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Article

Simultaneous Measurements of Dose and Microdosimetric Spectra in Clinical Proton Beam using scCVD Diamond Membrane Microdosimeter

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- 1 Abstract: A single crystal chemical vapor deposition (scCVD) diamond membrane based
- ² microdosimetric system was used to perform simultaneous measurements of dose profile and
- ³ microdosimetric spectra at Y1 proton passive scattering beamline of Center of Proton Therapy,
- ⁴ Institute Curie in Orsay, France. To qualify the performance of the set-up in clinical conditions of
- hadrontherapy, the dose, dose rate and energy loss pulse-height spectra in diamond microdosimeter
- were recorded at multiple points along depth of a water-equivalent plastic phantom. The dose-mean
- ⁷ lineal energy (\overline{y}_D) values were computed from experimental data and compared to silicon on insulator
- (SOI) microdosimeter literature results. In addition, the measured dose profile, pulse height spectra,
- and \overline{y}_D values were benchmarked with numerical simulation using TOPAS and Geant4 toolkits.
- ¹⁰ These first clinical tests of a novel system confirm that diamond is a promising candidate for tissue
- equivalent, radiation hard, high spatial resolution microdosimeter in beam quality assurance of
- ¹² proton therapy.
- ¹³ Keywords: Diamond, Proton therapy, Microdosimetry, Radiation detectors, Dosimeters, Sensors

14 1. Introduction

The use of proton beams for the treatment of cancers has gained considerable interest in recent 15 years. This is observable from the increase in the number of proton beam centres around the world. 16 For instance, in Europe there were 25 more proton beam centres constructed between 2009 and 2019 [1]. 17 This is a result of the comparative advantage proton therapy offers over conventional photon radiation 18 therapy. The absorbed energy of a proton beam increases with depth while that of photons decreases 19 with depth giving clinical proton therapy a higher conformal dose delivery and hence less damage 20 to critical tissues in patients than obtainable in photon radiation therapy. Like every other radiation 21 procedures, there are some concerns around the undesirable effects of proton therapy, including 22 necrosis of the healthy tissue in the proximity of treated tumor and cases of induced secondary cancers. 23 The occurrence of secondary effects depends on the radiation dose, volume and the region irradiated 24 [2]. Studies [3–5] have revealed the need for LET optimization to reduce any unwanted biological 25 effects in proton therapy. The relative biological effectiveness (RBE) of radiation is defined as the ratio 26 D_L/D_H where D_H is the absorbed dose of radiation, H at which the probability of a given biological 27 effect is equal to that at an absorbed dose D_L of a reference radiation, L [6]. The RBE has been found 28 to depend on the deposited physical dose, irradiated tissue and the quality of the beam which is 29 measured by the linear energy transfer (LET). The RBE is an experimental quantity obtained from 30

irradiation studies on living cells. A proton RBE value of 1.1 is usually used for clinical therapy with
photon radiation used as a reference [7]. Though the RBE model that proposes a value of 1.1 has been
widely accepted, studies have shown that this value varies with proton energies (i.e along the depth
dose profile), increasing significantly at the distal part of the Bragg Peak. Hence, an RBE weighted
treatment plan could lead to the optimized dose delivery to patients with less important secondary
effects occurrence, also in the case of proton therapy.

³⁷ Microdosimetry has been used in the investigation of microdosimetric quantities of radiation field. ³⁸ The probability density d(y) together with the dose averaged lineal energy, \bar{y}_D , are physical quantities ³⁹ correlated with the biological effectiveness of the therapeutic beam obtainable from microdosimetry ⁴⁰ measurements. Tissue Equivalent Proportional Counters (TEPC) are well established for clinical ⁴¹ microdosimetry. However, solid state microdosimeters have been introduced in clinical dosimetry as ⁴² they offer higher spatial resolution, more robust and easy integration than conventional TEPCs.

