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Modeling dose response to synchrotron X-rays in solid-state and biological systems

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The Monte-Carlo method is used to model perturbation to the dose response of solid-state detectors and biological systems in the vicinity of the K-edge of constituent elements. Diamond detectors are examined where silver-based (Ag) solders are used to form electrical contact with the diamond crystal. Perturbation from photoelectric interactions with Ag lead to a dose response that increases gradually above the K-edge of Ag (25.5 keV) reaching a maximum around 45 keV. Dose enhancements associated with synchrotron-based photon activation therapy (PAT) with platinum (Pt) are also examined. Perturbation from photoelectric interactions with Pt leads to a dose response that may increase to a maximum at the K-edge of Pt but falls dramatically above edge. For large volumes of irradiation, such as is typical for radiation therapy of the brain, self-absorption leads to a decrease in dose response above edge indicating that a high degree of localization of activating material is required for the treatment approach to be successful.

1. Introduction

In order for the many advantageous properties of solid-state dosimeters to be realized in clinic, strategies must be evolved for the calibration of detector systems for an ever expanding range of radiation sources including spectrally complex and mixed radiation fields. Monte-Carlo (MC) models of the source and detector systems provide a means to account in a precise way for energy absorbed in the detector, allowing for primary and secondary radiation processes in megavoltage radiotherapy [1] and for mixed radiation sources such as boron neutron capture therapy (BNCT) [2].

Third generation synchrotron electron storage-rings, with energies in excess of 1 GeV, are a source of highly intense, monoenergetic and coherent light. Synchrotron light is primarily used for X-ray crystallography but increasingly is being utilized in demanding applications in imaging including medical imaging and in more recent years has been considered for

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51 radiation therapy. The high intensities achievable with synchrotron X-rays mean that sub-mm
52 dose resolution, not possible with conventional radiation sources, can be considered.

53 Already several applications exploiting the high intensity of synchrotron light are being
54 actively examined. Micro-beam radiation therapy (MRT), for example, uses radiation beams
55 delivered in a rapid time-frame (microseconds) to effectively freeze patient motion and criss-
56 cross micron width slices of radiation dose to the region of the tumor. The advantage of
57 so-called spatial fractionation has yet to be fully demonstrated but the expectation is that such
58 radiation will be more damaging to the more highly disordered vasculature associated with
59 tumors [3].

60 We are in the process of examining several candidate dosimeters for synchrotron X-ray
61 dosimetry including diamond detectors [4], p-type silicon diodes, MOSFET [5, 6] and doped
62 optical fibers [7]. Solid-state dosimeters are needed at the sub-mm length scales typical of syn-
63 chrotron beams as conventional methods of dosimetry, such as gas filled ionization chambers,
64 are impractical due to low-sensitivity and difficulty of construction. The nature of solid-state
65 detectors, however, present new challenges, essentially due to perturbation of higher density
66 and non-tissue equivalent constituents and in the case of X-rays in the kilovoltage energy range,
67 the influence of high atomic number (Z) constituents due to the greatly enhanced photoelectric
68 effect in the vicinity of the atomic orbital edges.

69 The diamond detector has a number of important characteristics that support its suitability
70 as a primary dosimeter for synchrotron X-ray applied to medicine, in particular the tissue-
71 equivalent sensitive material and stability of response over long-time periods and repeat
72 exposures. Natural diamond dosimeters are commercially available (PTW, Freiberg). In the
73 kilovoltage energy range perturbations due to the presence of gold flash (Au) coatings on the
74 surface of the diamond and silver (Ag) solders attached to copper connective wiring need to
75 be considered along with the small variation in response below 100 keV due to the slightly
76 lower photon absorption and effective- Z of carbon compared with tissue.

