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Doped silica fibre thermoluminescence measurements of radiation dose in the use of ^{223}Ra

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ABSTRACT

Using tailor-made sub-mm dimension doped-silica fibres, thermoluminescent dosimetric studies have been performed for α-emitting sources of $^{223}RaCl_2$ (the basis of the Bayer Healthcare product Xofigo®). The use of $^{223}RaCl_2$ in the palliative treatment of bone metastases resulting from late-stage castration-resistant prostate cancer focuses on its favourable uptake in metabolically active bone metastases. Such treatment benefits from the high linear energy transfer (LET) and associated short path length (< 100 µm) of the α-particles emitted by ^{223}Ra and its decay progeny. In seeking to provide for in vitro dosimetry of the α-particles originating from the ^{223}Ra decay series, investigation has been made of the TL yield of various forms of Ge-doped SiO_2 fibres, including photonic crystal fibre (PCF) collapsed, PCF uncollapsed, flat and single-mode fibres. Irradiations of the fibres were performed at the UK National Physical Laboratory (NPL). Notable features are the considerable sensitivity of the dosimeters and an effective atomic number Z_{eff} approaching that of bone, the glass fibres offering the added advantage of being able to be placed directly into liquid. The outcome of present research is expected to inform development of doped fibre dosimeters of versatile utility, including for applications as detailed herein.

1. Introduction

In consideration of external-beam alpha particle therapy, unless use were to be made of α-particles accelerated to several 100 MeV, at the typical decay energies of radionuclide sources and associated elevated linear energy transfer (LET) penetration into tissue would be impractically small (Jayaraman and Lanzl, 2004). Conversely, for certain internal medicine cancer therapy treatments, the use of radionuclide α-emitting sources in targeted radiotherapy is proving to be of considerable interest (Allen et al., 2004). Of particular note is that the greatest loss of energy of α-particles within an absorbing medium is concentrated near the end of their paths. In regard to energy loss at depth, this manifests in the so-called Bragg peak, preceded by a considerably lower-valued plateau that starts from the surface of the absorptive medium through to the peak. In internal use, these features are now being harnessed in clinical trials, the aim being to deliver destructive energy to tumour cells while causing relatively little damage to nearby healthy cells. Key to this is controlled selective uptake, made possible through molecular tagging, the energy and hence the dose being delivered with considerable precision. The resulting α-particle radiotherapy is novel in treating highly distributed tumours located within sensitive normal tissues, a challenging situation familiar in seeking to deal with metastatic spread.

In requiring validation of dose deposition to support such charged particle therapy, it would be invaluable to have available a system of dosimetry which has the capacity to be placed in aqueous environments, that is sensitive to the range of doses delivered in radiotherapy and which can offer spatial resolution approaching cellular dimensions.

Over recent years the present group, part of a large collaboration, have been developing Ge-doped silica fibres as thermoluminescence (TL) dosimeters (Bradley et al., 2012; Yusoff et al., 2005), a particular intention being to extend versatility of application to beyond that of

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other passive forms of dosimetry, one example of which is the well-established LiF-based commercial phosphor product TLD-100. Particular performance characteristics of interest include: (i) sensitivity to radiation; (ii) a useful dynamic (linear) range over which response can be obtained; (iii) excellent spatial resolution, and; (iv) the capacity to be used in challenging environments, as in for instance in conduct of in vivo measurements. In evaluation of doped silica fibres, results of a range of such measurements have already been highlighted in previous publications (Abdulla et al.,; Noor et al., 2010, 2011; Issa et al., 2011; Hashim, et al., 2009; Abdul Rahman et al., 2011; Ramli et al., 2009; Hashim et al., 2010). The first such investigations of fibres by this group were of fibres of cylindrical shape, with an outer diameter of the order of 100 µm, providing for the spatial-resolution needs of for instance the fine beams applied in stereotactic ablative body radiotherapy (SABR), sometimes also referred to as stereotactic body radiotherapy (SBRT).

The key factor in providing for sensitivity towards irradiation measured by the TL produced, has been the use of an extrinsic dopant, most typically Ge (Youssef, 2003; Chen and McKeever, 1992). For dopant delivery, introducing Ge into the host silica, the predominant technique has been that of modified chemical vapour deposition (MCVD) (Jacqueline et al., 2004; Mat-Sharif et al., 2013; Liu et al., 1997). Such studies have now lead to considerable understanding being gained as to the origin of the TL from such fibres. A particularly notable defect type, albeit not uniquely important, is the germanium oxygen deficiency centre (GODC) (Awazu et al., 1990; Fujimaki et al., 1998; Alessi et al., 2008), manifestly contributing to the sensitivity of the TL signal resulting from such media. Details of this and other contributing defects resulting from controlled compositional manipulation are to be found in (Alessi et al., 2008; Siti Shafiqah, 2015; Abdul Sani, 2015), as are characterisation of these via various spectroscopic techniques, including glow-curve analysis (Bradley et al.,). Further apparent is that mechanical strain can be deliberately introduced into the fibres in order to generate strain-related defects (Bradley et al.). Spectroscopic study has shown that deep defects TL predominates, with the associated light being towards the blue end of the visible spectrum, limited fading being a desirable effect of deep trapping (Bradley et al.).

