Radiation Protection Dosimetry (2004), Vol. 110, Nos 1-4, pp. 851–857
doi:10.1093/rpd/nch203

EXPERIMENTAL EQUIVALENT CLUSTER-SIZE DISTRIBUTIONS IN NANOMETRIC VOLUMES OF LIQUID WATER

B. Grosswendt[1,*], L. De Nardo[2], P. Colautti[3], S. Pszona[4], V. Conte[3] and G. Tornielli[2]
[1]Physikalisch-Technische Bundesanstalt, Bundesallee 100, D-38116 Braunschweig, Germany
[2]Dipartimento di Fisica dell'Università di Padova, via Marzolo 8, I-35100 Padova, Italy
[3]INFN Laboratori Nazionali di Legnaro, viale dell'Università 2, I-35020 Legnaro (Padova), Italy
[4]Soltan Institute for Nuclear Studies, 05-400 Otwock/Swierk, Poland

Ionisation cluster-size distributions in nanometric volumes of liquid water were determined for alpha particles at 4.6 and 5.4 MeV by measuring cluster-size frequencies in small gaseous volumes of nitrogen or propane at low gas pressure as well as by applying a suitable scaling procedure. This scaling procedure was based on the mean free ionisation lengths of alpha particles in water and in the gases measured. For validation, the measurements of cluster sizes in gaseous volumes and the cluster-size formation in volumes of liquid water of equivalent size were simulated by Monte Carlo methods. The experimental water-equivalent cluster-size distributions in nitrogen and propane are compared with those in liquid water and show that cluster-size formation by alpha particles in nitrogen or propane can directly be related to those in liquid water.

INTRODUCTION

It is commonly accepted that the spatial distribution of energy deposition due to the interaction of ionising radiation in sub-cellular structures such as segments of the DNA is decisive for the initiation of radiation damage. These sub-cellular structures have volumes of a few nanometres in size and are not yet accessible to direct measurements. Because of this fact, our present knowledge on the initiation of radiation damage is almost exclusively based on Monte Carlo simulations. These simulations use more or less highly sophisticated models of the DNA including higher-order structures, such as nucleosomes and chromatin fibre loops [see, for instance, Nikjoo *et al.*[1] and Friedland *et al.*[2]], or they assume, as a substitute to radiosensitive sub-cellular target volumes, nanometric volumes of liquid water, which are, however, also not accessible to direct measurements. Common to all Monte Carlo calculations is the result that radiation damage to sub-cellular structures strongly depends on radiation quality and cannot always be described satisfactorily by macroscopic quantities like absorbed dose or linear energy transfer [see, for instance, Goodhead[3]]. Therefore, one of the great challenges of radiation physics is, to find quantities which are measurable and behave, as a function of radiation quality, in a similar manner as radiation damage to segments of DNA. Appropriately designed measuring devices based on such quantities could be used, for instance, in radiation therapy with heavy ions to simplify treatment planning.

*Corresponding author: Bernd.Grosswendt@ptb.de

If one considers the fact that the yields of clusters of multiple ionisation produced by ionising radiation of different quality within sites, 2–3 nm in size, correlate well with observed yields of double-strand breaks of DNA as was shown, for instance, by Brenner and Ward[4], it seems to be reasonable to base potential quantities for radiation quality on the probability of cluster-size formation in volumes comparable in size to segments of DNA. This ionisation cluster size is defined by the number ν of ionisations that are produced by an ionising particle in a specified volume. For particles of energy T passing the target volume at distance d from its centre, the distribution of cluster size is then characterised by the probability $P_\nu(T;d)$ that exactly the cluster size ν is formed. In this sense, the mean ionisation cluster size is given by the first moment of the $P_\nu(T;d)$-distribution:

$$M_1(T;d)=\sum_{\nu=0}^{\infty}\nu P_\nu(T;d) \quad \text{with} \quad \sum_{\nu=0}^{\infty}P_\nu(T;d)=1. \tag{1}$$

At the moment, the most promising method for determining such cluster-size distributions experimentally is a measurement in millimetric volumes of a low-pressure gas, using target volumes with dimensions of mass per area similar to those of DNA segments if a density of 1 g cm^{-3} is assumed. This procedure is the same as that used in traditional microdosimetry for many years, but it is extended to target dimensions of the order of a few nanometres (nanodosimetry). There are, however, at least two conditions that must be fulfilled when this procedure is applied for characterising radiation damage to sub-cellular structures. First, the interaction

mechanisms of ionising radiation in the counter gas must be similar to those in tissue-equivalent matter; and second, the requirement that the number of ionisations produced by a particle when penetrating the target volume is accurately counted by the measuring device. The problem with measurements in gases is that, in particular, the first condition is not really fulfilled. There is, however, a scaling procedure, which can be applied to nanodosimetric measurements in gases and, at the same time, allows the determination of ionisation cluster-size distributions that are very similar to those to be expected in specified volumes of liquid water. This scaling procedure is based on the mean-free ionisation path lengths of primary particles in gas and in liquid water [for the details, see Grosswendt[5]].