Most solid state microdosimeters are based on silicon and have been introduced as an alternative 43 to TEPCs. Due to the non-tissue equivalent nature of silicon, corrections must be made for effective ΔΔ extraction of dose parameters [9]. Over the years since the first publication on silicon microdosimeters, 45 there have been continuous improvements in the design, structure and its efficiency [10-14]. Due to 46 the limitations of silicon based microdosimeters, further development on the portability and efficiency 47 of the TEPCs are also being considered. A compelling work is that of Conte [15] and Bianchi [16] on 48 the use of sealed mini TEPC for proton beam therapy. Bianchi et al. observed similar microdosimetry spectra for mini TEPC and a $\Delta E - E$ silicon microdosimeters at linear energies higher than 8 keV / μm 50 with discrepancies observed at lower LET values. 51

Rollet [17] first reported the use of artificial diamond for microdosimeters. Diamond (Z=6) offers 52 advantage due to its radiation hardness, near tissue equivalence (Z=7.5) for photon radiation, resulting 53 in less variable function for energy loss spectra conversion to water compared for example to silicon (Z=14) [18]. In addition, some of the physical and electronic properties of diamond such as large-band 55 gap, temperature stability, fast drift velocity and low capacitance, make diamond an interesting 56 potential material for producing microdosimetric devices. Previous research works [20,21] have shown 57 that single crystal diamond detectors exhibit good charge collection efficiency, homogeneity in the 58 micro-sensitive volumes and can be used in measuring microdosimetric quantities in clinical beams. Using new device structures [22], improvements of the electric field geometry have also been proposed 60 to maximise the charge collection efficiency and full potential of these detectors. 61

A diamond guard ring microdosimeter previously reported [24] by this group has shown the possibility of obtaining a sensor with full charge collection efficiency over broad range of linear energy transfer of ions at various energies. The proof of concept has prompted the authors to pursue the integration of this detector to simultaneously measure the depth dose profile and the microdosimetric

spectra of a degraded 230 MeV clinical beam at the Proton therapy Center, Orsay, France.

67 2. Materials and Methods

68 2.1. scCVD diamond membrane Guard Ring (GR) prototype

The scCVD diamond membrane consists of four arrays of 16 sensitive volumes interconnected 69 with bridges and bonded on a DIL20 chip carrier. Structurally, it comprises of an intrinsic diamond 70 layer ($12\mu m$ thickness) sandwiched between two layers of metallic Aluminium electrodes. Further 71 patterning of the top electrode and a chemical etching process was performed for the realization of 72 multiple microsensitive volumes (μSVs) surrounded by the guard ring structure as shown in figure 73 1 (left). The critical dimensions have been chosen for the best signal to noise ratio in measurement 74 conditions. Detailed description of the fabrication process of a guard-ring (GR) scCVD membrane 75 microdosimeter and its charge transport characterization with an ion microbeam can be found in 76 previous published work [24]. 77



Figure 1. Left: the schematic representation of one microsensitive volume μSV of diamond GR microdosimeter prototype; Right: Optical micrograph of the diamond membrane with four sensistive microSVs arrays showing the μSVs marked with red(for microdosimetric read out) and yellow (dose read-out) color squares

As shown in figure 1 (right), the complete scCVD diamond membrane plate is arranged in four arrays hereafter referred to as Sensitive Volume Arrays (SVA). Each array comprises of 16 μSVs 79 interconnected with bridges and micro-bonded onto the chip carrier. In this device prototype, only two 80 (SVA1 and SVA2) of the four arrays of SVAs were used - one for microdosimetric spectra acquisition 81 and the other for dose measurements. The active area and lateral size of one SVA is $16 \,\mu SVs$ is 0.045 82 mm^2 with each microsensitive volume having 60 μm diameter. The total active area including bridges is 0.057 mm^2 . The thickness of the diamond membrane is 12 μm as confirmed from alpha particles 84 absorption spectroscopy and ion beam induced currrent technique with scanning trasmission ion 85 microscopy approach [22]. 86

