimeters [33, 35, 49], even providing historical background from before the seminal papers of Gore *et al* [50, 51] that initially established the 3D measurement potential of chemical dosimetry. There have been regular reviews of the fundamentals of Fricke gels [32, 52, 53], polymer gels [34, 54-57], radiochromic gels [23-25] and novel systems throughout the proceedings; each of the review papers providing a comprehensive list of references extending to the broader literature. These descriptions of the basic science of the various dosimeters were typically supplemented by details of how to best prepare and use the various systems to assure consistent and reproducible dosimetry.

This basic didactic component of the proceedings extends also to readout techniques including magnetic resonance imaging (MRI) [58-63], optical computed tomography (optical CT) [64-69], x-ray CT [70-72] and other potential readout systems [72]. These reviews typically describe the radiation properties of the irradiated materials that enable the various imaging modalities to readout the dose, and also provide detailed analyses that inform the imaging protocols required for reproducible and accurate readout. Thus the reviews consistently provide a valuable resource for establishing readout protocols when implementing 3D dosimetry. Additional invited papers further address data analysis

Table 1. A summary of some of the dose measurements and validation experiments required for implementing IMRT as initially summarized in the proceedings from DosGel 2006 [41]. The comments on the utility of volumetric 3D gel or plastic dosimeters in the shaded cells are personal reflections added in this current review based on past DosGel and IC3Ddose proceedings.

<i>Phase and Intent</i>	<i>Dosimetry / Test Required</i>	<i>Typical Tools and Approaches</i>	<i>Role for 3D Dosimetry</i>
1. Commissioning of treatment planning system and benchmarking of performance (both treatment planning and dose delivery)	Acquisition of beam data to dosimetrically characterize beam, and machine data to mechanically characterize linac	Ion chamber, water tank, film, detector arrays	no
		<i>Not strongly indicated for conventional beams but there is likely a role in small field and brachytherapy source commissioning</i>	
	Measurement of test cases planned in phantom under well-defined conditions to ensure correct performance and establish benchmark data for each particular treatment protocol	Regular and anthropomorphic phantoms; film; 2D dose QA systems (diode), portal imaging systems	yes
		<i>A strong role for 3D systems especially when used with complementary dosimetry techniques</i>	
2. Periodic QA	Routine testing of the delivery system; QA to ensure continued planning and delivery as at commissioning	Regular and anthropomorphic phantoms; film; 2D dose QA systems (ion chamber and diode), portal imaging systems	yes
	Including end to end QA	<i>A strong role for 3D systems especially when used with complementary dosimetry techniques</i>	
3. Routine patient specific treatment QA	QA of Monitor Unit (MU) calculations	Independent validated calculation system or direct measurements in phantom (see cell below) with ion chambers or other point dosimeters	possibly
		<i>Other techniques are much more reliable but, if validated, 3D systems may fill a complementary (not primary) role</i>	
	Testing of delivered dose distributions	Replace patient by standard phantom, expose phantom to same MLC sequence, trajectories and MUs as for patient. 2D dosimeters	yes
		<i>3D systems are powerful tools for initial testing of novel treatments techniques (e.g., small field irradiations, irradiation under motion management, etc.), especially when used to validate other pseudo 3D techniques used regularly for patient specific QA (see below)</i>	
	At treatment measurement of delivered dose and dose distribution.	In-vivo dosimetry or online exit beam dosimetry (using EPID or tomotherapy imaging detector)	no
<i>In general other techniques may be better indicated, however, new small field techniques (e.g., small field VMAT treatment of multiple brain metastases) may bring an increased clinical role</i>			

procedures required to go from imaging readout to dose, addressing such issues as accuracy and error analysis [73-76], calibration, data processing workflow and 3D dosimetry metrics enabling comparison of measured doses with planned distributions [77, 78]. Over the years the 100 or so invited reviews have presented a detailed set of courses on how to perform 3D dosimetry.

4. The Themes of IC3Ddose as Presented in Proffered Papers

The conference proceedings from the various DosGel and IC3Ddose meetings also review well the development of 3D dosimetry as reported by basic researchers, practical developers and clinical users (see Table 2). (Citing the many individual proffered papers that have advanced the practical and clinical role out of gel dosimetry is beyond the format of this review; but a narrative based on the conference proceedings is possible.)

