Real-time in vivo dose measurement using ruby-based fibre optic dosimetry during internal radiation therapy

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Abstract

In vivo dosimetry (IVD) in a commonly used liver cancer treatment of selective internal radiation therapy (SIRT) has been done based on the post-treatment image-based dosimetry approach. Real-time IVD is necessary to verify the dose delivery and detect errors during the treatment for better patient outcomes. This study aims to develop a fibre optic dosimeter (FOD) for in vivo real-time dose rate measurement during internal beta radiation therapy, e.g., SIRT. A ruby fibre optic probe was prepared and studied the radioluminescence (RL) characteristics, including its major challenge of stem effect arising from Cherenkov radiation and luminescence from the irradiated fibre. The stem signal was suppressed adequately using the stem removal technique of optical filtering, and only 2.3 ± 1. % stem signal was contributed to the measured RL signal. A linear dose rate response was observed during the exposure of the ruby probe to varying dose rates using a 6 MeV electron beam and a positron-emitting radionuclide fluorine-18. The ruby exhibited a temporarily non-constant RL signal, which increased the RL signal by $0.84 \pm 0.29 \text{ counts / sec}^2$ during the irradiation of the maximum dose rate used in this study of 9 Gy / min for 2 minutes. The ability of ruby FOD to measure the absolute dose rate with sufficient stem effect suppression and the linear RL dose rate response indicates its suitability for real-time IVD during internal beta radiation therapy. Future work will investigate the time-dependent RL characteristic of ruby and validate post-treatment image-based dosimetry using ruby-based FOD.

Introduction

Selective internal radiation therapy (SIRT) with a beta emitter, yttrium – 90 (Y-90), is a commonly used treatment for unresectable primary and metastatic liver cancers [1–4]. In SIRT, radiation dose is delivered by directly injecting Y-90 microspheres to the liver tumours through a catheter positioned in the hepatic artery as liver tumours are fed primarily with the blood supply from the hepatic artery, and normal liver parenchyma is fed primarily from the portal vein [5]. After the administration of Y-90, quantitative images can be obtained by single photon emission computed tomography/computed tomography (SPECT/CT) or positron emission tomography/computed tomography (PET/CT) to check the Y-90 distribution for the estimation of dose delivered to the patient. Y-90 bremsstrahlung SPECT/CT scanning suffers from low image quality and poor quantitative accuracy [6]. The time of flight (TOF) PET/CT can be used with better resolution [7] and improved quantification than SPECT/CT [8]. However, the post-treatment image-based dose measurement methods detect the unexpected variations in the overall delivered dose only after the treatment. The same scenario exists with internal beta radiation therapy for treating pancreatic cancer in which phosphorous-32 (P-32) microparticles are injected directly into the tumour to deliver the dose. SPECT/CT imaging of P-32 bremsstrahlung radiation is performed after the treatment to check the coverage of P-32 microparticles inside the tumour [9]. From the dosimetric perspective, the knowledge of actual dose delivered is essential to improve the understanding of absorbed dose-effect relationships. Accurate dosimetry methods enable to maximise therapeutic efficacy while minimising toxicity. There is a need to have real-time in vivo dosimetry (IVD) in place to measure the delivered dose during the treatment, detect significant errors and ensure that the treatments are carried out as intended. Implementation of
real-time IVD during internal beta radiotherapy can be used to validate the post-treatment image-based dosimetry. To our best knowledge, no such a system exists which measures the in vivo real-time dose during SIRT. Fibre optic dosimetry (FOD) is an attractive option available today for real-time in vivo dose rate measurement during radiation therapy [10].

A FOD system consists of a scintillator, which emits light spontaneously after excitation by ionising radiation, known as radioluminescence (RL). The scintillator is coupled to an optical fibre to guide the RL light emitted during irradiation. In general, the intensity of RL signal is regarded as proportional to the dose rate absorbed by a scintillator [11]. The availability in desirable size of FOD and the real-time dose rate measurement feature makes them suitable for IVD during internal radiation therapy. The small size of FOD probe allows them to be placed inside a catheter inserted in the tumour to deliver the Y-90 microspheres in SIRT or through the endoscope used to inject P-32 microparticles in pancreatic cancer treatment.