87 2.2. Measurement set-up

A battery powered diamond based dosimetric and microdosimetric measurement system has 88 been developed. Although not fully integrated and miniaturized yet, here we present the first 89 proof-of-principle of operation of such a modular system in clinical conditions of a hadrontherapy 90 facility. Figure 2 (right) shows a diagram of the used set-up. The electrical signal induced by the proton 91 beam in both SVA of the diamond sensor (enclosed in an electrically screened plastic housing), is fed 92 to both a charge sensitive preamplifier Amptek CoolFET (CSA) for the purpose of microdosimetric 93 spectra measurements and a high precision Keithley 6517A pico-ammeter (pAM) for dose/dose rate 94 measurement. A fixed bias voltage of 15V (equivalent to electric field of $1.2 V / \mu m$) is applied directly 95 to the back electrode of the diamond sensor from a voltage adjustment element (VADJ). The system is 96 powered by a 5V, 24 000 mAh PowerBank (PwBa). 97

Pre-amplified voltage pulses from CSA induced in the SVA1 of the diamond sensor by 98 single-particles are fed to a versatile, small size multi-channel analyzer (LabZY nanoMCA II [26]) with 99 integrated digital amplifier and WiFi module for data transfer. The MCA's digital amplifier shapes 100 and further amplifies the signal and processes the generated pulse-height spectra. Communication is 101 made with the personal computer (PC) through a wifi router. Physical connection between PC (placed 102 in control area) and the wifi router (placed in experimental area) is made by a 20 m long ethernet 103 cable. Beam induced DC current from the SVA2 of the sensor is fed to the picoammeter (placed in the 104 experimental) area through 2 m coaxial cable. Communication of the picoammeter with the PC, where 105 data is stored, is assured through a 20 m USB cable with three repeaters. 106



Figure 2. The Experimental set-up and the schematic of the experiment

2.3. Passive Scattering Beamline at the Proton Therapy Centre, Orsay

A proton beam of mean energy 230 MeV and energy spread 0.6 MeV (2σ) generated by an IBA 108 C235 cyclotron, is degraded to 89 MeV in the isocenter by a range shifter. The range shifter contains 109 a combination of lexan and lead layers of different thicknesses. The beam is further scattered by 110 lead foils before entering the treatment room. A large brass collimator of $4 \times 4 \ cm^2$ was placed at the 111 end-point of the beam line, in order to obtain a homogenous 2D beam profile and at the same time 112 protect readout electronics from radiation damage. The water equivalent phantom SP34 made of white 113 polystyrene, type RW3 [27] in the form of various thicknesses 10 mm, 5 mm, and 1 mm square plates 114 were used to create dose profiles within target depth. These plates were gradually placed directly 115 before sensor housing during irradiation. The uncertainty of positioning depth was estimated to be 116 less than 0.1 mm, and it is mostly related to precision of plate fabrication and presence of air gaps 117 between the plates. All the components of the experiment including the geometry of the beam line 118 (shown in figure 3) and the diamond sensor were included in obtaining the energy loss spectra in 119 Geant4 and TOPAS numerical simulations. The Geant4 electromagnetic and hadronic physics models 120 were used in the simulation for describing particle trajectories. Details of these models can be obtained 121 in reference [28]. 122

123 2.4. Energy calibration procedure for microdosimetric spectra measurements

Calibration was done in the laboratory prior to the measurements at a hadron therapy facility. The procedure includes a combination of two techniques: First, the measurement of 5.486 MeV alpha particles spectra from Am-241 with 300 μm thick fully absorbing scCVD diamond detector in a vacuum and secondly, a consecutive pulse generator calibration. A thick electronic grade scCVD detector was placed in a vacuum chamber biased at 300 V (1V/ μm). Using an alpha particles radioactive source, the pulse height spectra was recorded. A precise line spectra was obtained and fitted with a gaussian distribution. The centroid at a fixed channel number corresponds to 5.486 MeV and at full width half



Figure 3. Y1 beam line geometry of IC-CPO used in TOPAS/Geant4 simulation

maximum of the alpha line of 0.3 %. Consequently an ORTEC pulse generator amplitude was adjusted
to match perfectly the measured alpha spectra line. Then, the thick scCVD detector was replaced by the
scCVD diamond membrane microdosimeter reported in this work. The system was re-calibrated with
the pulse generator, introducing 5 spectral lines at 5.486 MeV, 2.743 MeV, 1.37 MeV, 0.685 MeV, 0.343
MeV. No shift in the pulse generator peak at 5.486 MeV was observed compared to the measurement
system with thick diamond detector, indicating negligible influence of different detector capacitance
on the calibration process.