To apply this scaling procedure for determining equivalent ionisation cluster-size distributions in nanometric volumes of liquid water, measurements were performed for alpha particles at an energy of 4.6 MeV crossing a cylindrical target volume of nitrogen on a diagonal at half the cylinder's height with a mass per area of the cylinder's diagonal between 0.1 and 1.3 μg cm^{-2}, and for alpha particles at 5.4 MeV using a cylindrical target of propane with a diameter of mass per area 2.04 μg cm^{-2}. In the latter case, special emphasis was laid on the investigation of ionisation cluster-size formation by secondary electrons. The ionisation cluster-size distributions in nanometric volumes of liquid water were calculated by Monte Carlo simulation and used afterwards for a comparison with the experimental results after the application of the scaling procedure.

It is the aim of the present paper to (i) describe briefly the measuring devices used for measurements of cluster-size frequencies, (ii) summarise the scaling procedure applied for determining cluster-size distributions that are equivalent to those in specified volumes of liquid water and (iii) give a coarse overview of the Monte Carlo models that were used to simulate the experiments and to determine ionisation cluster-size distributions in liquid water. Furthermore, experimental and numerical cluster-size distributions are compared and discussed from the point of view of application to characterise radiation damage to sub-cellular structures.

THE MEASUREMENT OF IONISATION CLUSTER-SIZE DISTRIBUTIONS

The measurement of ionisation cluster-size frequencies for 4.6 MeV alpha particles in nitrogen was performed with the so-called Jet Counter of Pszona *et al.*[6] or Grosswendt and Pszona[7] using alpha particles emitted from a gold-plated ^{241}Am source, after their attenuation from 5.4 to 4.6 MeV within the source walls. For a schematic view of the counter, see Figure 1. The gaseous volume for simulating a nanometric target at unit density was obtained by pulse expansion of nitrogen gas into an evacuated interaction chamber, which is of cylindrical shape, 10 mm in diameter and 15 mm in height. The clean vacuum environment is maintained by a turbo molecular pump of modest pump rate of 240 l s^{-1}. Pulse expansion is performed by means of a fast piezoelectric valve, which is connected to a second valve and injects the gas through a nozzle with an orifice, 1 mm in diameter, from a reservoir into the interaction chamber below the nozzle. The gas jet within the interaction chamber forms a cylindrical target volume of equal height and diameter. In the experiments, this target volume is crossed by a well-collimated beam of alpha particles on a diameter at half its height. After leaving the interaction chamber, the alpha particles are registered by a silicon detector. Ions created by each alpha particle upon its penetration through the interaction chamber during the flow of nitrogen are removed from the chamber by an electric field created by a grid. Afterwards, they are guided and accelerated to an ion-counting device using an electric field created by a second grid. To separate the ions at the ion-counting device, the time-of-flight technique is applied. Only those ions are accepted, which are produced within the interaction chamber by a single alpha particle and are, at the same time, in coincidence with the gas jet within a time window that ensures an almost constant gas density along the particle track. In a typical experiment, the mass per area of the target volume's diameter and height was varied between ~0.1 and 1.3 μg cm^{-2}. These data were determined by measuring the transmission of low-energy electrons through the gas layer across the diameter of the interaction chamber, as a function of the time elapsed after operating the piezoelectric valve. The overall detection efficiency of the Jet Counter was estimated to decrease from ~50% at small mass per area of the target diameter to ~40% at a larger value. This decrease is probably caused by the fact that with increasing the number of ions, which are produced within the target volume if the mass per area of its diameter is increased, the probability that all ions can be separated by the applied time-of-flight technique also decreases.

The measurement of ionisation cluster-size frequencies for 5.4 MeV alpha particles in propane was performed with the track-nanodosimetric counter of De Nardo *et al.*[8,9] using alpha particles emitted from a ^{244}Cm source, after their attenuation from 5.8 to 5.4 MeV within the source walls. For a schematic view of the counter, see Figure 2. The counter is mounted on a platform, which can be moved relative to the alpha particle beam, and is defined by two collimators in front of a solid-state

