In-situ radiation dosimetry based on Radio-Fluorogenic Co-Polymerization

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Abstract. A fluorimetric method of radiation dosimetry is presented for which the intensity of the fluorescence of a (tissue equivalent) medium is linearly dependent on accumulated dose from a few Gray up to kiloGrays. The method is based on radio-fluorogenic co-polymerization (RFCP) in which a normally very weakly fluorescent molecule becomes highly fluorescent when incorporated into a (radiation-initiated) growing polymer chain. The method is illustrated with results of in-situ measurements within the chamber of a cobalt-60 irradiator. It is proposed that RFCP could form the basis for fluorimetric multi-dimensional dose imaging.

1. Introduction
Many methods for measuring the energy deposited in materials by high-energy radiation have been developed over the years based on a variety of physico-chemical effects resulting from the interaction of radiation with matter. Of these only a few are capable of monitoring in-situ and in real-time the dose rate or the accumulated dose after a given exposure. The most commercially viable and generally accepted methods used at present are based on the current generated by “ionizing” radiation in gaseous (Geiger counter) or solid (semiconductor) media. Optical methods of in-situ monitoring have been proposed based on the radio-luminescence or optically-stimulated luminescence of (doped) crystals or glasses. However, the latter have not, as yet, been generally accepted as suitable alternatives within the field of radiotherapy dosimetry. The increasing refinement of radiotherapeutic techniques and the necessity of better definition and in-vivo control of the geometrical dose distribution profiles has made it essential (and possibly legally imperative) that suitable dosimetry methods are available.

In this article we present a new method of monitoring in-situ and in real-time the accumulated dose within a small (<< 1 cc) volume of a medium which is close to tissue equivalent in its attenuation properties. In addition, the method requires no electrical wiring or applied voltages, depending for the transmission of information from the monitoring site on optical fibers. The method is based on the process of radio-fluorogenic co-polymerization (RFCP), first demonstrated by one of the present authors in 1997 [1]. In RFCP, polymerization of a bulk monomeric medium is initiated by radiation. Also present in the medium is a small concentration of a compound which is normally non-fluorescent but which on co-polymerization into the growing polymer chains becomes fluorescent. The resulting intensity of the fluorescence is then proportional to the degree of polymerization which in turn is proportional to the yield of initiating free-radicals produced by the radiation, and hence to the radiation dose.

The RFCP method has been used in the past to study radiation-induced polymerization of methylmethacrylate with particular attention given to the “gel effect” [2], in which autoacceleration of
polymerization takes place at relatively high total doses (kiloGrays). It was realized more recently that the effect could be used in the low dose regime to monitor accumulated dose. Demonstration of this potential is the subject of the present article. The fact that the fluorescent product is a high molecular weight polymer indicates that RFCP could be applied to obtain fixed multidimensional fluorescent images of dose distribution using semirigid films or bulk gel phantoms.

2. Experimental
The overall experimental set-up, using optical fibre transmission components, is illustrated in Fig. 1.

The apparatus consists of an “excitation light source” (ELS); a shutter/optical-filter holder (S/F1); a fiber splitter (S); the “radio-fluorogenic probe” (RFP); a second shutter/optical-filter holder (S/F2); a “spectrophotometric detector” (SPD); and computer hardware and software for analysis and storage of the photometer output. The ELS used was either a pulsed N₂ laser (LTB Lasertechnik Berlin, MSG 800) or a CW 360 nm light-emitting diode (Avalight-LED360, Avantes). A UG11 long-wavelength cut-off filter was used in S/F1 to remove the visible wavelength tail of the LED. The SPD was a miniature spectrophotometer capable of spectral resolution from 200 to 900 nm (Ocean Optics SD2000 with data analysis software provided). If considered necessary a GG420 short-wavelength cut-off filter was used in S/F2 to remove any residual light from the excitation source. The optical cable connecting to the probe consisted of a central 200 µm fiber core surrounded by 6 200 µm fibers.
At the splitter, the fibers were separated into two cables with the inner fiber going to the SPD and the outer fibers going to the ELS.