138 3. Results

139 3.1. Dosimetric performance of the system

Figure 4 presents beam induced current curves measured under 30s irradiations at various depths 140 of plastic water phantom. The plateaus of the presented curves corresponds to relative dose rate of used 141 proton beam. A remarkably low leakage current (less than $10^{-13}A$) can be observed on the diamond 142 sensor for beam-off conditions. The beam induced charge was obtained by integrating the induced 143 current over the irradiation window (the induced charge corresponds to relative absorbed dose). The 144 maximum dose (induced charge) is obtained at 54 mm of plastic water depth marking the maximum 145 peak of the depth dose profile. Comparison between dose rate, instantaneous induced current at the 146 plateau level and dose integrated induced current curves (induced charge) within the irradiation time 147 window is presented in figure 5. It shows a perfect agreement between both quantities indicating 148 the possibility of fast scanning in water phantoms if only constant beam current is guaranteed at the 149 accelerator level. 150

To check reproducibility of the dose measurements, additional runs were performed for each depth of the depth dose profile. Three irradiations were performed at each depth and at the same irradiation times. Spread between measured values for each profile point was below 2%. This includes uncertainty of precision of dose delivery by accelerator. The result also shows the good quality of the underlying diamond material. Additionally, to our knowledge the presented sensor is the smallest volume $6.84 \times 10^{-4} mm^2$ dosimeter available, which could be a perfect instrument for precise dose measurements in small-field, microbeams and mini beam dosimetry.

158 3.2. Energy loss spectra

The energy loss spectra obtained from labZY MCA of the calibrated diamond GR microdosimeter is presented in figure 6. Only three measurements, related to the characteristics points of the depth dose profile are shown. i.e (a) at the plateau (30 mm), (b) at the Bragg peak (BP) maximum (55 mm depth) and (c) the distal end of the BP (69 mm). The corresponding Geant4 simulated energy spectra at



Figure 4. Proton Beam Induced Current in diamond GR microdosimeter at various depth of plastic water phantom



Figure 5. Comparison between measured induced current (dose rate profile) and measured induced charge (dose profile) for 230 MeV proton beam degraded to 89 MeV



Figure 6. Selected measured calibrated pulse-height spectra obtained along depth dose profile at (a) 30 mm (b) 55 mm (c) 69 mm. Counts have been normalised to the primary proton peak.

each characteristic point is included in figure 6. There is a very good agreement between the measured
spectra and the simulation result in terms of distribution shape, peak position and its width.

In addition, a progressive shift of the peak position of the energy loss spectra towards higher 165 energies and broadening of the spectrum is observable with depth of water. This is due to protons 166 being slowed down towards the BP. Also, there is an expected reduction in the intensity with depth. A 167 low energy tail at around 22.25 keV is observed and become more pronounced at higher depth. This 168 low energy tail was previously associated with the incomplete charge collection efficiency (CCE) due 169 to the charge sharing between µSV and the guard ring electrode [24]. The measured spectra have a 170 cut-off at 20 keV that corresponds to the current limit of the measurement set-up due to the electronic 171 noise. 172

173 3.3. Water-equivalent microdosimetric spectra

By using a diamond-water conversion factor of 0.32 [25], the measured energy deposition spectra obtained with the diamond GR microdosimeter was converted to water-equivalent microdosimetric spectra yd(y). In general, we observe that microdosimetric distributions shift towards higher energy values with increasing depth in plastic water phantom. Due to the nature of the spectra transformation



Figure 7. Experimental microdosimetric spectra obtained from GR diamond microdosimeter in plastic water phantom at depth of 0, 40, 52, 55, 60 and 69 mm. Inset: A zoom on the spectra at 60 and 69 mm. Proton edge at 35 kev/ μ m corresponds to protons of 1.3 MeV with stopping range of approximate 12 μ m in diamond equal to the sensor thickness.