77 High- Z atoms are used for biologically targeted dose enhancement in radiation therapy, also
78 known as photon activation therapy (PAT). Several targeting system are currently under investi-
79 gation including I and Gd contrast media [8] and Pt bearing cytotoxic drugs [9]. Other inventive
80 delivery systems include localized application of Au atoms [10] through nanoparticle-bearing
81 liposomes that will target the leaky and disordered vasculature associated with tumors. Particu-
82 larly impressive results were achieved by Biston *et al.* (2004) [9] where glioma disease bearing
83 Fischer rats, infused with cis-diamminedichloroplatinum (II) (CDDP) at Pt concentrations
84 approaching 0.5 mg/mL, demonstrated greatly enhanced survival.

85 MC calculations have been used to predict the response of a diamond detector to synchrotron
86 X-rays demonstrating agreement better than 5% over a wide energy (5 keV–5 MeV) [11, 12]. In
87 this work we use the MC method to examine perturbations to a water equivalent ideal detector
88 material from (1) Ag constituents and (2) Pt which is close in atomic number to Au, often used
89 to surface-coat solid-state detectors, but more particularly in response to recent biological
90 data demonstrating the effects of high- Z materials on dose when used in combination with
91 kilovoltage X-rays.

92 93 94 **2. Method**

95
96 MC method has been utilized to predict variation in detector response for monoenergetic syn-
97 chrotron beams in the vicinity of the K-edge of Ag, typically used in the bonding of electrical
98 contacts in a variety of solid-state detector systems. The code EGS4 [13] has been used with
99 additional physics introduced by the KEK (High Energy Accelerator Research Organization,
100 Japan) [14–16] and ourselves [17, 18] for low energy and synchrotron X-ray applications

including near-edge Compton and Rayleigh elastic scattering processes and photon polarization. Calculations were performed for a 1 cm wide, 1 mm thick, 99% polarized, synchrotron X-ray beams. Ten million photons per energy point were used leading to approximately 2% (2 s.d.) uncertainty in dose response relative to water utilizing only photon transport and PHOTOX (RSIC Data Package DLC-136) cross-sectional data. Electron transport has not been utilized where the highest energy photons used in this study lead to electrons with ranges of less than 0.1 mm.

Figure 1 shows MC calculations of the variation in response near the K-edge of Ag (25.5 keV) due to the presence of Ag (1 mg/g) in the closely water equivalent diamond detector. The dose response has also been calculated assuming a model that takes into account attenuation in the overlaying medium and the absorption of the sensitive material within the detector relative to that of water. A ratio of the dose response of the detector to that of a water equivalent material is given as follows:

$$\text{Ratio} = \exp[-(\mu/\rho)_{\text{Water}} * t_1 * \rho_1] * \exp[-(\mu/\rho)_{\text{Diam}} * t_2 * \rho_2] * \left[\frac{(\mu_{\text{en}}/\rho)_{\text{Diam}}}{(\mu_{\text{en}}/\rho)_{\text{Water}}} \right],$$

where (μ/ρ) and (μ_{en}/ρ) are the photon mass-attenuation and absorption coefficients (Hubbell and Seltzer, NIST IR 5632), t_1 and t_2 are the thickness of the overlaying medium and detector respectively. The mass-attenuation coefficient in the diamond detector material is calculated to be,

$$(\mu/\rho)_{\text{Diam}} = (1 - \alpha)(\mu/\rho)_{\text{Water}} + \alpha(\mu/\rho)_{\text{Ag}},$$

where α represents the mass-fraction of Ag with a similar expression used for the mass-absorption coefficient. In particular the approximation over-estimates the response immediately above edge by about 2% compared to a MC calculation which correctly accounts for the dispersal of much of photoelectrically absorbed energy by fluorescent photons. The maximum perturbation to the detector response occurs more than 20 keV above edge.