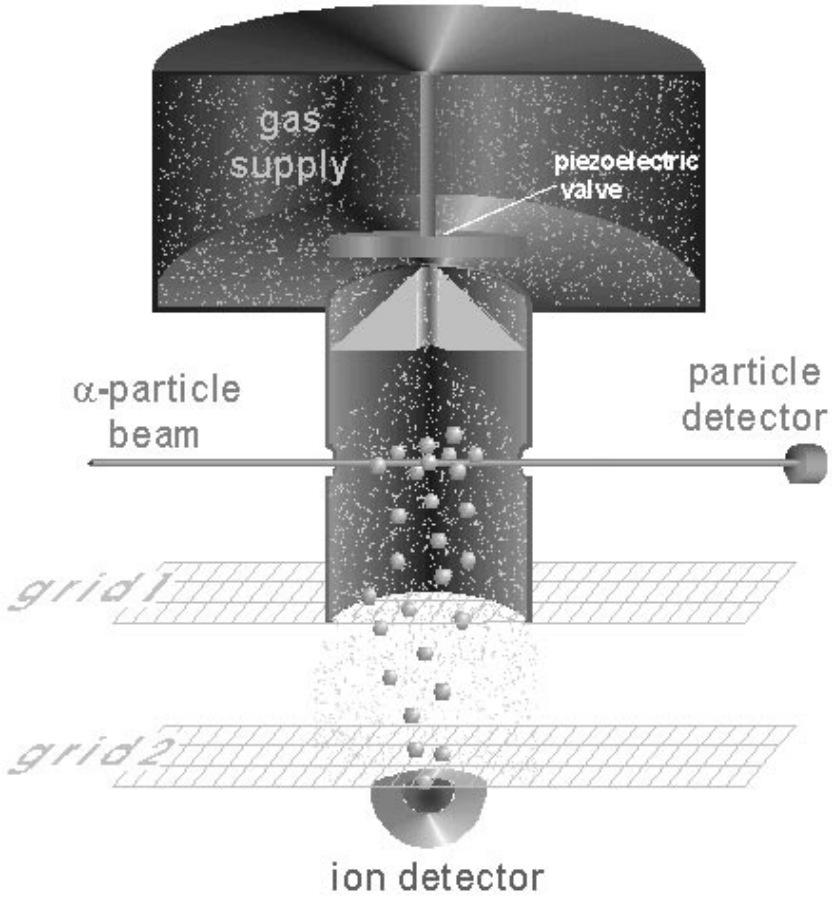

Figure 1. Schematic view of the Jet Counter of Pszona *et al.*[6]: alpha particles of a narrow beam are detected by a silicon detector after penetration through a gaseous target volume formed by pulse expansion of molecular nitrogen into an evacuated interaction chamber. The ions produced by each alpha particle within the target volume are guided to an ion detector where they are counted using time-of-flight techniques.

detector. The detector signal is used for data acquisition. Due to the movable platform, the nanodosimetric counter can be applied to investigate the formation of ionisation cluster size as a function of distance to the particle beam. It essentially consists of an electron collector and a single-electron counter. The electron collector is formed by a system of electrodes, which encloses an almost wall-less millimetric volume, representing the sensitive volume of the counter. The shape of this volume is that of a cylinder, the height of which is equal to its diameter (3.7 mm). The detection efficiency of the counter within its sensitive volume, however, is spatially dependent and was calculated by Monte Carlo simulation[8]. Its mean detection efficiency is ~25%. Electrons generated within the sensitive volume by ionising interactions are transferred into the single-electron counter, which consists of a long cylindrical drift column and an electron multiplier. This electron multiplier uses the measuring principle applied by convention in multi-step avalanche chambers. Electrons created inside the sensitive volume enter the drift column of the single-electron counter and arrive at the multi-step avalanche chamber at different time intervals. Here, each single electron generates an electronic avalanche which is used to produce a detectable signal. Since each signal, independent of its height, is considered to represent one electron, the fluctuation of the amplification (gas gain) is not important. Each electron cluster collected from the sensitive volume gives rise to a pulse trail which is used to count the number of ionisations in a cluster. In typical experiments with 5.4 MeV alpha particles, the diameter of the sensitive volume has a mass per area of ~2 μg cm^{-2} which corresponds to 20 nm at unit density.