One main drawback of FOD is the generation of Cherenkov radiation and fibre luminescence in the irradiated optical fibre called the stem effect. The stem effect is mainly due to Cherenkov radiation [12]. The stem effect adds additional signal to the RL signal from the scintillator and therefore it must be removed. Four stem removal techniques have been used: background fibre method [13], optical filtering technique [14], air core fibre method [15] and temporal separation technique which is compatible only with a pulsed source of radiation [16]. Among these methods, the optical filtering method is the easiest and cheapest method suitable for in vivo applications. The optical filtering method is used effectively when the scintillator has an RL emission spectrum in a longer wavelength region where the Cherenkov radiation is less significant as Cherenkov radiation is dominant in the blue to ultraviolet spectrum region [17]. However, the Cherenkov radiation spectrum is continuous, and there is also light emission due to Cherenkov effect at longer wavelengths [18].

Jordan [19] investigated ruby-based FOD for dose measurement in external beam radiotherapy. It was demonstrated that the dose depth profiles obtained with the ruby detector for 4 MV photon beams and 9–12 MeV electrons were in good agreement with the ionisation chamber data. Teichmann [20] further investigated ruby-based FOD with an external beam radiation source. A slight increase in RL signal with an accumulated dose of 2 Gy was observed. This was considered to be due to the admixture of impurities in ruby other than Cr$^{3+}$ as previously suggested by Bessonova [21]. In the studies by Jordan [19] and Teichmann [20], the temporal separation technique was used to suppress the stem effect, but it is not applicable for internal radiation therapy where a time decaying radioactive source is used. Kertzscher and Beddar [22] tested a ruby-based fibre optic detector for IVD during high dose rate (HDR) brachytherapy. Depending on the admixture of impurities in ruby, time-dependent (non-constant) scintillation was observed during 50 Gy irradiation with Iridium-192 (Ir-192) and the stem removal technique of background fibre method was used. In the background fibre method, a second optical fibre without a scintillator, i.e., a background fibre is employed parallel to the ruby detector to measure the stem signal. The background fibre technique is not suitable for in vivo applications as it makes the FOD system bulky. Kertzscher and Beddar [22] concluded by simulations that the stem signal suppression would be better by
narrowing the bandpass wavelength region of the bandpass filter to \( \leq 20 \) nm when the optical filtering technique is used. Using a scintillator such as a ruby which has a narrow RL main emission peak at 694 nm with a narrow bandpass filter will effectively suppress the stem effect, making the FOD technique suitable for IVD during internal radiation therapy.

The objective of this study is to assess the potential use of ruby FOD during SIRT for real-time dose measurement to validate the image-based dosimetry. We have investigated the stem effect suppression using the optical filtering stem removal technique with a filter of 10 ± 2 nm bandpass wavelength. The RL characteristics of ruby FOD have been studied with the therapeutic 6 MeV electron beam using a linear accelerator (LINAC) and a readily available positron-emitting radiopharmaceutical fluorodeoxyglucose [F-18] FDG.

**Methods**

**2.1. Fibre optic dosimetry system**

The experimental set-up of the fibre optic dosimetry system is illustrated in Fig. 1. A ruby FOD probe was fabricated by attaching a half-sphere ruby of 1 mm diameter (49558, Edmund optics Inc, USA) to a 15 m long silica fibre (FP600ERT, Thorlabs) with optical glue (NOA61, UV-curing glue, Thorlabs). The length of the silica fibre was 15 m to transmit the RL signal emitted by ruby to the light detection system or a reader, outside the irradiation facility. The ruby FOD probe is coupled to the reader via a multimode connector (B30670G3, Thorlabs).

The reader consists of a photomultiplier tube (H7360-01, Hamamatsu, Japan) and a data acquisition card (DAQ), National Instruments (USB-6341, National Instruments Inc. USA) with four 32-bit counter and time base of 100 MHz. A customised LabVIEW™ software (National Instruments Inc. USA) reads the counters of USB-DAQ and displays the count rate in proportion to RL light. The sampling rate of 1 Hz, with 1 sec integration time, is used throughout the experiments.

