Evidence of Fraud in the Department of Radiology, at the New Jersey Medical School

US District Court, District of New Jersey, Case # 03-4837

Plaintiffs: United States of America Ex Rel. Dr. Helene Z. Hill

Defendants: University of Medicine and Dentistry of New Jersey, Dr. Roger W. Howell and Dr. Anupam Bishayee

Expert Report prepared by Michael E. Robbins, PhD on behalf of Dr. Helene Z. Hill

Here is a summary of the basis for allegations of fraud:

1. Dr Anupam Bishayee, a post-doctoral fellow in the laboratory of Dr. Roger Howell, Division of Radiation Research, and Department of Radiology, New Jersey Medical School, was noted to have fabricated experiments on two occasions, one in 1999, observed by Dr. Hill, the other in 2001 observed by Dr. Hill and Dr. Lenarczyk, also a post-doctoral fellow in Dr Howell's laboratory.

2. Experiments that were reported in two publications and used as preliminary data in a funded grant application have not and indeed cannot be replicated.

3. Observations recorded by Dr. Bishayee in the course of performing published experiments using a cell counting instrument (Coulter Counter) appear statistically impossible to have been generated experimentally – there is a probability of greater than 50 billion to one that they are fabricated.

4. Results presented in the same publications and used as preliminary evidence in the funded grant application are scientifically impossible based on the conditions prevailing in Dr. Bishayee's experiments.

5. The strong likelihood that the tubes that were used in Dr. Bishayee's experiments produced hypoxic (low concentration of oxygen) conditions that would have prevented the results presented from occurring.

Outline of the Experiments in Question

The experiments, collectively called either 100% experiments, or 50% experiments, follow one of two similar protocols. In the 100% experiments, V79 hamster lung fibroblasts, a cell line that has been used extensively in radiation biology studies for over 40 years, are placed in tubes and incubated overnight with varying amounts of tritiated thymidine (^{3}H-TdR). During this time the cells that are synthesizing DNA in a portion of the cell cycle called the S-phase (synthesis phase), will take up the ^{3}H-TdR and incorporate this into their DNA. Cells that are in other phases of the cell cycle (G_1, G_2 and M) will not take up the ^{3}H-TdR. The following morning, the cells are washed with medium to remove any of the ^{3}H-TdR that has not been taken up by cells and then placed in narrow 400 μL tubes (called Helena tubes) and then gently centrifuged (spun down) to form "clusters" of cells. The Helena tubes are then incubated for 3 days at ~ 10^{o}C to allow the ^{3}H to decay without any cell replication taking place. Those cells that have incorporated ^{3}H-TdR into their DNA will be irradiated. The type of radiation produced by the ^{3}H-TdR, called beta (β) radiation, will only travel a short distance, and will therefore only kill cells that contain the ^{3}H-TdR. The cells are then placed in new larger tubes, washed, and counted

for both cell number (performed in a machine called a Coulter Counter) and radioactivity, diluted, and then placed in tissue culture dishes containing growth medium. The cells are diluted such that each plate will contain between 50-250 colonies. Once plated, each cell will divide several times forming a colony of cells that can be counted about 1 week later. The number of colonies present is used to determine the surviving fraction of cells following treatment with ^{3}H-TdR. This is determined by dividing the average number of colonies in the dishes containing cells exposed to ^{3}H-TdR by the average number of colonies in control dishes that were not exposed to ^{3}H-TdR.

In the 50% experiments, half of the tubes are incubated overnight without the radioactive ^{3}H-TdR; these will be the bystander cells, described in more detail later. These cells are subsequently mixed with an equal number of cells treated with ^{3}H-TdR overnight prior to the 3 day incubation. The rest of the experiment is performed as described above for the 100% experiment.

Experimental Results

The results of the experiments in question were reported in a successful grant application submitted by Dr. Howell to the NIH as well as in two published papers; Bishayee et al, Radiat Res 152:88-97, 1999; Bishayee et al, Radiat Res 155:335-344, 2001. These 100% experiments showed that the cells were extremely sensitive to irradiation. There was an exponential decline in cell survival (seen as a decrease in surviving fraction on a log (surviving fraction)-linear (dose of radiation) plot) down to around 3 logs, or in other words, a surviving fraction of around 0.001 or 0.1% (99.9% of the cells had been killed; see ***Figure 1***). These results are impossible to generate due to the following three reasons:

1. ^{3}H-TdR blocks the movement of cells through the various phases of the cell cycle. Thus, cells that are not in the S phase of the cell cycle during the overnight incubation with ^{3}H-TdR cannot enter S phase, will not incorporate ^{3}H-TdR into their DNA, and will not be killed by the subsequent radioactive decay of the ^{3}H.
2. No deoxycytidine (dCyd) was present in the medium at the time the cells were exposed to ^{3}H-TdR. Previous studies have shown that the inclusion of dCyd in the medium prevents the ^{3}H-TdR from blocking cell movement through the cell cycle leading to an exponential decrease in cell survival.
3. No attempt was made to synchronize the cells into the same phase of the cell cycle prior to their treatment with ^{3}H-TdR. If all the cells were in the same phase of the cell cycle then there is a possibility that they would all have been in the S phase of the cell cycle at the time the ^{3}H-TdR was added. However, as will be discussed below, special experimental procedures are required to ensure that the cells are synchronized, and these were not used in the experiments performed by Bishayee.

It should be noted that additional 100% experiments performed by Drs. Lenaryczyk and Howell failed to confirm the data generated by Dr. Bishayee. In these studies no dCyd was added to the medium, nor were the cells synchronized prior to addition of the ^{3}H-TdR. In marked contrast to the surviving fraction of 0.001 reported by Bishayee et al, these latter studies noted a surviving fraction of 0.3 (30%, or in other words 70% of the cells were killed) or less, a value 300 times greater than reported in the experiments performed by Bishayee, and a value entirely consistent with the experimental conditions used and published in the literature.

For the 50% experiments, Bishayee et al reported that the surviving fraction of the cells declined exponentially down to a value of 0.01. Subsequent attempts by Drs. Lenarczyk and Howell to reproduce these findings were singularly unsuccessful. These investigators were unable to demonstrate any bystander effect, although one would have expected to see such a response.

The likely explanation for the absence of any bystander effect in these cells is the presence of hypoxia in the Helena tubes.

The radiobiological bases for these arguments in support of the allegations of fraud are discussed below.

Effect of ^{3}H-TdR on the Cell Cycle: Tritium is a radioactive form of hydrogen. When tritium decays, it releases low-energy β radiation in the form of an electron that will break the DNA present in the cell nucleus resulting in cell death or mutations that can lead to cancer.

Deoxyribonucleic acid (DNA) is a nucleic acid that contains the genetic instuctions used in the development and function of all living organisms. DNA can be compared to a set of blueprints or a code, since it contains the instructions needed to construct other components of cells, such as proteins. The DNA segments that carry this genetic information are called genes. Chemically, DNA consists of two long polymers of simple units called nucleotides, with backbones made of sugars and phosphate groups joined by ester bonds. These two strands run in opposite directions to each other and are therefore anti-parallel. Attached to each sugar is one of four types of molecules called bases. Two of these bases are called purines (adenine (A) and guanine (G)) and two are called pyrimidines (cytosine (C) and thymidine (T)). These bases are incorporated into DNA in the form of triphosphates, namely dATP, dTTP, dGTP, and dCTP.

^{3}H-TdR causes an imbalance in the precursors by increasing dGTP and decreasing dCTP, so that DNA synthesis stops. Adding deoxycytidine (dCyd) to the medium that contains dThd prevents dThd from decreasing dCTP and restores the precursor balance so that DNA synthesis can proceed. In order to get into DNA ^{3}H-TdR needs to be converted to ^{3}H-dTTP. There are enzymes in the cell that can make this conversion.

Thymidine (TdR) blocks the cell cycle at the beginning of the DNA synthesis phase (G_1/S interface): In the presence of TdR those cells that are in the S phase stop making DNA (as described above) and the cells that are in the other phases of the cell cycle move round to the point of entry into S but then stop. If the TdR is ^{3}H-TdR, it will be incorporated into the DNA that is made during the S phase and be converted to ^{3}H-dTTP. It will then irradiate the DNA causing lethal damage; it will also block cells in other phases of the cell cycle from entering S phase. (Mortensen et al 1986; Bjursell & Reichard 1973; Tobey et al 1966; Galvazi et al 1966). Upon removal of the thymidine block, progress through the cell cycle resumes. Indeed, Tdr has been used as an S-phase blocking agent in V79 cells (Sinclair, 1986; Hagan et al 1984), the same cells used in the studies by Dr. Bishayee. It should be noted that this TdR-mediated block can be released by the addition of dCyd to the medium (Morris & Fischer, 1960; Bjursell & Reichard, 1973; Fox et al, 1980; Wheater & Roberts, 1987, Hiramoto et al 1990).