THE DETERMINATION OF EQUIVALENT CLUSTER-SIZE DISTRIBUTIONS FOR LIQUID WATER

From the point of view of radiation damage to subcellular targets, the ionisation cluster-size distributions of interest should be as close as possible, at least, to those to be expected in cylindrical volumes

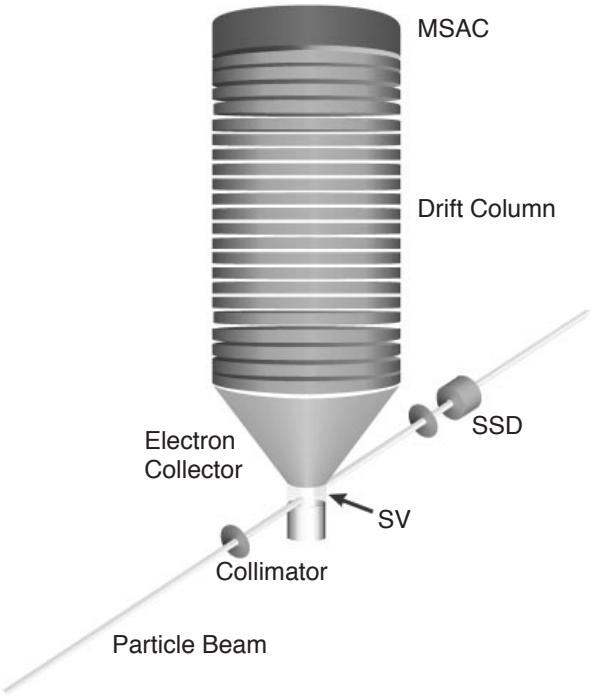

Figure 2. Schematic view of the track-nanodosimetric counter of De Nardo *et al.*[8]: alpha particles of a collimated narrow beam pass the sensitive volume (SV) and are detected by a solid-state detector (SSD). The low-energy secondary electrons produced by each alpha particle within the SV are collected to a single-electron counter, which consists of a drift column and a multi-step avalanche chamber (MSAC). Here, they are counted using time-of-flight techniques.

of liquid water comparable in size to a DNA segment. It seems, therefore, to be of doubtful value to measure cluster-size distributions in gases since it is well known that radiation interaction in gaseous systems well suited for proportional counter experiments is quite different from radiation interaction in liquid water. This argument is generally true as far as excitation processes are concerned, but it is not so serious from the point of view of ionisation cluster-size formation because the energy distribution of secondary electrons set in motion by impact ionisation does not strongly depend on the type of target molecules.

Based on the results of De Nardo *et al.*[9] in their analysis of general aspects of ionisation cluster-size formation, a scaling method was derived by Grosswendt[5], which allows a scaling of the sizes of gaseous volumes to those of a liquid water target and can be used for measuring cluster-size distributions in gases with mean cluster sizes almost equal to those of specified volumes of liquid water. The scaling procedure is founded on the constraint that, at least, the mean cluster sizes of the distributions in a measuring gas and in liquid water should be the same. This leads to the following condition:

$$(D\rho)^{(\mathrm{water})} = \eta \times (D\rho)^{(\mathrm{gas})} \times \frac{(\lambda\rho)_{\mathrm{ion}}^{(\mathrm{water})}}{(\lambda\rho)_{\mathrm{ion}}^{(\mathrm{gas})}} \times \frac{m_1(T,d)^{(\mathrm{gas})}}{m_1(T,d)^{(\mathrm{water})}} \approx \eta \times (D\rho)^{(\mathrm{gas})} \times \frac{(\lambda\rho)_{\mathrm{ion}}^{(\mathrm{water})}}{(\lambda\rho)_{\mathrm{ion}}^{(\mathrm{gas})}}. \quad (2)$$

Here, η is the detection efficiency in the gaseous measurement, $(D\rho)^{(\mathrm{water})}$ and $(D\rho)^{(\mathrm{gas})}$ represent the mass per area of the target diameter in liquid water or in a gas, $(\lambda\rho)_{\mathrm{ion}}^{(\mathrm{water})}(T)$ and $(\lambda\rho)_{\mathrm{ion}}^{(\mathrm{gas})}(T)$ are the mean-free ionisation path lengths of a particle at energy T, and $m_1(T,d)^{(\mathrm{gas})}$ or $m_1(T,d)^{(\mathrm{water})}$ are parameters characterising the transport of secondary electrons produced by a primary particle if the particle beam passes the target centre at a distance d. If it is assumed that the production of secondary electrons and the electron degradation are similar in both materials, the last factor in the middle part of Equation 2 can be set equal to one. As a result, the mass per area of each length in a gas must be scaled to the comparable length in liquid water by a multiplication with the product of the detection efficiency and the ratio of the mean ionisation path length in water to that in a gas. For further details, see Grosswendt[5].