The radio-fluorogenic probe consisted of a 20 mm long poly-tetrafluoroethylene (PTFE) closed cylinder of 8 mm OD and 4 mm ID which could be tightly fitted onto the end of the optical cable as shown in Figure 1. This was filled with the radio-fluorogenic solution which, in the experiments presented here, consisted of methylmethacrylate (MMA, Merk) as bulk solvent which had been passed over a DHR4 hydroquinone-stabilizer removal column, with a ca millimolar concentration (Optical density at 360 nm ca 2 per cm) of maleimido-Fluoroprobe (MFP, for molecular structure see Figure 2). The MFP was synthesised by the group of prof. J.W. Verhoeven. (University of Amsterdam). The solution was deaerated by bubbling with nitrogen within a continuously nitrogen-flushed glove box. The solution was transferred to the probe cylinder and the cylinder was attached to the end of the fiber cable within the glove box.

![Figure 2](image)

Figure 2. The molecular structures of two of the fluorogenic probe molecules used in RFCP studies; AnMA and MFP (present work) together with their fluorescent moieties anthracene (An) and Fluoroprobe (FP).

The attached probe was placed in the centre of the raised irradiation chamber of a Gammacell 200 cobalt-60 irradiator (Atomic Energy of Canada Ltd). Measurement of the fluorescence emanating from the probe was made prior to and after lowering the chamber into the irradiation zone. The dose rate of ca 5 Gy/min was accurately known and continuously corrected for the natural decay of $^{60}\text{Co}$. Using cylindrical lead attenuators the dose rate could be reduced by factors of 4.15 and 14.6.

### 3. Results and Discussion

In Figure 3 is shown the spectrally-resolved light emanating from the radio-fluorogenic probe before (lowest trace) and after lowering the probe into the irradiation zone. The dominant feature, with an emission maximum at 530 nm (150 channel numbers in the figure), is the fluorescence of the FP chromophore which increases with time due to the RFCP effect. The fluorescence spectrum prior to irradiation, corresponds to a quantum yield of less than 0.01. The sharply-peaked short-wavelength emission is residual light from the excitation source. The fluorescent component alone was obtained by taking the integral from 450 to 600 nm.

The integrated fluorescence was automatically recorded every 30 seconds using an integration time of 10 seconds. The results, from which the initial, preirradiation value has been automatically subtracted, are shown in Figure 4 for the 3 dose rates used. It should be pointed out that these three plots were obtained sequentially using the same probe by raising and lowering the chamber and inserting the required lead attenuator.
Figure 3. The increase in the spectrally resolved fluorescence emanating from a radiofluorogenic probe containing a solution of MFP in MMA as a function of time after lowering into the irradiation zone of the cobalt-60 source. The maximum in the fluorescence at ca 150 channel numbers corresponds to a wavelength of 530 nm. The maximum irradiation time was 90 minutes corresponding to an accumulated dose of ca 400 Gy. Several spectra were taken after irradiation was stopped to illustrate the lack of post-irradiation growth. The sharp, peaked spectral feature at short wavelengths is remnant light from the excitation source.

As can be seen in Figure 4, the fluorescence obeys a very good linear dependence on exposure time (or dose) for the three dose rates used. Importantly the data show no indication of an initial delay which would result from the presence of trace amounts of oxygen in the solution. For the highest dose rate the linearity extends up to a total accumulated dose of 160 Gy. In other measurements, the linearity has in fact been found to extend up to at least 1.6 kGy.

As expected from the nature of the underlying polymerization process, the slopes of the traces in Figure 4 show a very good linear dependence on the square root of the dose rate. This results from the fact that the ultimate degree of polymerization is determined by radical-radical recombination [3]. While a linear dose rate dependence might be considered to be preferable a perfect square root dependence should not be too difficult to take into account in quantifying data, and has the advantage that the method is most sensitive to the lowest relative dose rates.
Figure 4. The dependence of the increase in the integrated fluorescence on irradiation time for the three dose rates given using a radiofluorogenic solution of MFP in MMA.

4. Conclusions
We have shown that radio-fluorogenic co-polymerization, RFCP, can provide a method of monitoring in-situ and in real-time (seconds) the accumulated radiation dose within a small volume (<< 1 cc) using a probe which is tissue equivalent and biologically compatible. In addition, the method requires no electric wiring or applied voltages making it more suitable for potential in vivo applications than existing methods. A linear dependence on dose from a few Gray up to kiloGrays has been found for a methylmethacrylate based solution, allowing multiple use of the same probe. Extension of the sensitivity to lower or higher dose ranges could be achieved by the choice of other polymerizable monomers and fluorogenic probe molecules. The fact that the fluorescent product of RFPC is a polymer indicates that this process could be applied to multi-dimensional dose imaging using semi-rigid, gel matrices.

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