^{3}H-TdR can modulate the cell cycle: Addition of ^{3}H-TdR to the medium has been shown to cause significant biological changes, including mutations, chromosome aberrations, cell death, and growth retardation (Wimber 1964; Setlow & Setlow (1972). Incubating cells with as little as 1 μCi/mL ^{3}H-TdR can lead to changes in progression through the cell cycle, specifically a delay in their progression through the S and G_2 + M phases and decreased proliferation (Pollack et al 1979; Beck, 1981, 1982; Hoy et al 1990; Yanokura et al 2000). A similar ^{3}H-TdR-mediated perturbation of the cell cycle has also been observed in V79 cells (Ehmann et al 1975; Iuzhakov & Lychev 1985).

Addition of dCyd to the medium prevents the cell cycle block effect of ^{3}H-TdR: As noted previously, the G_1/S phase cell cycle block observed when cells are incubated with TdR can be prevented by the addition of dCyd to the medium (Morris & Fischer, 1960; Bjursell & Reichard, 1973; Fox et al, 1980; Wheater & Roberts, 1987, Hiramoto et al 1990).

Synchronization of the cell cycle: Many different techniques have been developed to synchronize cells at specific phases of the cell cycle (Davis et al, 2001). Some of these require special equipment or specialized techniques that were not called for in the protocols used. The only technique that might conceivably have been used was that of "contact inhibition (Dietrich et al, 1997). However, previous studies (Chapman et al, 1970) have observed that this methodology is only "an approximate synchronization method," and fails to yield pure populations of cells in any phase of the cell cycle. These findings were confirmed by later studies, in which it was shown that V79 cells in plateau phase, commonly though to reflect a non-mitotic population, in fact exhibited considerable turnover, with at least 50% of the cells cycling (Stevenson and Lange, 1989; Stevenson et al, 1989). Indeed, Nelson et al (1984) reported that it was necessary to hold CHO-K1 cells for 18 days under conditions of nutrient deprivation to obtain about 98% of the cells in the G_1 phase. If these conditions were achieved then one would predict that irradiating these cells would lead to a surviving fraction of 0.02, a value that is 10 times higher than the lowest surviving fraction value obtained by Bishayee on his survival curves.

To illustrate this point, let us examine documents ***B00894-00913*** which describe flow cytometric analysis of the cell cycle for V79 cells performed by Dr. Bashayee, 11/24/2000. Cells sent for FACS analysis were either ~ 50% confluent (L) or 90-95% confluent (H). The standard protocol used in the Howell lab was as follows: cells were plated and cultured for 24 h (L) or 3 days (H) before harvest, at which time they were sent for FACS analysis. The results after harvest show that for the L cells, 38% were in S phase at the time rolling of the cells started and for the H cells, 20% were in S. In the 100% and 50% labeling experiments, ^{3}H-TdR would be added after 3 h. At that time, the trailing edge of the cells in S would be in G_2 and about 30% of cells would have entered S (3 h represents about 30% of the total cell cycle time for V79 cells). Adding the ^{3}H-TdR would lead to killing all the cells present in the S phase, but the ^{3}H-TdR block on cell cycle progression would prevent any additional cells entering the S phase. There is no way that 99.9% of the cells could enter S phase during the 12 h of rolling. Only those cells that enter S would be killed during the course of the experiment, and thus one would expect that survival would decline to a value of about 50%. Indeed, this is the value obtained by Drs. Lenarczyk and Howell in their experiments.

Lack of dCyd in the medium: A point that cannot be overemphasized is that there is no evidence that dCyd was added to the medium in any of the protocols used in the Howell lab. As discussed previously, the only way to prevent the effects of ^{3}H-TdR on blocking cell cycle progression is to add dCyd to the medium. Since this was not added, all of the deleterious effects of ^{3}H-TdR on the cell cycle did occur in the experiments carried out by Drs. Bishayee, Lenarczyk and Howell.