MONTE CARLO MODEL OF CLUSTER-SIZE FORMATION

The Monte Carlo model applied for simulating the ionisation cluster-size formation in both measuring devices and in liquid water is based on the assumption that, for alpha particles at ~5 MeV, which penetrate through a material layer of mass per area of 2 μg cm^{-2} or less, the elastic scattering and charge-changing processes can be neglected. In consequence, the ionisation component of the structure of alpha particle track segments is exclusively founded on the particles' path lengths between successive ionisation events, on the spectral and angular distribution of secondary electrons set in motion on these occasions, and on the properties of secondary electron degradation. In contrast to alpha particles, the cluster-size formation by secondary electrons is simulated by taking into account elastic electron scattering, a series of different excitation processes, and impact ionisation. At each point of interaction, the electron's flight direction in the case of elastic scattering, or its energy loss and flight direction in the case of inelastic scattering, is determined, supplemented by the energies and flight

directions of potential secondary particles. As external electromagnetic fields are not taken into account, it is assumed that the electrons travel along straight lines which connect successive interaction points. In the case of elastic interaction, the polar angle of the electron's flight direction after scattering is determined relative to its initial direction; the azimuthal scattering angle is assumed to be uniformly distributed between 0 and 2π. On the occasion of excitation events, the initial electron energy is reduced by the appropriate excitation energy; assuming, however, that the electron direction remains unchanged. In the case of impact ionisation (only single ionisation is taken into account), a secondary electron is liberated which is treated in the same way as the initial electron. The history of each electron is simulated until it leaves the interaction volume, or until its energy has been degraded to a value smaller than the ionisation threshold of the stopping system. The analysis of ionisation clusters is performed after each ionisation event taking into account the detection efficiency of the measuring device. For a detailed description of the Monte Carlo models used in the present work for propane, nitrogen and liquid water see the publications by De Nardo *et al.*[9], by Grosswendt and Pszona[7] and by Grosswendt[10], respectively.

EXPERIMENTAL EQUIVALENT IONISATION CLUSTER-SIZE DISTRIBUTIONS

To give an impression of experimental equivalent cluster-size distributions based on the scaling method, Figures 3 and 4 show distributions $P_\nu(T)$ due to 4.6 MeV alpha particles crossing a cylindrical volume of molecular nitrogen on a radius at half its height, measured with the Jet Counter of Pszona *et al.*[6]. The data for a target cylinder with a diameter and height of mass per area $(D\rho)^{(\text{nitrogen})} = 0.22\ \mu\text{g cm}^{-2}$ for the case of a detection efficiency of 50% are presented in Figure 3, and those for a diameter and height of mass per area of $0.88\ \mu\text{g cm}^{-2}$ for the case of a detection efficiency of 40% are presented in Figure 4. In both figures, the measured data are compared, at first, with the results of Monte Carlo simulations of Grosswendt and Pszona[7] for nitrogen, showing a very satisfactory agreement of measured and calculated data. Due to this fact, it can be assumed that also the Monte Carlo results for nitrogen, which assume a 100% detection efficiency, are realistic estimates of cluster-size formation in nitrogen. Second, a comparison is made with the results of Monte Carlo calculations for cylindrical target volumes of liquid water the sizes of which are based on the scaling factor $\eta \times (\lambda\rho)_{\text{ion}}^{(\text{water})}(T)/(\lambda\rho)_{\text{ion}}^{(\text{nitrogen})}(T)$ of Equation 2. For this purpose, a factor of 0.693 was applied for alpha particles at 4.6 MeV in the case of a detection efficiency of

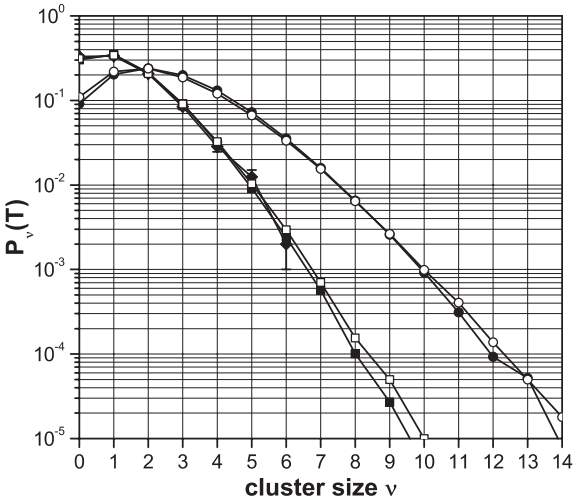

Figure 3. Comparison of ionisation cluster-size distributions $P_\nu(T)$ for alpha particles at $T = 4.6$ MeV, which penetrate a cylindrical volume of nitrogen or liquid water with a diameter and height of mass per area $(D\rho)^{(\text{nitrogen})}$ or $(D\rho)^{(\text{water})}$ on a radius at half its height (the measurements were performed with the Jet Counter of Pszona *et al.*[6] using molecular nitrogen): (closed diamonds) experimental results with $(D\rho)^{(\text{nitrogen})} = 0.22\ \mu\text{g cm}^{-2}$ and a detection efficiency of 50%, (solid lines with open squares) Monte Carlo simulation of the experimental data, (solid lines with open circles) Monte Carlo simulation in nitrogen at a detection efficiency of 100%, (solid lines with closed squares) Monte Carlo simulation for liquid water with a diameter of 0.76 nm calculated using Equation 2 with $\eta = 0.5$, (solid lines with closed circles) Monte Carlo simulation for liquid water with a diameter of 1.5 nm calculated using Equation 2 with $\eta = 1.0$.