The stem effect removal method of optical filtering is used for all the measurements. A bandpass filter FL694.3-10 (Thorlabs Inc, USA), 6.3 mm in thickness, with 694.3 ± 2 nm centre wavelength and 10 ± 2 nm FWHM bandpass, is placed between the end of the fibre and the photomultiplier tube. All measurements are carried out at room temperature and in a dark room to minimise light contamination, which contributes background signal.

**2.2 Radioluminescence response using 6 MeV electron beam**

A 6 MeV electron beam from a TrueBeam (Varian Medical Systems, Palo Alto, CA) linear accelerator (LINAC) is used to study the stem effect and RL dose rate response of the ruby FOD system. The measurements were performed by placing the ruby FOD probe at a depth of 1.3 cm in a solid water phantom (Gammex RMI, Middleton, U.S.A) at the centre of a field size of 10 x 10 cm² and at a source to
surface distance (SSD) of 100 cm as shown in Fig. 2. The electron beam output is specified at the maximum depth dose ($Z_{\text{max}}$), 1.3 cm for a 6 MeV electron beam in the solid water phantom.

2.2.1 Stem effect

The background fibre stem removal method with a second silica fibre (FP600ERT, Thorlabs), 15 m long without a scintillator, i.e., a background fibre, is employed to evaluate the stem effect contribution in the filtered ruby RL signal, which is still allowed by the optical filtering stem removal technique. The ruby FOD probe was connected to the reader, and the filtered ruby RL signal using a bandpass filter was measured when irradiated with a 6 MeV electron beam with a dose rate of 9 Gy / min. The background fibre replaced the ruby FOD probe to measure the stem signal with the bandpass filter when irradiated with a 6 MeV electron beam with a dose rate of 9 Gy / min. The light detected by the background fibre approximates the stem signal contribution in the filtered ruby RL signal, which the optical filtering technique could not remove.

2.2.2 Dose rate linearity and stability of radioluminescence signal

Linear RL response with changing dose rate is required to effectively use ruby FOD as the RL intensity is proportional to the dose rate. This feature is verified by exposing ruby FOD with varying dose rates, from 1, 3, 5, 7 and 9 Gy / min for 2 minutes. Also, RL signal stability with accumulated dose has been examined from this same data.

2.3. Radioluminescence response using fluorine-18

The RL response of the ruby FOD system to a continuously decaying radioisotope was studied with a positron-emitting F-18 source. An unsealed F-18 source with the initial activity of 334 MBq and volume ~ 0.02 ml was placed inside a polypropylene syringe cap to create a point source. The ruby probe was positioned opposite the cap in the immediate vicinity, as shown in Fig. 3. RL count rate response of ruby FOD with the time decaying activity of F-18 is investigated by collecting RL signal data for 3.5 hours, i.e., about two half-lives of F-18.

Results

3.1. Radioluminescence response using 6 MeV electron beam

3.1.1. Stem effect

Figure 4 shows the RL signal, i.e., light output in terms of counts / sec or count rate, from the ruby FOD probe and the background fibre when irradiated with a 6 MeV electron beam with a dose rate of 9 Gy / min for 2 minutes. From the average RL count rate measured by background fibre and ruby FOD probe
with uncertainties corresponding to two standard deviations, it is estimated that 2.3 ± 1. % of the ruby RL signal comes from the stem effect allowed by the optical filtering technique. The afterglow effect, i.e., luminescence after the irradiation, was observed for the ruby.

### 3.1.2 Dose rate linearity and stability of radioluminescence signal

The dose rate linearity was assessed from the response of the ruby FOD probe upon irradiation with a 6 MeV electron beam, dose rates of 1, 3, 5, 7 and 9 Gy / min, for two minutes, approximately 1 minute apart. Figure 5 plots the average RL count rates against the exposure dose rates. The RL count rate response was observed to be linear over the investigated dose rate interval with R² of 0.9992.