<u>Protocols used by Dr. Bishayee and Howell</u>

The failure of Dr. Howell to duplicate the results generated and published by Dr. Bishayee could reflect differences in the experimental protocols used. This clearly is not the case. Howell (***experiment #5 B007433 ff, 7/16/2001***) has the same protocol with minor variations as that

used by Bishayee (***experiment #2, B012735 ff, 11/30/1998***) in 100% cluster experiments except for the range of the ^{3}H-TdR concentrations used. The uptakes are comparable. However, the experiment performed by Bishayee claims an exponential decrease in surviving fraction, to a value less than 0.5%. In contrast, the data generated by Dr. Howell shows, as predicted, a biphasic decrease in surviving fraction, with a minimal value of some 50%, a level of survival 100 times greater than Bishayee's (see ***Figure 2***).

This marked discrepancy between the data generated by Bishayee and Howell is evident for the 50% experiments as well. Howell ***experiment #3 (B007397 ff, 5/30/2001)*** has the same protocol as Bishayee experiment #1 (***B008243 ff, 12/29/1998***) except for the range of ^{3}H-TdR concentrations used. The uptakes are different, but at 10 mBq/cell, Bishayee's survival has fallen to 0.009 (0.9), while Howell's has fallen to 0.6 (60%), a level of survival 67 times greater than Bishayee's (see ***Figure 3***).

These findings indicate that the protocols used by Bishayee and Howell were the same, and thus the pronounced differences in the level of cell kill observed between the two investigators cannot reflect differences in experimental procedures.

<u>Comparison of the experiments performed by Drs. Lenarczyk and Howell</u>

The 100% experiments performed by Drs. Lenarcyzk and Howell completely failed to duplicate the results published by Bishayee et al (Radiat Res 152:88-97, 1999; Radiat Res 155:335-344, 2001). To illustrate this, we will look at 4 experiments using the V79 cells performed by Lenarczyk; ***B019439 ff, 10/2/2000; B019456 ff, 5/3/2001; B019628 ff, 5/21/2001; and B019611, 6/21/2001***. In each of these, the surviving fraction shows a biphasic decline with increasing dose that plateaus at a value of about 0.6, or 60% (***Figure 4 left upper panel***).

Two experiments performed by Dr. Howell, namely experiment #5, ***B007433 ff, 7/16/2001*** and experiment #6, ***B07463, 9/27/2001***, also give a biphasic decline in surviving fraction, with a plateau value of approximately 0.3 or 30% (***Figure 5 left pane***l). Finally, an experiment performed by both Dr. Lenarczyk and Howell, ***B019476 ff, 12/14/200***, also demonstrated a biphasic response, with a minimal value of about 0.2, or 20% (***Figure 4 left upper panel***). Averaging the data from these 7 experiments indicates the following:

- Survival decreases in a biphasic manner with increasing dose
- The average break point in these survival curves is 0.50 (50%) at greater than 0.3 mBq/cell.

In three additional 100% experiments (***B019537 ff, 11/10/200; B019980, 11/28/2000; and Len exhibit 21, 2/19/2001***) performed by Lenarczyk using a different Chinese hamster cell line, CHOK1-A_1, a biphasic decrease in survival is again clearly evident (***Figure 4 left lower panel***). The average break point with this cell line is 0.29, or 29%.

- Thus, in ten 100% experiments performed by Drs. Lenarczyk and Howell, the survival curves seen when cells were treated with ^{3}H-TdR gave the expected biphasic response, reflecting the lack of synchrony and the lack of dCyd present in the medium to prevent the ^{3}H-TdR-mediated cell cycle block.

- These results are completely at odds with those generated by Bishayee et al, who reported an exponential decline in cell survival down to levels less than 0.1%. Based on the radiobiological principles outlined above, it seems clear that the data generated by Bishayee from his 100% experiments could not have been generated without falsification of the data.

The 50% experiments performed by Drs. Lenarcyzk and Howell similarly completely failed to duplicate the results published by Bishayee et al (Radiat Res 152:88-97, 1999; Radiat Res 155:335-344, 2001). To illustrate this point we will look at experiments using V79 cells performed by Dr. Lenarczyk; ***Len exhibit #25, 12/26/2001; Len exhibit # 26, 1/15/2001; Len exhibit #27, 2/5/2001; and Len exhibit #28, 6/14/2001*** (***Figure 4, upper right panel)***. These data show a biphasic response with a break at a surviving fraction of approximately 0.7 or 70%. An additional experiment, performed by both Dr. Lenarczyk and Bishayee (***Len exhibit #29, 7/5/2001***) gave essentially identical results.