100%, and scaling factors of 0.347 or 0.277 in the case of the real existing detection efficiencies of 50 or 40% [for the data, see Grosswendt[5]]. The comparison of the appropriate cluster-size distributions in liquid water with those for nitrogen at a detection efficiency of 100%, or with those at a detection efficiency of 50 or 40% is excellent. It can therefore be stated that, for 4.6 MeV alpha particles, a cylindrical target volume of nitrogen gas with a diameter and height of a mass per area of $0.22\ \mu\text{g cm}^{-2}$ is equivalent to a cylindrical target of liquid water with a diameter and height of 0.76 nm if a detection efficiency of 50% is used, and it is equivalent to a liquid water target with a diameter and height of $\sim$1.5 nm at a detection efficiency of 100%. Similarly, a gaseous cylinder of molecular nitrogen with a diameter and a height of mass per area of $0.88\ \mu\text{g cm}^{-2}$ at a detection efficiency of 40% is equivalent to a cylindrical volume of liquid water with a diameter and height of about 2.4 nm, and the same gaseous cylinder at a detection efficiency of 100% to a liquid water cylinder with a diameter and height of 6.1 nm.

In order to study equivalent cluster-size distributions $P_\nu(T; d)$ in case of a primary particle beam

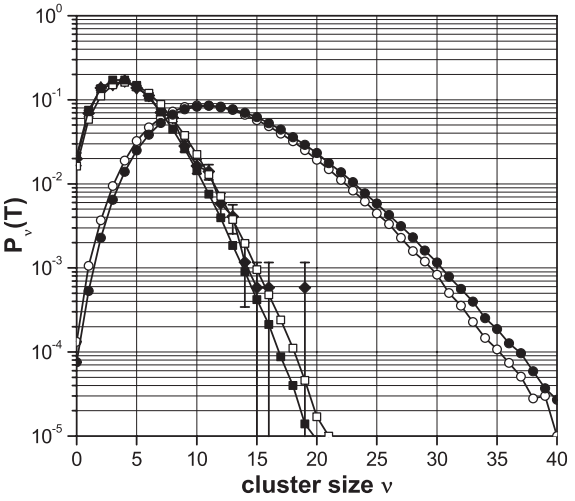

Figure 4. The same as Figure 3, but: (closed diamonds) experimental results with $(D\rho)^{(\text{nitrogen})} = 0.88$ μg cm^{-2} and a detection efficiency of 40%, (solid lines with open squares) Monte Carlo simulation of the experimental data, (solid lines with open circles) Monte Carlo simulation in nitrogen at a detection efficiency of 100%, (solid lines with closed squares) Monte Carlo simulation for liquid water with a diameter of 2.4 nm calculated using Equation 2 with $\eta = 0.4$, (solid lines with closed circles) Monte Carlo simulation for liquid water with a diameter of 6.1 nm calculated using Equation 2 with $\eta = 1.0$.

