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# Real-time in-vivo dosimetry for DaRT

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Abstract. Diffusing alpha-emitters radiation therapy (DaRT) is a revolutionary brachytherapy technique used to treat solid tumours. Implant seeds are coated with <sup>224</sup>Ra which, along its shortlived daughter atoms, emits alpha particles of high linear energy transfer (LET) and of high relative biological efficiency (RBE), creating a tumour-killing dose distribution a few mm wide. Those alpha particles are of energy between 5.67 and 8.78 MeV. DaRT is under investigation in clinical trials, but there currently is no obvious solution for dosimetry aimed at quality assurance of treatment. This study introduces alpha-RAD, a dosimeter based on a metal-oxidesemiconductor (MOS) sensor technology. Alpha-RAD was characterized with <sup>241</sup>Am, which emits alpha particles of energy 5.49 MeV. The results showed that alpha-RAD had good linearity with dose, with the signal increasing linearly in the range from 0 to 6.84 Gy. Also, an external bias in the range between 15 and 60 V, applied on the gate of alpha-RAD during irradiation, would optimize sensitivity to alpha particles of energies typical of DaRT. Alpha-RAD, owing to its compactness, can fit into a brachytherapy needle, to be placed next to <sup>224</sup>Ra seed implants in the tumour, for real-time in vivo dosimetry.

#### **1. Introduction**

Diffusing alpha-emitters radiation therapy (DaRT) is a new revolutionary brachytherapy technique that exploits alpha particles to treat solid tumours. Implant seeds are coated with Radium-224 (224Ra) and inserted into the tumour. The daughter atoms of <sup>224</sup>Ra (<sup>220</sup>Rn, <sup>216</sup>Po, <sup>212</sup>Pb, <sup>212</sup>Bi, <sup>212</sup>Po, <sup>208</sup>Ti and <sup>208</sup>Pb), which are released from the seeds, diffuse and convect into the tumour. Alpha particles of energy between 5.67 and 8.79 MeV, which have high linear energy transfer (LET) and high relative biological efficiency (RBE), are emitted in the process, delivering a lethal dose only around the seed, sparing adjacent critical structures [1, 2]. Theoretical modelling predicts that, over 14 days a dose of more than 10 Gy is delivered in a sphere of radius 5-6 mm centred on the seed of activity density of 0.4 - 0.8 MBg  $g^{-1}[2, 3]$ . Ongoing clinical trials are showing promising results [4].

However, theoretical modelling of a DaRT dose distribution is insufficient for quality assurance of treatment. Also, information on absorbed dose over a target volume does not yield biological information due to the complicated interaction between human cells and alpha particles. For those reasons, it is necessary to devise devices to assess, in vivo within the framework of a DaRT treatment, dose deposited by, and RBE based on radiobiological model of, alpha particles.

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This study tackles the first of those two challenges, and it introduces alpha-RAD, a point-like dosimeter to assess in real-time and *in vivo* dose in DaRT. We performed a characterization of alpha-RAD considering parameters such as sensitivity, and dose linearity of response, to alpha particles of energy 5.49 MeV emitted by <sup>241</sup>Am.

# 2. Material and methods

Alpha-RAD is based on metal-oxide-semiconductor (MOS) sensor technology. With accumulated dose of ionizing radiation the voltage drop across the sensor is increasing. Fabricated first generation of sensors were wire bonded in a dual in-line (DIL20) package with sensitive volume of the sensor face up and without any lead to minimize perturbations to the fluence of incident particles. In our experimental setup, alpha-RAD was irradiated from the top with an Americium-241 (<sup>241</sup>Am) source (figure 1), which emits alpha particles (5.49 MeV) and gamma photons (59.54 keV). The energy of the alpha particles is of the same order of those in DaRT. The fluence of <sup>241</sup>Am was verified with a silicon Hamamatsu PIN diode with a sensitive area of 1x1 cm<sup>2</sup>, operated with an external bias of -100 V. The distance between the die and the emitting surface of <sup>241</sup>Am was 1.45 mm, and this is negligible compared to the range of the alpha particles in air (41.84 mm for  $E_{\alpha}$ =5.5 MeV). The same experimental setup was used for all measurements.