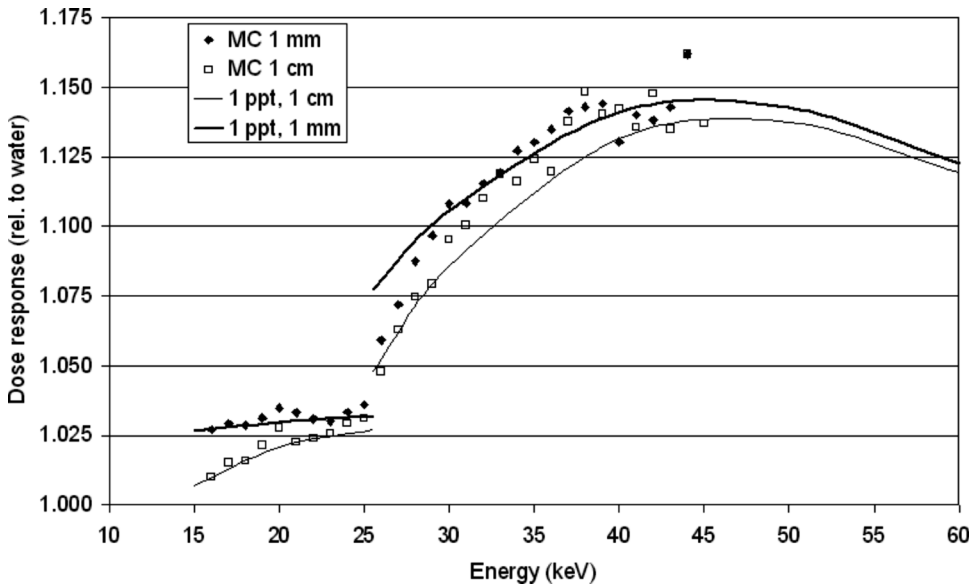
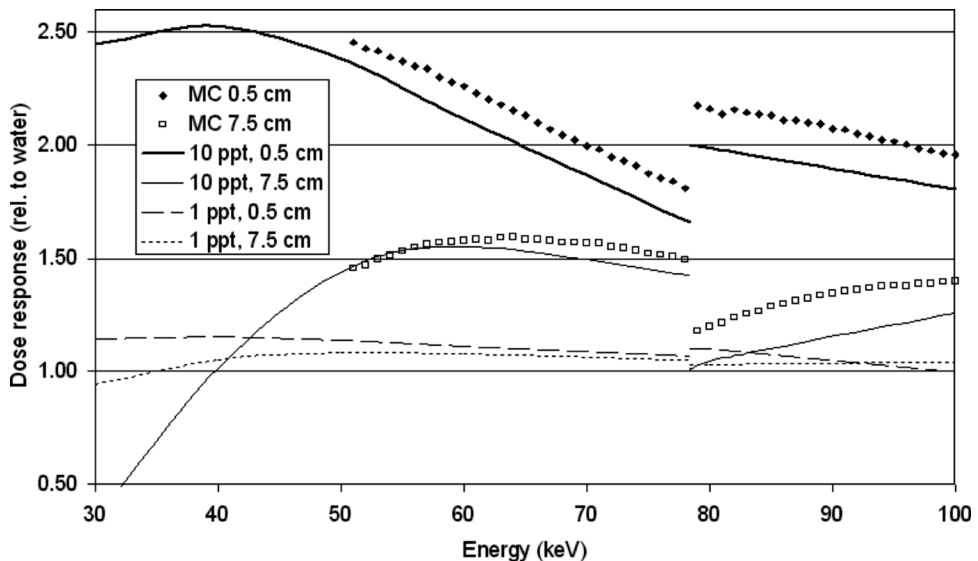


Figure 1. Variation in the dose response with monoenergetic X-ray energy due to perturbations from a Ag constituent (1 mg/mL) in a water equivalent detector of 1 mm (diamonds) and 1 cm (squares) diameter surrounded by water calculated using MC. Models ignoring photon scattering processes are also shown (trend lines).

