Radiochromic 3D Detectors

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Abstract. Radiochromic materials exhibit a colour change when exposed to ionising radiation. Radiochromic film has been used for clinical dosimetry for many years and increasingly so recently, as films of higher sensitivities have become available. The two principle advantages of radiochromic dosimetry include greater tissue equivalence (radiologically) and the lack of requirement for development of the colour change. In a radiochromic material, the colour change arises direct from ionising interactions affecting dye molecules, without requiring any latent chemical, optical or thermal development, with important implications for increased accuracy and convenience. It is only relatively recently however, that 3D radiochromic dosimetry has become possible. In this article we review recent developments and the current state-of-the-art of 3D radiochromic dosimetry, and the potential for a more comprehensive solution for the verification of complex radiation therapy treatments, and 3D dose measurement in general.

1. Introduction

End-to-end verification measurements of radiation dose distributions delivered to phantoms has long been a key component of comprehensive radiation therapy QA programs [1]. These measurements are typically performed during an intensive commissioning phase, when the accuracy of a new technique is established prior to implementation on patients in the clinic. Historically, in the absence of dosimetry tools that can measure the dose in 3-dimensions (3D), commissioning measurements were typically made at selected planes and points, utilizing film, TLD’s, diodes, and ion chambers [2]. These low-sampling methods have important uses, but are incapable of providing comprehensive verification in 3D throughout the relevant volume at high resolution. The advent of sophisticated and complex radiation treatments has led researchers to consider whether 3D radiochromic dosimetry techniques can provide a more comprehensive solution to the problem of verification of complex radiation treatments. This review builds on work in Oldham [3], describing the development and current state-of-the-art of 3D radiochromic dosimetry.

The term 3D dosimetry was discussed in Oldham et al [4] who introduced the Resolution-Time-Accuracy-Precision (RTAP) criteria as a performance goal for clinical use. To meet RTAP, a dosimetry system should deliver a 3D dosimetric analysis of a treatment plan with 1mm isotropic spatial resolution, within 1hour, with an accuracy of within 3% of the true value, with 1% precision. The RTAP remains a useful benchmark, although others have noted that lower resolution is sufficient for some clinical situations, and a shorter time criteria would be ideal. Partial-3D dosimetry systems such as Delta4 and arc-check, have planes or surfaces of point detectors and interpolate to 3D dose [5-7]. These approaches represent momentum toward the ideal of a truly comprehensive 3D dosimetry system, but are not discussed further here.
3D dosimetry systems in current use include those illustrated in figure 1. These are chemical dosimetry systems, where a material exhibits a physical response to radiation that can be quantified and imaged by a readout system. Three categories of materials are shown: polymer gels, radiochromic gels, and radiochromic plastics. These three materials and associated readout (imaging) methods have been discussed recently in [3]. Polymer gel dosimetry has been much studied and while many applications and uses have been demonstrated [8, 9] the limitation to MRI or slower optical readout techniques have led some researchers to investigate the potential of radiochromic dosimetry. Radiochromic dosimeters are compatible with cheaper and potentially faster optical readout techniques, by virtue of relative insensitivity to stray-light artifacts (discussed below). Here we focus on developments in the radiochromic detectors – both materials and readout techniques. Alternative 3D dosimetry systems have also been recently proposed utilizing scintillation [10] and the Cerenkov effect [11], but are not discussed further here.

2. Methods of 3D Radiochromic Dosimetry

2.1. Radiochromic Gels

The ferrous sulphate (or Fricke dosimeter) has been used for many years as both an absolute and relative dosimetry system [12, 13]. The Fricke dosimeter consists of a ferrous solution containing Fe2+, contained in small vials compatible with optical attenuation measurement in a spectrophotometer. Fricke dosimeters are tissue and water equivalent even for lower energy radiation fields [14]. When irradiated, Fe2+ is oxidized to Fe3+, and the quantification of the proportion of Fe3+ (which is proportional to absorbed dose) is determined by spectrophotometry [15]. To achieve accurate measurements, the temperature of the reaction must be carefully controlled. Another challenge can be the limited sensitivity caused by the modest optical-density (OD) change of the Fe3+ ions at the probing light wavelength (224nm). Imaging at such a short wavelength is possible for small volumes of Fricke solution contained in optical cuvettes (with an optical path length of 1cm) but not feasible for large volumes due to strong light attenuation.