The initial meeting [1] focussed on Fricke and polymer gel dosimeters as the main systems of interest. But soon reports of new dosimeter systems appeared, often for the first time, in these proceedings. Fong introduced normoxic polymer gels in Brisbane [2]. In Ghent's DosGel04 [3], the first of the proceedings to be reported in the open Journal of Physics: Conference Series, Venning *et al* reported on PAGAT, the normoxic formulation of the more common polyacrylamide gel, while Adamovic and Maryanski described the polyurethane radiochromic systems that developed into PRESAGE. The reduced toxicity N-isopropylacrylamide (NIPAM) system was introduced by Senden *et al* two years later in Sherbrooke [4]. The proceedings from Dosgel08 in Hersonissos [5] had reports of the development and use of the normoxic N-Vinylpyrrolidone polymer (VIP) gel by various Greek researchers and introduced the new family of micelle radiochromic gels through Babic *et al*'s proffered work. The reports of new dosimetry systems has continued in more recent conference series [8] with reports of the development of novel deformable polydimethylsiloxane and silicone based dosimeters by De Deene *et al* and Høye *et al*, respectively. As Juang *et al* showed in the IC3Ddose 2013 [7], the development of these dosimeters enables dose measurements that can validate advanced deformable dose calculation algorithms in modern treatment planning systems. This small sample clearly shows that the proceedings provide a solid account of the historical development of 3D dosimetry systems.

The proceedings do not just report the development of new dosimeters; they also compile a considerable literature on the practical aspects of their use. For example, Keller *et al* showed in the initial DosGel [1] that the then commonly held view that adding mM amounts of benzoic acid during the preparation of the dosimeter would increase sensitivity was false, since the presence of 5% gelatin provided overwhelming alternate reaction pathways already increasing the chemical yield. In Ghent [3], McAuley *et al* confirmed the observation of enhanced dose response at the edge of high dose gradient regions in polyacrylamide polymer gels through mathematical modelling of monomer diffusion in irradiated gel. This modelling was later extended to brachytherapy applications and in Hilton Head [6] the group reported that the perturbation of polymer formation around low dose-rate brachytherapy sources would make dose calibration of polymer gels problematic in LDR brachytherapy. Each of the proceedings over the years has also presented a full set of proffered papers that describe practical issues in sample preparation, particularly highlighting the importance of establishing, and sticking to, careful preparation protocols (including setting timescales for various steps in the preparation of the dosimeters, periods between sample preparation and irradiation, and then time to readout) to ensure consistent and reproducible dosimetry. The proceedings offer a compendium of preparation caveats and practices to avoid; in fact, a search of the proceedings before undertaking the use of a particular dosimeter is well indicated, since this will help the new user set good protocols at the start of their work (see also [31]).

The papers proffered over the last two decades of these international conferences also present a complete review of the potential clinical utility of 3D dosimetry as first promised by Scheib [38]. Even an abridged review of a limited set of conferences makes this clear. In Sherbrooke [4] Oldham reported on IMRT verification with optical CT readout and radiochromic plastic, Pappas reported on small field profile measurement with polymer gels, while Månsson *et al* and Oldham *et al* reported on 4D measurements made with dynamic phantoms simulating respiratory tumour motion. Later, in 2008 in Crete [5], Petrokokkinos *et al*, Moutsatos *et al* and Papas *et al* reported on the use of VIP gels for dosimetry applied to HDR brachytherapy, Gamma Knife and stereotactic radiosurgery commissioning, respectively; Ceberg *et al* discussed RapidArcTM treatment validation using MRI and polymer gels; while Wu reported on the commissioning of a high definition multileaf collimator using polymer gels and optical readout. Ceberg *et al* showed more on the use of gels for 4D treatment validation in Sydney, reporting the measurement of interplay effects in VMAT delivery on a breathing motion phantom. Over the years our group from Kingston has reported on the use of 3D dosimetry, mainly with optical readout of Fricke gels, for example for stereotactic body radiation therapy with IMRT and VMAT dose delivery validation [7, 8, 48], noting that complete characterization in the clinical setting can benefit from the correlation of measurements from multiple dosimeters such as ion chamber, film and 3D dosimeters [48,47].

Table 2. A summary of the proceedings content (✓ indicates significant content, ~ indicates limited or no presentations in a given year, there may still have been some discussion).