Three experiments performed by Dr. Howell, namely e***xperiment #2, B007382 ff, 4/19/2001, experiment #3, B007396, 5/3/2001, and experiment #4, B007419 ff, 6/28/2001*** also give a biphasic decline in surviving fraction, with a plateau value of approximately 0.7 or 70% (***Figure 5 right panel***). Combining the data from these 8 experiments indicates the following:

- Survival decreases in a biphasic manner with increasing dose

- The average break point in these survival curves is 0.70 (70%)

In three additional 50% experiments (***B019500 ff, 11/20/200; B019979, 11/28/2000; and B019670 ff, 2/15/2001***) performed by Lenarczyk using a different Chinese hamster cell line, CHOK1-A_1, a biphasic decrease in survival is again clearly evident (***Figure 4 right lower panel***). The average break point with this cell line is 0.7, or 70%.

Thus, in ten 50% experiments performed by Drs. Lenarczyk and Howell, the survival curves seen when cells were treated with ^{3}H-TdR gave a biphasic response, with a level of cell kill similar to that seen in the 100% experiments. It is important to recollect the design and purpose of these 50% experiments.

In the 50% experiments, half of the tubes are incubated overnight without the radioactive ^{3}H-TdR; these will are known as the bystander cells. These cells are subsequently mixed with an equal number of cells treated with ^{3}H-TdR overnight prior to the 3 day incubation. The rest of the experiment is performed as described above for the 100% experiment. The expected survival of the 100% labeled cells is approximately 50%. These will make up 25% of the survivors in the 50:50 clusters present in the 50% experiments. If we consider the bystander cells, if all survive then 75% of the cells in the clusters will be survivors. In contrast, if none survive, then 25% of the cells in the clusters will be survivors. Thus, the predicted bystander effect should be evident between 25% survival and 75% survival.

- In the 50% experiments carried out by Lenarczyk and Howell, survival appeared to be in the order of 70%, indicating little or no bystander effect. These results are completely at odds with those generated by Bishayee et al, who reported an exponential decline in cell

survival down to a survival of 0.01, or 1%. Based on the radiobiological principles outlined above, it seems clear that the data generated by Bishayee from his 50% experiments could not have been generated without falsification of the data.

Helena tubes and radiobiological hypoxia:

Why did Lenarczyk and Howell fail to observe a bystander effect? It should be noted that experiments recently published by Persaud et al (2005) do indicate a bystander effect, with survival of the bystander cells appearing to be around 40% (***Figure 6***). What is the difference between these studies? There is a major difference in the protocols used by the two groups. Persaud et al used microfuges tubes with 100 μL of air present above the cells. In contrast, Lenarczyk and Howell used Helena tubes in which no air was present above the cells. In this situation the cells would have been hypoxic, a condition in which they are much more resistant to the killing effects of radiation. Data in support of this conclusion are shown in Figure 6. This shows data from studies performed in the Howell lab as well as data published in the literature. In ***experiment #1, B007921***, performed by Bishayee 9/7/98, a colony forming assay was obtained using V79 cells cultured in Falcon tubes, in which the cells were aerobic and therefore radiosensitive. The cell survival curve shown in ***Figure 7*** indicates a marked decline in surviving fraction, as expected. These data are in agreement with survival data for V79 cells obtained from the literature (Cox et al, 1977; Goodhead & Thacker, 1977; Han & Elkind, 1977; Hill et al, 1988; Millar et al, 1978; Raaphorst & Kruuv, 1976; Radford & Hodgson, 1987) and shown as a star on the graph. These data show the average dose at which a surviving fraction of 0.1, or 10%, was observed. The remaining plots are from cell survival assays performed by Drs. Bishayee (***B07927/B07910-B007911, B07984***), Lenarczyk (***B019656***) and Bogdan (***B002754-B002760***) using Helena tubes and irradiating the cells as clusters or in suspension. In all of these experiments, the survival curves are much shallower, reflecting radioresistant cells due to their being hypoxic. Thus, given the experimental protocol used in the Howell lab, the cells were hypoxic when cultured in the Helena tubes, and thus would be radioresistant. Thus, the lack of a bystander effect observed by both Lenarczyk and Howell is a result of the cells being hypoxic.

Bishayee's conditions and protocols were the same as those used by Lenarczyk and Howell and thus the cells would have been hypoxic. The marked radiosensitivity of the cells on the 50% experiments indicates that his results could not have been generated without falsification of the data.