process, the previously identified low energy tail in pulse-height spectra is still visible but does not 178 significantly contribute to the microdosimetric spectra area and thus to the calculated \overline{y}_D values. To 179 confirm this, we performed a cut-off for four measured pulse height distributions removing low energy 180 tails prior to the transformation to microdosimetric distributions. Four \overline{y}_D values calculated from 181 corrected microdosimetric spectra are displayed in figure 8 with open triangles following the trend of 182 \bar{y}_D values obtained from not-corrected spectra. Furthermore, the typical "proton edge" can be seen 183 from an enlarged view of the microdosimetric spectra measured at the BP and its distal part (see inset 184 of figure 7). 185

The maximum lineal energy observed at this edge was approximately $35 \text{ keV}/\mu m$ in water. This lineal energy corresponds to a proton energy of 1.3 MeV with a stopping range of approximately 12 μm in diamond equalt to the sensor thickness. Therefore, this observed proton edge validates the energy calibration performed with the α -particle source and the pulse generator. Observed threshold in experimentally derived microdosimetric spectra amounts to 0.6 keV/ μm water equivalent. This is comparable to frequently reported sensitivities of silicon based solid-state microdosimeters [29].

192 4. Discussion

4.1. Comparison of calculated \overline{y}_D and literature results

The calculated dose-mean lineal energies \overline{y}_D from experimentally measured microdosimetric spectra is presented in figure 8. The microdosimetric spectra and \overline{y}_D values measured with the diamond GR microdosimeter are in agreement with expected trends. The measured microdosimetric spectra shift to higher values of lineal energy with increasing penetration depth. The spectra shift and thus, a steep increase of \overline{y}_D is expected towards the end of the proton range, where the protons deposit more



Figure 8. \overline{y}_D along dose profile both measured with diamond GR microdosimeter compared with dose profile and LET_d from TOPAS simulations

energy in µSVs. The obtained result is also consistent with microdosimetric spectral trends observed 199 for silicon solid-state microdosimeters in clinical proton beams [30–32]. The dose-mean lineal energy 200 \bar{y}_D values in the entrance region of the BP (0 mm to 40 mm) were approximately 2 keV/ μ m. Identical 201 values were reported for SOI microdosimeter for 159 MeV proton pencil beam [30]. In the proximal 202 and distal part of the BP (52 mm to 69 mm), the measured values went from 3 to 10.7 keV/ μ m, while 203 maximum measured \overline{y}_D value was reached at very distal part of BP at 69 mm depth at the point of only 204 1% relative dose distribution. Similar values were reported for SOI microdosimeter ranging from 3 to 205 10.3 keV/ μ m, with the maximum \overline{y}_D value reached at 20% of relative dose distribution in BP distal 206 fall-off. It must be noted, that if we compare the dose profile at the BP distal fall-off and \overline{y}_D values, in 207 general, diamond measured \overline{y}_D values for a degraded 230 MeV proton beam are lower compared to 208 reported \overline{y}_D values for SOI microdosimeter measured for lower proton beam energies. For instance, if 209 we consider the measured value of \overline{y}_D = 5.3 keV/ μ m in diamond, it corresponds to a position at 50% 210 of relative dose in BP distal fall-off part of degraded 230 MeV proton beam. For SOI microdosimeter, 211 the \overline{y}_D at 50% of relative dose in BP distal fall-off part is 8.4 keV. Again such a trend is expected since, 212 with the increase of the initial beam energy, the maximum \overline{y}_D , decreases. The longer travelling path 213 from a higher-energy beam can result in more energy straggling close to the maximum range at the 214 corresponding locations. This will result in a higher mean energy and a lower \overline{y}_D , accordingly [33]. 215 To further benchmark our experimental results of \overline{y}_D , we performed numerical simulations using 216 TOPAS Simulation Toolkit [34] to obtain dose-weighted LET_d values. The complete Y1 beam line 217 218 geometry (figure 3) with configuration identical to experiment was implemented in the simulation. We used a water phantom placed in the isocenter to obtain dose and LET_d profiles. The TOPAS 219 ProtonLET scorer gives the LET_d of primary and secondary protons, including the energy deposited 220 by associated secondary electrons. More details about LET_d scoring technique in TOPAS/Geant4 221 can be found in [35,36]. TOPAS simulated LET_d profile is displayed in figure 8 (in black solid line) 222