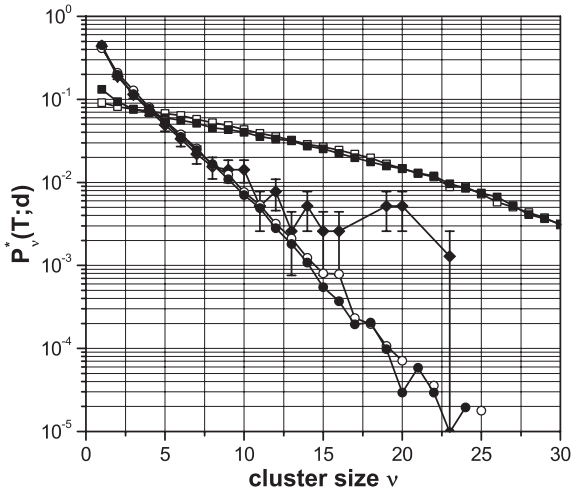

Figure 5. Comparison of conditional cluster-size distributions $P_\nu^*(T;d)$ with $\nu \geq 1$ for alpha particles at $T = 5.4$ MeV, which pass a cylindrical volume of propane or liquid water with a diameter and height of mass per area $(D\rho)^{(\text{propane})}$ or $(D\rho)^{(\text{water})}$ on a radius at half its height, at a distance from the target's main axis of mass per area $(d\rho)^{(\text{propane})}$ (the measurements were performed with the track-nanodosimetric counter of De Nardo *et al.*[8] using gaseous propane): (closed diamonds) experimental results with $(D\rho)^{(\text{propane})} = 2.04$ μg cm^{-2} at a distance of mass per area $(d\rho)^{(\text{propane})} = 2.09$ μg cm^{-2}, (solid lines with open circles) Monte Carlo simulation of the experimental data taking into account the spatially dependent detection efficiency, (solid lines with open squares) Monte Carlo simulation of the experiment assuming a constant detection efficiency of 100%, (solid lines with closed circles) Monte Carlo simulation for a volume of liquid water with a diameter and height of 6.3 nm at a distance of 6.5 nm calculated by applying the scaling method defined by Equation 2 with $\eta = 0.25$, (solid lines with closed squares) Monte Carlo simulation for a volume of liquid water with a diameter and height of 25.3 nm at a distance of 25.9 nm according to the scaling method defined by Equation 2 with $\eta = 1.0$.

which passes the target volume at a distance d greater than the target radius, measurements were performed with the track-nanodosimetric counter of De Nardo *et al.*[8] for alpha particles at an energy of 5.4 MeV. Such distributions represent the cluster-size formation by secondary electrons and can be characterised at best by the conditional distributions $P_\nu^*(T;d) = P_\nu(T;d)/[1 - P_0(T;d)]$ that, at least, a cluster size $\nu = 1$ is formed. To give an impression of such data, Figures 5 and 6 show conditional cluster-size distributions for a cylindrical target volume of propane with a diameter and height of mass per area $(D\rho)^{(\text{propane})} = 2.04$ μg cm^{-2}, caused by an alpha particle beam passing the target volume at a distance of mass per area $(d\rho)^{(\text{propane})}$ from its main axis, in the plane at half its height. The distribution at a distance of $(d\rho)^{(\text{propane})} = 2.09$ μg cm^{-2} is presented in Figure 5, and that at $(d\rho)^{(\text{propane})} = 3.76$ μg cm^{-2} in Figure 6. In addition to the experimental data, four curves are plotted in the figures, two of them showing the results of Monte Carlo simulations in propane which either take into account the spatially dependent detector efficiency or assume a constant detection efficiency of 100%; the other two representing the results of Monte Carlo simulations in liquid water if the scaling method of Equation 2 is applied to the sizes of the target volume and to the distance d. Based on the data of Grosswendt[5], the scaling factor $\eta \times (\lambda\rho)_{\text{ion}}^{(\text{water})}(T)/(\lambda\rho)_{\text{ion}}^{(\text{propane})}(T)$ was set equal to 1.24 in the case of a detection efficiency of 100%, and to 0.31 in the case of a constant mean detection efficiency of 25%, which was used to represent the spatially dependent efficiency applied in the measurements. As is obvious from both figures, the experimental data are in a rather satisfactory agreement with the Monte Carlo results in propane if the spatially dependent detection efficiency is taken into account. The deviations at greater cluster sizes are probably caused by the fact that the measured data could not be corrected for background contributions [for details, see DeNardo *et al.*[9]]. Because of the satisfactory agreement of measured and calculated data, it can be assumed that the results of the Monte Carlo simulation are also close to reality in the case of a constant detection efficiency of 100%. If one now compares the appropriate conditional cluster-size distributions in liquid water with those for propane at a detection efficiency of 100%, or with

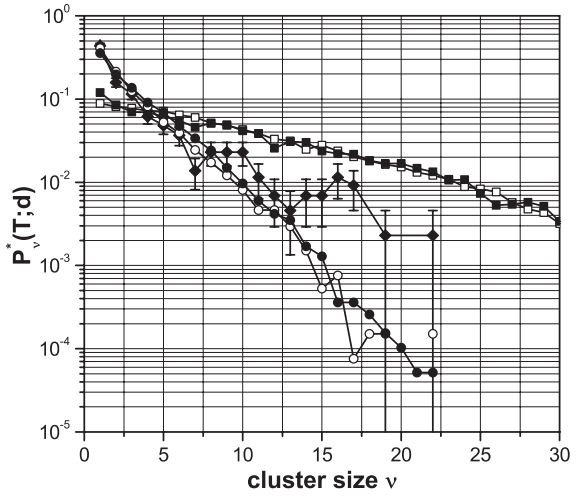

Figure 6. The same as Figure 5, but: (closed diamonds) experimental results with $(D\rho)^{(\text{propane})} = 2.04$ μg cm^{-2} at a distance of mass per area $(d\rho)^{(\text{propane})} = 3.76$ μg cm^{-2}, (solid lines with open circles) Monte Carlo simulation of the experimental data taking into account the spatially dependent detection efficiency, (solid lines with open squares) Monte Carlo simulation of the experiment assuming a constant detection efficiency of 100%, (solid lines with closed circles) Monte Carlo simulation for a volume of liquid water with a diameter and height of 6.3 nm at a distance of 11.7 nm calculated by applying the scaling method defined by Equation 2 with $\eta = 0.25$, (solid lines with closed squares) Monte Carlo simulation for a volume of liquid water with a diameter and height of 25.3 nm at a distance of 46.6 nm according to the scaling method defined by Equation 2 with $\eta = 1.0$.