151 The conclusions drawn from this system can be generalized to other dosimeters also being
 152 considered for synchrotron X-ray dosimetry including silicon diodes where the dose response
 153 of a Si-based detector system varies substantially, up to eight-times that of tissue, in the kilo-
 154 voltage range. For the micron-scale dosimetry required for MRT, the highly localized sensitive
 155 volumes of MOSFET detectors have been investigated [5, 6]. Optical fiber technologies offer
 156 similar possibilities where radiation sensitive inner cores on micron-scale are possible using
 157 dopants like Al, Ge, and Er [7] but which will also lead to K-edge discontinuities and near
 158 edge perturbation in the response.

159 Figure 2 demonstrates significant differences (>20%) between MC calculations for Pt
 160 bearing tissue and the scatter-free approximation used, for instance, by Adam [10] to examine
 161 dose enhancement from I and Gd. For the case of a small (*e.g.* 0.5 cm radius) localized
 162 concentration of Pt (10 mg/mL of 0.5 cm diameter) embedded in a water medium, the two
 163 models give a comparable prediction; that the response increases immediately at edge but
 164 decreases above edge. The change to a decrease in dose enhancement appears to be due
 165 to decreased attenuation by the medium at these energies which is dominated by Compton
 166 scattering. If the Pt concentration is more diffusely distributed, say for the typical dimensions
 167 of the human brain, the dose enhancement falls at edge from increased competition between
 168 attenuation and absorption near the K-edge of Pt (78.2 keV) also known as self-absorption,

169 The data shows that significant dose enhancement occurs only at extremely high concentra-
 170 tions of Pt. Although the results obtained for 10 mg/mL Pt reflect the magnitude of the
 171 biological response reported by Biston *et al.* (2004), the concentrations reported in this study
 172 were significantly smaller (<0.5 mg/mL) supporting a mechanism for improved survival that
 173 goes beyond a dose enhancement model. Enhancement in the biological dose may be due to
 174 variations in the Pt concentration at smaller length scales, for example a microdistribution of
 175 Pt that includes high (~10 mg/mL) concentrations of Pt, or from increases in the quality of
 176 the photoionization products (the microdosimetry).



197 Figure 2. Variation in the dose response with monoenergetic X-ray energy for due to perturbations from a Pt
 198 constituent (1 mg/mL and 10 mg/mL) in a water equivalent biological system of diameter 1 cm and 15 cm with the
 199 dose determined at a depth of 0.5 cm and 7.5 cm respectively. MC methods are used to calculate the response at the
 200 higher concentrations due to multiple scattering effects. Models ignoring photon scattering processes are also shown
 (trend lines).

3. Conclusion

Previous work has already shown that solid-state dosimeters including Si diodes, MOSFET, diamond detectors can be calibrated for dose in monoenergetic synchrotron X-rays in the range 5–50 keV, for quasi-monoenergetic X-rays sources from 20–200 keV and for megavoltage X-rays and proton sources, such as are used in radical radiation therapy. With careful consideration of the elemental composition of the detector it is possible to achieve high quality agreement (2–3%) between measurement and MC models of the variation of the detector response over a wide energy range. This information is needed in radiation therapy dosimetry where, for large external X-rays beams, detectors see a mixture of high energy primary photons and low energy (*e.g.* Compton scattered and pair-production-annihilation) photons. Typically, for solid-state detectors, different cavity theories are required for the two energy groups. In addition, high-Z constituents in detectors lead to an enhanced photoelectric absorption, which in the case of pure silicon detectors is up to eight times greater than the tissue equivalent response.

Furthermore, MC models are also being developed for determining the influence of electron transport on the response of detectors, including microdosimetric response. Current MC codes are able to handle large variations in density that typify tissue equivalent gas-filled proportional counters (TEPC) and on the sub-micron scale in candidate solid-state microdosimetry systems such as MOSFET and thin films, where it is anticipated that intercomparison with experiment will help to validate the use of such codes for the microdosimetry predictions on the sub-cellular scale in radiobiological systems. MC based microdosimetry calculations are also expected to assist in explaining LET dependencies found in many solid-state detector systems.

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