is in close agreement with the experimentally measured \overline{y}_D profile for all depth. Frequently, due

to the fundamental difference between LET_d and \overline{y}_D , literature reported comparisons between both 224 differ especially in the entrance part of the BP [31]. In general, this difference arises from the different 225 volumes (voxels) used for LET_d calculation (typically \approx 1 mm) and \overline{y}_D measurement (typically \approx dozens of microns) and are related to the energy transfer differences by the delta-rays. Both quantities 227 frequently differ at entrance part of the BP where delta-rays have higher range, exceeding the volume of 228 interest used in measurement. In the distal part, delta-rays range becomes comparable with the volume 229 of interest used in measurement, thus both values are in close agreement. In our case, volumes in 230 simulation (0.05 mm) and measurement (\approx 39 microns water-equivalent) were comparable, resulting in close agreement of \overline{y}_D and LET_d in the whole range. A comprehensive review of volume size influence 232 on LET_{*d*} calculations can be found in [33]. 233

The TOPAS simulated dose profile (shown in dash line of figure 8) reproduces very well the 234 distal part of the measured diamond GR microdosimeter dose profile (shown in solid blue line) and 235 the position of the BP. However, its amplitude differs from measured one. Both profiles have been 236 normalized to the entrance point. At this stage of sensors development, we believe that the observed 23 difference arises from characteristics of the diamond sensor, most probably due to the charge collection 238 inefficiency or induced proton beam DC current saturation in the peak region for the measurement. 239 Our second hypothesis (less probable) assumes that this difference arises from the over-response 240 of the sensor in the entrance part due to the presence of non-tissue equivalent materials around 241 diamond sensor. Further experiments with reference ionization chambers are planned to clarify this 242 issue. Nevertheless, measured dose profile already allows precise sensor positioning and proton range 243 verification. 244

²⁴⁵ 5. Conclusions and current perspectives

A diamond GR microdosimeter with energy calibrated response has been fabricated and tested in 246 a proton therapy facility. A demonstration of simultaneous measurement of the dose depth profile and 247 microdosimetry spectra has been reported. The possibility of measuring both the depth dose profile 248 and pulse-height spectra using one sensor allows precise positioning of the device for microdosimetric 249 spectra acquisition in the selected points-of-interest - a very useful feature for future beam quality 250 assurance system in hadron therapy. The measured calibrated pulse-height spectra of energy loss of 251 protons in diamond have been benchmarked with Geant4 simulation, showing very good agreement, 252 in terms of peak maximum position and widths. The dose-mean lineal energy \overline{y}_D have been compared 253 and discussed with the experimental data measured with silicon based solid-state microdosimeters as 254 reported in literature, as well as with numerical calculations of LET_d values. We observed all these 255 values in close agreement at the entrance, the proximal and distal part of the BP. Finally, we reported a very good correlation between TOPAS simulated dose profile and our measurement for the distal part 257 of the BP. A difference in dose profile amplitude at the BP could be associated with charge collection 258 characteristics of the diamond sensor. 259

In ongoing work, the system is being miniaturized by integrating the CSA on the same printed circuit board with the sensor and the modular elements can be integrated in one water-proof PMMA housing to assure full portability. Thus, the entire system is expected to be compact, battery powered and with wireless data transfer capability. In order to improve the quality of the pulse height spectra, a new type of diamond membrane microdosimeter with truly isolated 3D microSVs, surrounded by a tissue equivalent non-electrically active material is envisaged in future developments of the microdosimetry system.

267 6. Patents

Patent pending: System for Dosimetric and Microdosimetric Ionizing Radiation Charcaterization–

²⁶⁹ I.A. Zahrdnik, M. Pomorski, EP20305733.6, 30 June 2020

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