Gore et al 1984 [16] first proposed 3D Fricke based dosimetry by showing that ferric ions have a greater influence on proton relaxation times than ferrous, enabling 3D dose imaging by MRI [16, 17]. A linear relationship between spin-lattice relaxation rate R1 and dose was reported [18]. R1 relaxation measurement was preferred to spin-spin relaxation (R2) for Fricke gels, because of higher dynamic range (the unirradiated Fricke dosimeter exhibits low R1) [19]. A key limitation arises from diffusion.
of small Fe$^{3+}$ ions in the gel immediately post irradiation, leading to degradation of the dose distribution. To mitigate this effect, the gel needs to be imaged within ~1 hour [20-22]. Attempts to stabilize the Fricke solution in gels were performed by a number of investigators ([14, 16, 23-26]. Early work reported low spatial resolution (thick slices) owing to the challenge of obtaining low noise with high spatial resolution using MRI. Recent work involving fast 3D MRI sequences has shown promising results: 1mm isotropic, in a 20 minute imaging session [27].

![Figure 2.](image.png)

Figure 2. A) calculated dose distribution of a 4-field box irradiation (6MV and 4x4cm). B) Corresponding optical-CT scan through an irradiated FBX gel. C) Line profile comparison along the line indicated in A and B. D) The change in absorbance spectrum of an irradiated FBX dosimeter, indicating optimal readout wavelength of ~535nm. From Kelly *et al* [28].

The Fricke 3D dosimeter requires access to MRI, which is restrictive for many medical centres. Much effort has therefore been devoted to developing Fricke gels that could be imaged by optical-computed-tomography (optical-CT). The addition of a metal ion indicator (e.g. xylenol orange) leads to a visible colour change in the presence of ferric (Fe$^{3+}$) ions [29]. This development opens up the facility for optically imaging larger Fricke dosimeters using longer wavelength light with greater penetrating power [17]. Kelly *et al* [28] demonstrated the feasibility of 3D optical-CT dosimetry of Fricke-benzoic-xylenol (FBX) gels (see figure 2). Their system used a scanning laser beam and was able to achieve sub mm spatial resolution and an accuracy of reconstructed attenuation values of within 2%, corresponding to dose measurement of within 5% in dose range 1-10Gy. A key advantage of the FBX dosimeter for optical-CT dosimetry, is the nature of the radiation induced optical contrast, which is absorbing in nature, incurring minimal stray light. This enables fast broad-beam scanning systems [30, 31]. The Fricke and FBX gels are relatively easy and convenient to make [32]. The main challenges relate to the need for an external casing to support the gel (largely a cost and convenience factor), and the diffusion limitation, requiring the gel to be imaged within 1 hour of irradiation.

### 2.2. Radiochromic Plastics

A radiochromic plastic material ‘Presage’ was first introduced in 2006 for 3D dosimetry by optical-CT [33]. Presage consists of a firm polyurethane matrix doped with a halogenated hydrocarbon free
radical initiator and a leucodye (leuco-malachite-green). The polyurethane matrix is highly transparent: more so than gelatin or agarose. Radiation induced optical-contrast is generated through the oxidation of LMG to malachite green (figure 3). Presage thus maintains the advantage of radiochromic gels in the minimization of stray light through an absorptive radiation induced contrast mechanism. The hard polyurethane substrate removes the requirement of an external casing. Presage has proved highly versatile for moulding [34], and embedding cavities and channels (e.g. in brachytherapy applications [35, 36]). 3D printing of Presage dosimeters of various shapes, including anatomical shapes defined on CT scans, is an exciting new capability that has recently been demonstrated [37].