The stability of RL signal with accumulated dose was investigated from the same data used to check the dose rate linearity where the ruby FOD probe was irradiated with 1, 3, 5, 7, and 9 Gy / min dose rate for 2 minutes. Time dependence in the RL signal was observed, and the RL count rate increased as the dose accumulated with time, as shown in Fig. 6. The linear regression approach estimates the increase in RL count rate per second with uncertainties corresponding to two standard deviations of about 0.040 ± 0.11, 0.12 ± 0.16, 0.18 ± 0.21, 0.41 ± 0.29, and 0.84 ± 0.29 counts / sec² during the irradiation with the dose rate of 1, 3, 5, 7, 9 Gy / min, respectively.

The afterglow effect was observed for at least 20 sec, as shown in Fig. 6. The average afterglow half-life for ruby scintillator, after the irradiation of dose rate 1, 3, 5, 7 and 9 Gy / min for 2 minutes, estimated by fitting the exponential decay to the data with uncertainties corresponding to two standard deviations, is found to be 0.57 ± 0.1 sec. These results are consistent with the afterglow half-life of the ruby of less than 1 sec, as estimated by Kertzscher [22].

### 3.2 Radioluminescence response using fluorine-18

The initial activity of F-18, \( A_0 \), decays with time \( t \) according to the fundamental radioactive decay law. The activity at a time \( t \), \( A_t \), is specified as, \( A_t = A_0 e^{-\lambda t} \), where \( \lambda \) is the decay constant of F-18. As the F-18 with initial activity, \( A_0 = 334 \text{ MBq} \), decays with time, the ruby FOD was simultaneously exposed to the different dose rates. \( A_t \). Figure 7 shows the RL response in terms of count rate to the decaying activity \( A_t \) of F-18. The linear regression analysis approach is used to find the relationship between RL count rate and the time decaying activity \( A_t \) of exposure. \( R^2 = 0.9935 \) represents the linear RL response of ruby FOD to the activity \( A_t \) of F-18, ranging from the initial activity of 334 MBq to 89 MBq, after 3.5 hr.

By rearranging the RL count rate data from used to plot Fig. 7, the decay constant for F-18 is evaluated to estimate the half-life of F-18. The measured half-life of F-18 from the RL count rate data obtained during the first two hours with uncertainties corresponding to two standard deviations, 109 ± 1 min agrees with the 109.77 min reported in the literature [23], which indicates the linear response of ruby FOD to the decaying activity of F-18.
Discussion

This study aimed to assess the use of ruby FOD for the real-time dose rate measurement during internal beta radiation therapy by checking its desirable characteristics. The stem signal, a major disadvantage of FOD is effectively suppressed using stem removal technique of optical filtering with a narrow bandpass filter. The stem signal contribution was found to be $2.3 \pm 1.\%$ of the ruby RL signal which is negligible compared to fluctuations in the ruby RL signal associated with the FOD system noise. This finding agrees with previous studies, which have shown by simulations that narrowing the wavelength region of bandpass filter improves the stem signal suppression in ruby-based FOD system [22].

Figure 5 demonstrated that ruby FOD exhibits dose rate linearity over the investigated range of dose rates. A temporally non-constant RL signal and afterglow effect have been observed as illustrated in Fig. 6. Bessonova [21] suggested that the ruby RL intensity builds up during the constant dose rate exposure depends on the admixture of impurities in the ruby crystal, and the introduction of 0.5% vanadium to the ruby crystal prevents the build-up. Bessonova [21] speculated that the introduction of $\text{Ti}^{3+} V^{3+}$ and $\text{Mn}^{3+}$ ions prevent the mechanism of causes the RL build-up. The manufacturer has provided that the Ti, Mg and Mn are the main impurities in the ruby scintillator used in this study. The time dependence of the RL signal observed in this study could be that the ruby does not contain the correct admixture of impurities. However, for the lowest dose rate of the 1 mGy / min, the ruby RL signal appears stable.