	Meeting	DosGel					IC3Ddose		
	Year	1999	2001	2004	2006	2008	2010	2012	2014
	Venue	Lexington USA	Brisbane Australia	Ghent Belgium	Sherbrook Canada	Hersonnisos Greece	Hilton Head USA	Sydney Australia	Ystad Sweden
No of papers	Invited Review/ Refresher	9	9	12	11	10	21	17	12
	Proffered	36	41	39	46	55	80	93	79
Basics of Dosimetry Systems	3D systems (history, background)	✓	✓	✓	✓	✓	✓	✓	✓
	Fricke Gels	✓	✓	✓		✓	✓	✓	
	Polymer Gels	✓	✓	✓	✓	✓	✓	✓	✓
	Other Radio- chromic Gels	~	~	~	~	✓	✓	✓	✓
	Radio- chromic Plastics	~	~	✓	✓	✓	✓	✓	✓
Readout Systems	MRI	✓	✓	✓	✓	✓	✓	✓	~
	Optical-CT	✓	✓	✓	✓	✓	✓	✓	✓
	X-ray CT	~		✓	✓	✓	✓	✓	✓
	other	~	✓	✓	~	✓	✓	✓	✓
Practical/Clinical Issues	Clinical Role	✓	✓	✓	✓	✓	✓	✓	✓
	Data Evaluation	~	~	✓	✓	✓	✓	✓	✓
	Equipment/ source Commissionin g	~	~	✓	✓	✓	✓	✓	✓
	Dosimeter preparation protocols	✓	✓	✓	✓	✓	✓	✓	✓
	End to End QA	~	~	~	~	✓	✓	✓	✓
Complementary Dosimetries	EDID based	~	~	~	~	~	✓	✓	✓
	Point Dosimeter Arrays	~	~	~	✓	~	✓	✓	✓
	Film	~	~	~	✓	✓	✓	✓	~
	Scintillators	~	~	~	~	~	✓	✓	✓
	Others	~	~	~	✓	✓	~	✓	✓

Over the years the groups from Duke and the M.D. Anderson have also investigated the potential for volumetric 3D dosimeters for end-to-end quality assurance in the clinic and in credentialing programs (for example, two papers by Sakhalkar in 2009 [5], work by Newton in 2010 [6], and by Thomas in 2013 [7]). The work outlined in this paragraph is, in large part, the basis for my long held view of a strong role for 3D dosimetry in the clinic as described in the final section (Clinical role - reprise) of the 2015 review article on true 3D dosimetry [21]. A quick read of the submissions for this year's IC3Ddose suggests that proffered papers will again indicate an increased role for 3D dosimetry in the modern radiation therapy clinic.

Over the years attendees at the 3D dosimetry conferences have also reported on one other important factor in 3D dosimetry: data analysis and workflow. Initially the focus was typically on the scientific fundamentals of converting readout to dose, with emphasis on uncertainty and error analysis. Eventually the reports evolved more to description of the analytic tools required for fast efficient data analysis and for the comparison of 3D measurements to the dose distributions from treatment planning as described, for example, by Kozicki in two papers in Crete [5], by Deasy in Hilton Head [6], and by Alexander in Ystad [8].) These papers illustrate the advances in data analysis provided by dedicated systems initially developed in-house and often later commercialized or offered in open source environments.

Finally, the various 3D dose conferences have benefited increasingly over the years by the attendance of commercial vendors offering a variety of services from dosimeter preparation, to sales of dosimeter readout systems (especially optical-CT scanners for radiochromic gels and solids and polymer gels), to actual readout and dose calculation service to clinical users lacking the required facilities in their clinics for in-house preparation and processing. The companies are listed in Table 3 along with some references to proffered papers that touched on the initial research that lead to commercializing, to later reports of the development of protocols for use, or to presentations of clinical applications performed in collaboration with the vendors. The increased availability of these commercial partners is an encouraging development, as it can only help further advance the clinical adoption of 3D dosimetry.

Table 3: A list of commercial service providers and vendors and an open-source system that have contributed to the various IC3Ddose meetings and that offer various 3D dosimetry readout and analysis systems and dosimeters; citations are to select proceedings reports related to their wares.

Provider	Vendor Website	Select DosGel / IC3Ddose papers related to vendor products
GeVero, Poland	www.polygevero.com	[79, 80]
Heuris Pharma, USA	www.presage3d.com	[22, 81-87]
MGS Research Inc., USA	www.mgsresearch.com	[88-90]
Modus QA, Canada	www.modusqa.com	[91-93]
RT Safe, Greece	www.rt-safe.com	(based on [94, 95])
Slicer-RT, Canada	www.slicerrt.org/	[21, 96, 97]

5. Conclusions

This review is intended to provide the reader a comprehensive set of references from past International Conferences on 3D Radiation Dosimetry on which to build their new work. This compendium offers a unique open source library detailing the scientific fundamentals of 3D dosimetry and outlining the development of clinical practice over nearly two decades. It represents a fruitful outcome from meetings born from a perceived need some 20 years ago of the requirement to establish a forum for researchers in a new field [98-100]. It also sets the stage for the remaining 9 invited and 64 proffered papers in these current proceedings. I wish you good reading.

6. References

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