![Figure 3](image)

**Figure 3.** A) The transparent leuco-dye (LMG) and the absorbing oxidative product malachite green [33]. B) A cylindrical PRESAGE dosimeter (11cm diameter) which inserts into a poly-urethane head-phantom for radiosurgery verification [38]. C) post-radiation temporal stability of radiation sensitivity of several Presage variants, illustrating how minor changes in formulation can yield substantially different effects [34], D) linearity and stability of a presage formulation (unpublished data).

A linear optical dose response of Presage has been demonstrated up to doses as high as 100Gy [33, 39-41]. Some studies have reported negligible energy or dose-rate dependence in the region 145kVp to 18MV [33, 40-42]. However other studies have reported conflicting results as to the stability of the radiochromic response and the relative 3D distribution [43]. Substantial variations in sensitivities between formulations of the same batch, and even the same batch but different volumes have been reported [44]. These results suggest caution when evaluating and using different Presage formulations. The poly-urethane substrates part A and part B can be varied, in different proportions, to create dosimeters with markedly different hardness. Recent data from our lab (figure 3C) show wide variability in post irradiation stability associated with relatively minor changes in poly-urethane components. Like many materials (including PAGs, and EBT film) under-response has been reported in the Bragg-peak when using Presage in proton beams [45, 46].
2.3 MRI Dose Readout Techniques
MRI was first used for 3D gel dosimetry by imaging R1 (spin-lattice) relaxation of water molecules in Fricke gels. R1 imaging has higher dynamic range than R2 (spin-spin) relaxation. The mechanisms underlying the relaxation and paramagnetic molecules have been described previously [16, 18]. The main challenges for MRI 3D dosimetry of radiochromic Fricke gels include difficulty generating high resolution low noise images, and stabilizing the irradiated dose distribution. The diffusion of small Fe$^{3+}$ ions within the gel degrades the dose distribution [13]. Given the challenges associated with accurate quantitative imaging with MRI, it is essential that the appropriate sequences and system characterization is implemented prior to 3D dosimetry studies. A number of limitations and challenges have been identified, leading to concern that expertise in MR imaging is a pre-requisite for accurate 3D dosimetry [47-49]. While some expertise is necessary, the prospect has been greatly simplified by recommendations in a recent report by De Deene et al [19].

2.4 Optical-CT readout of radiochromic gels
Optical-computed-tomography appears to have arisen independently in three specialty fields [50-54]. Optical-CT is analogous to x-ray CT, except visible light is used as the imaging modality. In both optical and x-ray CT, line integrals of attenuation are acquired at various views through the object to be imaged. The relatively small size of 3D dosimeters makes it practical to rotate the dosimeter, rather than the source and detector. The same reconstruction algorithms (e.g. filtered back-projection) can be used to reconstruct 3D maps of the local attenuation coefficients (x-ray or optical), and both modalities are susceptible to artefacts including scattered radiation, rings, beam-hardening, attenuation, motion, etc [55, 56]. Several different configurations of optical-CT systems for 3D dosimetry have been investigated as shown in figure 4. The primary advantages of optical-CT for 3D dosimetry, include reduced cost, increased accessibility, and potentially higher accuracy and precision in shorter imaging times [4].

The presence of scattered light (or stray light) poses challenges to obtaining accurate optical attenuation maps, in the same way that x-ray scatter can corrupt cone-beam-CT images [57, 58]. Accurate optical-CT is feasible if the stray light contribution to the line-integral measurements in projection images are minimal. The first optical-CT system for 3D dosimetry, the ‘OCTOPUS’ [52, 53], utilized a 1st generation scanning laser configuration, operating in a translate rotate manner. These systems are quite effective at reducing scatter, and can be used to image dose in dosimeters with high scattered light component, like PAGS [8, 59]. Several groups have investigated the performance of the OCTOPUS [42, 59-61]. Variations on the scanning laser system were also explored [4, 28].