Ramli et al. (2009) have investigated the Ge-doped SiO_2 optical fibre response to α-particles emitted from a source of ^{241}Am (activity 1.77 MBq), with α-particle energies of 5.443 MeV (I_α =13.2%) and 5.486 MeV (I_α =84.5%), a comparison of TL characteristics being made with that of TLD-100 rods. In that work, at the irradiation distance of 1 cm and with an air kerma dose-rate estimated to be 0.57 Gy h^{-1} per unit mass, the TL yield of the TLD-100 was reported to be approximately ten times that of Ge-doped fibres and approximately 30 times that of Al-doped fibres, each of 5 mm length. However, considerable progress has since been made in improving the sensitivity of the silica fibres and, unlimited by the hygroscopic nature of TLD phosphors, the results to be presented herein are intended to indicate considerable potential for use of SiO_2 optical fibres in targeted α-radiotherapy dosimetry, offering the possibility of improved positional sensitivity (fibre diameters are sub-millimetre, typically ~125 µm compared with the ~ millimetre dimensions of the phosphor dosimeters) and dose sensitivity well beyond that of TLD-100. Moreover, SiO_2 optical fibres offer many advantages over conventional dosimetry systems including the calcified tissue equivalence of the dosimetric material, the value of Z_{eff} being close to that of bone (being for the fibres, in the range 11.6 − 13.8) (Hashim et al., 2013).

Using tailor-made doped-silica fibres, thermoluminescent dosimetric studies of a formulation of $^{223}RaCl_2$ (the basis of a product called Xofigo™ (Bayer (Norway)) have been carried out. Due to the intrinsic high LET, the short path length (< 100 µm) of the α-particles emitted by the ^{223}Ra (and its decay progeny) and the high uptake in metabolically active bone metastases, the radiopharmaceutical is being used for treatment of bone metastases resulting from late-stage castration resistant prostate cancer (Heymann, 2014). Specifically, in this study, the TL yield of various forms of doped SiO_2 optical fibres have been investigated for in vitro dosimetry of α-particles originating from the ^{223}Ra decay series.

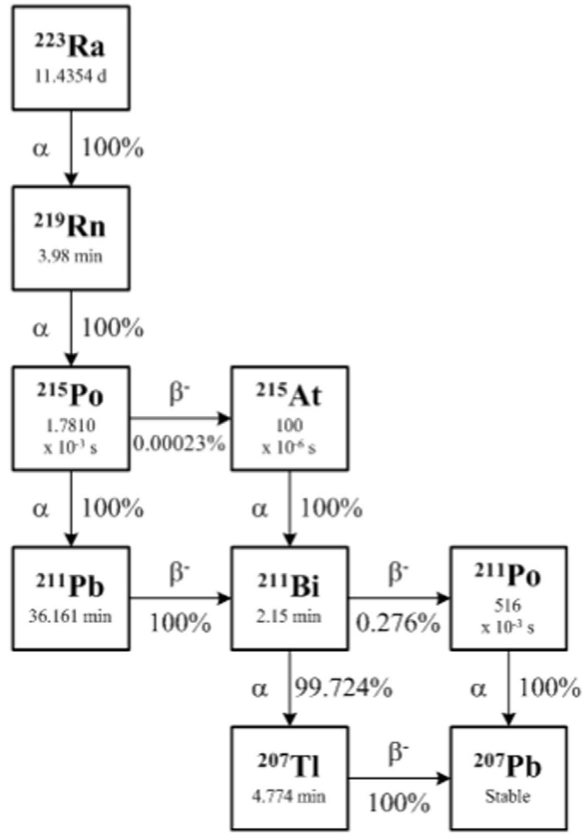

Fig. 1. Decay series of ^{223}Ra. The half-lives, decay mode and branching ratios of each radionuclide in the decay series are included.

The α-particle-emitting isotope ^{223}Ra mimics the uptake of calcium in bone and forms complexes with the bone mineral hydroxyapatite in areas of increased bone turnover, such as bone metastases. Jafari et al. have reported on calculated mass attenuation coefficients of glass (silica) beads, from a few keV to 100 keV, closely matched to that of NIST B-100 Bone Equivalent Plastic (Jafari et al., 2014). The effective atomic number, Z_{eff} of glass beads was calculated to be 10.6 (Jafari et al., 2014) whereas the Z_{eff} optical fibre was found to be in the range 11.6 − 13.8 (Hashim et al., 2013), close to that bone. The outcome of the current research is expected to be useful in developing and characterizing tailor-made doped optical fibres as new potential candidate TL dosimeter materials for skeletal radiation dosimetry.

1.1. Key features of ^{223}Ra

The six-stage-decay of ^{223}Ra to ^{207}Pb occurs via short-lived progeny, and is accompanied by a number of alpha, beta and gamma emissions with different energies and emission probabilities (Fig. 1). Fig. 2 shows measurement of the alpha spectrum obtained in use of a ^{227}Th source in equilibrium with its daughter progeny. The fraction of energy emitted from ^{223}Ra and its daughters as alpha particles is 95.3% (energy range of 5.0 − 7.5 MeV). The fraction emitted as beta-particles is 3.6% (average energies are 0.445 MeV and 0.492 MeV), and the fraction emitted as gamma-radiation is 1.1% (energy range of 0.01 − 1.27 MeV) (Summary of Product Characteristics, 2015). A detailed gamma emission spectrum of ^{223}Ra is shown in Fig. 3. The half-lives of ^{223}Ra and its decay progeny ^{211}Pb have recently been measured and, using selected experimental values, the recommended half-life values of 11.4354 (17) d and 36.161 (17) min have been evaluated (Collins et al., 2015). Due to the relatively short-lived half-lives of the decay progeny ($T_{1/2}$ (max)