First, we characterized the response of alpha-RAD in terms of sensitivity to alpha particles. The sensitivity was defined as the change of voltage drop per unit of accumulated dose (unit: mV/Gy). The sensitivity, other factors being equal, varies as a function of the external bias applied on the Al gate (across MOS structure) of alpha-RAD during irradiation [5]. We investigated biases in the range from 15 to 90 V (15, 30, 40, 60 and 90 V). At each applied bias, the total irradiation time was 60 minutes and voltage drop was recorded every 30 minutes, 3 times in total. Dose was independently calculated from fluence measurements with the PIN diode under the same air gap 1.45 mm. Second, we characterized the dose-response relationship of alpha-RAD. In that case, we used a bias of 30 V, irradiating alpha-RAD with alpha particles emitted by <sup>241</sup>Am for 180 minutes, and recording the threshold voltage every 30 minutes, 3 times in total.

Our study of sensitivity, and of dose-response relationship, assumed that the dose contribution due to gamma particles emitted by  $^{241}$ Am was negligible. We verified this hypothesis by measuring the threshold voltage drop when there was a piece of paper (cellulose fibres, thickness of 0.1 mm) interposed between the die of alpha-RAD and  $^{241}$ Am. Alpha particles emitted by  $^{241}$ Am were stopped by the paper because their range in that material is less than 50 µm. For this measurement we used a bias of 30 V.

All measurements were repeated at least twice, and data are shown as the mean with uncertainty described by 1 standard deviation. Dose is always reported as dose-to-water for alpha particles with energy 5.49 MeV unless otherwise specified. The voltage drop of alpha-RAD was read out in real-time with a data acquisition system designed and developed in-house at the Centre for Medical Radiation Physics (CMRP) at the University of Wollongong; its accuracy was within  $\pm 1 \text{ mV}$  [6].

# 3. Results

# 3.1. Fluence of $^{241}Am$

The fluence of alpha particles emitted by  $^{241}Am$  was measured with the PIN diode as 800,190  $\pm$  49 particles per cm<sup>2</sup> over 5 minutes; this corresponds to a dose of approximately 0.19 Gy , assuming an LET of 150 keV/µm.

## 3.2. Sensitivity

Figure 2 shows the sensitivity of alpha-RAD as a function of external bias applied on the gate during irradiation. The sensitivity was 60 mV/Gy when the bias was 15 V, and  $85 \pm 5$  mV/Gy when the bias was 30 V. That value was 103 mV/Gy when the bias was 40 V, and 130 mV/Gy when the bias was 60 V. Increasing the bias from 15 V to 60 V roughly doubled the sensitivity from 60 to 130 mV/Gy. For a

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bias of 90 V, the sensitivity was 132 mV/Gy. The error was within  $\pm$  3 mV/Gy unless otherwise specified.





**Figure 1.** Experimental setup: DIL package with alpha-RAD, <sup>241</sup>Am source, battery for providing external bias to the gate of alpha-RAD during irradiation, and data acquisition system.





**Figure 3.** The threshold voltage drop of alpha-RAD, operated with a 30 V bias, as a function of the fluence of alpha particles emitted by <sup>241</sup>Am. Threshold voltage was measured every 30 minutes. Error bars did not exceed the symbol size.



**Figure 4.** The threshold voltage drop as recorded when irradiation was on the bare die between minutes 0 and 30, 60 and 90, and then 150 and 180 min. During other intervals, irradiation was with a piece of paper interposing between the die and <sup>241</sup>Am to stop alpha particles emitted by <sup>241</sup>Am. In that way, we assessed the contribution to alpha-RAD response of gamma radiation only. Error bars did not exceed the symbol size.

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#### 3.3. Dose-response relationship

Figure 3 shows the threshold voltage drop recorded as a function of the fluence of alpha particles. In the first 30 minutes (i.e., after a total of 2.5 x  $10^6$  particles per cm<sup>-2</sup>), the voltage drop of alpha-RAD changed by 94 mV, reaching 204 mV after 60 minutes ( $5.0 \times 10^6$  particles per cm<sup>-2</sup>) and 600 mV after 180 minutes ( $15.1 \times 10^6$  particles per cm<sup>-2</sup>), calculated with respect to the initial voltage drop. The voltage drop increased linearly by 100 mV every 30 minutes (i.e.,  $2.5 \times 10^6$  particles per cm<sup>-2</sup>). The error was within  $\pm 1$  mV unless otherwise specified.