The limitation of the laser scanning configuration is that long imaging times are needed to translate and rotate the dosimeter to acquire all required line profiles. Scanning times of several hours were reported for large volumes [4, 53, 61, 62]. Recent scanning laser systems have achieved faster speeds by up to a factor 4 [62, 63], and still faster scans are possible utilizing rotating mirrors [64]. For smaller samples good quality results are reported [65-67]. Despite these advances, it was not until the introduction of broad-beam scanning systems that 3D dosimetry became feasible in time frame within the RTAP criteria[4]. The first prototype broad beam optical-CT scanners were proposed at the turn of the millennium [68, 69]. The image quality from these systems was not ready for preclinical use, a result compounded by the lack of radiochromic (low-scatter) dosimeters at that time. Other groups also developed in-house broad beam systems with more sophisticated components and configuration [31, 69-71].
Figure 4. Optical-CT scanning configurations. A) first generation scanning laser (from Gore et al [53]), b) cone-beam-CT arrangement (from Wolodzko et al [68]), c) parallel beam arrangement (from Krstajic et al [72]), d) a fully bi-telecentric system (Thomas et al [73]).

Two categories of fast broad-beam optical-CT scanning configurations can be identified: parallel beam, and cone-beam, illustrated in figure 4. Cone-beam-CT systems are low cost, but have the potential disadvantage of reduced accuracy arising from stray-light artefacts [30, 31, 74-76]. Telecentric systems are more expensive (due to the inclusion of sophisticated lenses) but have the capacity for high accuracy through minimisation of stray-light [70, 77]. The precise limitations and balance of this trade-off is yet to be fully determined. Stray light artefacts have been reported when using cone-beam-CT scanners and high scatter polymer gels [30, 31]. A continued increase in sophistication of broad beam optical-CT scanners is evident in the literature [30, 31, 68-72, 77, 78].

Perhaps the current state-of-the-art broad-beam system was introduced by Thomas et al [73], consisting of a powerful large field-of-view matched bi-telecentric scanning system. This system was commissioned and benchmarked for clinical use, and set a new standard for 3D dosimetry capability [38, 73, 79]. Accompanying articles addressed minor corrections associated with stray-light reflections (mostly within the lenses) and spectral artefacts [80, 81]. These corrections are negligible except under extreme conditions (e.g. small field dosimetry).

3. Summary and Conclusion

3D dosimetry has proved an innovative field of research and clinical development for over two decades. The original motivation was to develop more comprehensive methods for verification of complex radiation therapy treatments. This goal is potentially even more relevant today with continued increase in sophistication of modern RT treatments. Current areas of innovation and further development are occurring in 3 areas: materials development, readout development, and novel applications. For radiochromic materials, key challenges include the development of more stable dosimeters for remote credentialing activities [82], and re-useable dosimeters for improved economics within an institution [34]. New approaches to dosimeters have emerged from micelle technology [83-85] to new radiochromic materials [86]. The challenge of a 3D dosimetry material without an LET
dependence is also an active area of development [45, 87]. A recent development is the use of novel 3D printing technology to create anatomically accurate 3D dosimeters [37].

For 3D radiochromic dosimetry readout, improved optical-CT scanners and protocols are being developed, that are faster, more accurate (reduced scatter), cheaper, and with higher resolution [30, 73], as well as scanning configurations which require substantially less (or even no) fluid matching [88-90]. MRI sequences have been developed that minimize problems due to sample heating while preserving low noise and higher spatial resolution [47, 83]. For x-ray-CT readout, more sensitive formulations are being developed [91, 92].

A review of the current status of the field reveals that radiochromic approaches have contributed strong progress toward the long-sought goal of a reliable, practical, and cost-effective 3D dosimetry system that can match the RTAP criteria [4]. Several systems have demonstrated they can meet this goal, but are not yet realized in the commercial world. This will hopefully occur in the next few years, and will represent an important strengthening of core QA practices in radiation therapy, contributing to safer and more accurate treatment of our patients. A fairly comprehensive summary of the diversity of applications of 3D dosimetry in the clinical and pre-clinical worlds is given in Oldham [3].

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