Afterglow is observed for ruby, which could be due to the presence of shallow traps concentrations. Shallow traps influence the RL signal by competing with the recombination process when irradiation starts and releasing electrons to give rise to the afterglow signal at the end of the irradiation [24]. The afterglow effect is not a concern for internal radiation therapy as the microparticles of radioisotope are injected into the tumour at once, and the ruby FOD probe will be exposed to time decaying activity of radioisotope when placed in the tumour.

Conventionally, post treatment Y-90 image-based dosimetry used in SIRT performed using Medical Internal Radiation Dose (MIRD) schema. According to MIRD, the dose rate absorbed by the tissue upon exposure to radionuclide varies directly with the activity in the tissue [25], and the mean absorbed dose to tissue over the dose integration period is calculated from the time-integrated activity of radionuclide [26]. Recently developed more accurate voxel-based dosimetry with dose point kernel (DPK) is the widely used method for image-based dosimetric calculations, which uses the activity quantification based on tomographic imaging [27]. The image-based dosimetry relies on the amount of activity for the estimation of absorbed dose rate. The linear RL response to the activity is the desirable characteristic required to the validate of image-based dosimetry using FOD. The results in Fig. 7 confirms that the ruby RL response is linear to the investigated range of activity of F-18. In addition to linear dose rate response, the ability of ruby FOD to determine the absolute dose rate with adequate stem signal elimination shows the feasibility of in vivo real-time dosimetry during internal beta radiation therapy.
The limitation of ruby FOD was the temporally non-constant RL signal. The pre-irradiation technique has been proposed to remove the non-constant scintillation in the case of carbon-doped aluminium oxide (Al₂O₃:C) [28]. Kertzscher and Beddar [22] showed that the re-irradiated ruby with the pause 500 sec from the first irradiation, maintained the strong time-dependent scintillation and the RL signal was ~4% greater than during the first irradiation. Pre-irradiation technique is not preferred to achieve the stable RL response. The strategy to overcome this challenge would be to use the ruby sample with the right admixture of impurities for the stable RL signal. Further studies are planned to investigate the desirable characteristics of the ruby FOD system including temperature dependence and RL signal stability by adopting the proposed strategy to validate the image-based dosimetry system used in internal beta radiation therapy.

Conclusion

A ruby fibre optic probe has been prepared by considering the internal beta radiation treatment procedures and their requirements. It has been found that the ruby FOD has the potential to be used for in vivo real-time dose rate measurement. The most suitable stem removal technique for internal beta radiotherapy, optical filtering, achieves adequate stem signal suppression due to the ruby's narrow peak RL emission at 693.2 nm. The ruby FOD response was linear over the investigated range of dose rates using an external electron beam of 6 MeV and the activity of F-18. Ruby exhibited the time dependent RL response. More investigation is required regarding impurities in chosen ruby samples responsible for the stable RL response.

Declarations

Funding

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Competing interest

The authors have no relevant financial or non-financial interests to disclose.

Ethical approval

This study did not involve animals or humans. No ethical approval is required.

Informed consent
This study used solid water phantoms and no human participants. No informed consent was required.

References


Figures

![Experimental set-up of the ruby fibre optic dosimetry system](image)

**Figure 1**

Experimental set-up of the ruby fibre optic dosimetry system
Figure 2

Set-up of the solid water phantom with the ruby FOD and background fibre placed perpendicular to the beam and in the central axis of the 10 x 10 cm² field size for 6 MeV electron beam measurements.
Figure 3

Set up of ruby probe and F18-FDG source

Figure 4

Ruby probe, average RL count rate
= 2174+/−108 counts/sec

Background fibre, average RL count rate
= 50+/−26 counts/sec
RL count rate from ruby FOD probe and background fibre at 9 Gy / min dose rate

Figure 5

The response of ruby FOD to 1-9 Gy / min irradiation dose rates. The error bars represent ± 1 standard deviation of RL count rates.
Figure 6

RL count rate response with time for 1 to 9 Gy / min dose rates
Figure 7

RL count rate response to the activity of F-18, $A_t$