#### 3.4. Gamma contribution to the response of alpha-RAD

Figure 4 shows the threshold voltage drop recorded with and without a piece of paper interposed between the die of alpha-RAD and <sup>241</sup>Am. During the first 30 minutes, the die of alpha-RAD was bare, and at minute 30 we measured a voltage drop of 104.5 mV, calculated with respect to the initial voltage drop. We interposed a piece of paper between the die and the <sup>241</sup>Am during the subsequent 30 minutes (i.e., from 30 to 60 minutes), and recorded a voltage drop within 2 mV. We repeated the same procedure up to 180 minutes. Over three repetitions of the procedure, the average voltage drop when the die was bare was of  $101 \pm 3$  mV, whereas that value when the die was covered was  $2 \pm 2$  mV.

#### 4. Discussion and conclusion

This was a feasibility study of alpha-RAD for DaRT dosimetry. The rationale for using <sup>241</sup>Am to model alpha particles in DaRT is that <sup>241</sup>Am emits alpha particles with an energy of 5.49 MeV, which is close to the energy of alpha particles released in the <sup>224</sup>Ra decay chain (energy in the range from 5.67 to 8.79 MeV). It should be noted that, in DaRT, the activity is in the range from 15 to 150 kBq per <sup>224</sup>Ra seed [2], much stronger than that of the used <sup>241</sup>Am, which was measured by the PIN diode and estimated to be approximately 5.2 kBq. Dose measurements in DaRT with alpha-RAD would accumulate faster than from Am-241 source and can be measured in time with better signal/noise ratio; future work will investigate this.

First, we showed that alpha-RAD, when operated with a bias in the range from 15 to 90 V, had a good sensitivity to alpha particles. Sensitivity was maximized at a bias of 60 V, and the plateau beyond 60 V is due to full charge collection in alpha-RAD responsible for voltage drop. Based on results, a bias between 15 and 60 V is suggested to optimize alpha-RAD sensitivity to alpha particles in DaRT dosimetry. Second, alpha-RAD had a linear dose-response between 1 and 6.84 Gy; an increase of 100 mV in threshold voltage corresponded to approximately 1.14 Gy. This result agreed with Rosenfeld's previous study that the dose-response of an n-type MOSFET to alpha particles emitted by  $^{241}$ Am was linear up to the total fluence of  $10^8$  particles per cm<sup>2</sup> [7].

 $^{241}$ Am emits both alpha and gamma radiation, and the sensitivity of alpha-RAD to the latter is expected to be about 4 times higher than that to alpha particles [8]. However, our results showed that the voltage drop had insignificant shifts when alpha-RAD was covered by a piece of paper used to stop all alpha particles incident on the die. This result can be explained by low dose rate of gamma radiation from this source that provided confidence that most signal was associated with alpha radiation within 2% error.

In conclusion, we have shown that alpha-RAD is a suitable solution for real-time *in vivo* dosimetry in DaRT. Alpha-RAD had a linear dose-response relationship and a good sensitivity when irradiated with alpha particles of 5.49 MeV. As a limitation of this study, the investigated dose range was limited to between 0 and 6.84 Gy, whereas it is broader in DaRT, where the average dose to the target at 5 mm distance from the needle is expected 10 Gy.

#### 5. Reference

- [1] Arazi L et al 2010 Phys. Med. Biol. 55 1203-18
- [2] Arazi L et al 2007 Phys. Med. Biol. 52 5025-42
- [3] Arazi L 2020 Phys. Med. Biol. 65 015015
- [4] Popovtzer A et al 2019 Int. J. Radiat. Oncol. 50 S26-27

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Journal of Physics: Conference Series

**1662** (2020) 012031 doi:10.1088/1742-6596/1662/1/012031

- [5] Sze S M and Kwok K N 2006 *Physics of semiconductor devices*. John Wiley & Sons
  [6] Kwan I S *et al* 2008 *Radiat Meas*. 43 929-32
- [7] Rosenfeld A et al 1996 IEEE T. Nucl. Sci. 43 2693-700
- [8] Biasi G et al 2020 IEEE T. Nucl. Sci. 67 534-540