those for the spatially dependent efficiency, the agreement of the distributions is obvious. As a result, it can be stated that the measured conditional distributions in propane with $(D\rho)^{(\text{propane})} = 2.04$ μg cm^{-2} at distances of $(d\rho)^{(\text{propane})} = 2.09$ or 3.76 μg cm^{-2} correspond to distributions to be expected in a water cylinder with a diameter and height of 6.3 nm, at a distance of 6.5 nm (in Figure 5) or of 11.7 nm (in Figure 6). Similarly, the conditional cluster-size distributions in case of a detection efficiency of 100% correspond to distributions for a liquid water cylinder with a diameter and height of 25.3 nm at a distance of 25.9 nm (in Figure 5) or of 46.6 nm (in Figure 6). It should be noted that the dependence of the conditional cluster-size distributions on distance is almost negligible (see Figures 5 and 6).

CONCLUSIONS

Based on a scaling method derived from general aspects of ionisation cluster-size formation, measured cluster-size distributions caused by 4.6 and 5.4 MeV alpha particles in millimetric volumes of nitrogen or propane at low gas pressure were compared with ionisation cluster-size distributions to be expected in volumes of liquid water with sizes of the order of a few nanometres. As a result of this comparison, it can be stated that the application of the scaling procedure leads to cluster-size distributions in a gaseous system, which are quite similar to those to be expected in nanometric volumes of liquid water, at least, for alpha particles at energies of ~5 MeV. In consequence, measurements in gases could be used in future to determine equivalent ionisation cluster-size distributions for nanometric volumes of liquid water, as a substitute to subcellular structures.

ACKNOWLEDGEMENTS

This work was supported by the European Community within the Access to Research Infrastructure action of the Human Potential Programme under contract No. HPRI-1999-CT-00083.

REFERENCES

1. Nikjoo, H., O'Neill, P., Terrissol, M. and Goodhead, D. T. *Quantitative modelling of DNA damage using Monte Carlo track structure method*. Radiat. Environ. Biophys. **38**, 31–38 (1999).
2. Friedland, W., Jacob, P., Paretzke, H. G. and Stork, T. *Monte Carlo simulation of the production of short DNA fragments by low-linear energy transfer radiation using higher-order DNA models*. Radiat. Res. **150**, 170–182 (1998).
3. Goodhead, D. T. *Initial events in the cellular effects of ionising radiations: clustered damage in DNA*. Int. J. Radiat. Biol. **65**(1), 7–17 (1994).
4. Brenner, D. J. and Ward, J. F. *Constraints on energy deposition and target size of multiply damaged sites associated with DNA double-strand breaks*. Int. J. Radiat. Biol. **61**(6), 737–748 (1992).
5. Grosswendt, B. *Recent advances in nanodosimetry*. Radiat. Prot. Dosim. (this issue), xxx–xxx (2004).
6. Pszona, S., Kula, J. and Marjanska, S. *A new method for measuring ion clusters produced by charged particles in nanometre track sections of DNA size*. Nucl. Instrum. Meth. Phys. Res. A **447**, 601–607 (2000).
7. Grosswendt, B. and Pszona, S. *The track structure of alpha-particles from the point of view of ionization-cluster formation in 'nanometric' volumes of nitrogen*. Radiat. Environ. Biophys. **41**, 91–102 (2002).
8. De Nardo, L., Alkaa, A., Khamphan, C., Conte, V., Colautti, P., Ségur, P. and Tornielli, G. *A detector for track-nanodosimetry*. Nucl. Instrum. Meth. Phys. Res. A **484**, 312–326 (2002).
9. De Nardo, L., Colautti, P., Conte, V., Baek, W. Y., Grosswendt, B. and Tornielli, G. *Ionization-cluster distributions of alpha-particles in nanometric volumes of propane: measurement and calculation*. Radiat. Environ. Biophys. **41**, 235–256 (2002).
10. Grosswendt, B. *Formation of ionization clusters in nanometric structures of propane-based tissue-equivalent gas or liquid water by electrons and alpha-particles*. Radiat. Environ. Biophys. **41**, 103–112 (2002).