Response to Document #B018319: Summary of Experiments

As outlined above, attempts to reproduce the data generated by Dr. Bishayee and published in Bishayee et al, Radiat Res 152:88-97, 1999; Bishayee et al, Radiat Res 155:335-344, 2001, as well as in NIH applications, failed completely. These failures reflect the experimental conditions present::

1. ^{3}H-TdR-mediated cell cycle block;
2. Lack of dCyd in the medium at the time the cells were exposed to ^{3}H-TdR. Previous studies have shown that the inclusion of dCyd in the medium prevents the ^{3}H-TdR from blocking cell movement through the cell cycle leading to an exponential decrease in cell survival.
3. Lack of any attempt to synchronize the cell into the same phase of the cell cycle prior to their treatment with ^{3}H-TdR.

4. Presence of hypoxia in the Helena tubes used for the 50% labeling studies prevented the anticipated bystander effect

In response to this failure, Dr. Howell presented document # ***B018319***, Summary of Experiments, in which he proposed a number of possible factors that might explain the differences in the data generated. However, as discussed below, these fail to provide any evidence that might explain the marked differences in the experimental data generated by Bishayee compared with that of Lenarczyk and Howell.

- Variable source of microfuges tubes: It seems highly unlikely that "contamination" of the microtubes used with trace elements would explain the failure to replicate Bishayee's findings. No experiments were performed by Howell to substantiate this "claim."

- pH of media: This is not a valid concern. If the pH changed during the course of the experiment then it would be noted by the color of the phenol red in the medium; any acidification due to contamination would lead to stopping the experiment.

- Level of trace elements in the water: Without any evidence to indicate that this either occurred or would have any significant impact on the data generated, this response provides no explanation.

- Wetting agents on filter apparatus: Without any evidence to indicate that this either occurred or would have any significant impact on the data generated, this response provides no explanation.

- Methods used to clean bottles: It is not clear how this might impact the studies or serve as a potential explanation for the inability to duplicate Bishayee's data.

- Sodium bicarbonate product changed: As long as the final concentration of chemical used was the same, there would be absolutely no difference in the experimental conditions.

- Different incubator: Laboratories change incubators on a regular basis as the equipment ages or breaks down. As long as the gas concentrations and temperature are maintained, and the incubator is kept clean, then no difference would be seen in the cells being cultured.

- Fetal calf serum: Without any evidence to indicate that different sources of media used in the Howell lab led to differences in cell survival ranging from 0.1% to 70%, this point is invalid.

- Different V79 cells used: A review of the literature reporting cell survival for V79 cells after irradiation indicates very little difference in the radiation response of these cells over several decades and being cultured in numerous laboratories in Europe and the United States (Cox et al 1977; Goodhead and Thacker 1977; Han and Elkind 1977; Hill et al 1988; Millar et al 1978; Raaphorst and Kruuv 1976; Radford and Hodgson 1987). There are no data showing the 100-fold difference in survival of V79 cells following irradiation noted between Bishayee and Lenarczyk and Howell.

In summary, none of these variables explain the inability of Lenarczyk and Howell to replicate Bishayee's findings. As discussed above, the data generated by Lenarczyk and Howell are exactly what would be expected based on the experimental protocols used and the radiobiological principles discussed. The inabilities to reproduce Bishayee's findings reflect the fact that these data were generated falsely.

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Statement of Qualifications

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Dr. Robbins obtained a BSc (Hons.) degree in Applied Biology in 1976 and a PhD in Renal Physiology in 1980 at Thames Polytechnic, London, UK. He then joined the Cancer Research Campaign (CRC) Normal Tissue Radiobiology Group, Churchill Hospital, and University of Oxford, Oxford, UK as a Research Officer. In 1987, he was promoted to Deputy Director, a position he maintained until moving to the US in 1993 as Associate Professor and Director of Research in the Radiation Research Laboratory, Department of Radiology, at the University of Iowa. He was promoted to Full Professor in 2000, and moved in September 2001 to take up his current appointment as Professor and Head, Section on Radiation Biology, Department of Radiation Oncology at Wake Forest University School of Medicine (WFUSM). He is recognized internationally as an expert in radiation-induced late normal tissue morbidity, with particular emphasis on the pathogenesis of radiation injury in the kidney and brain as well as the role of oxidative stress in radiation-induced late effects. Since moving to WFUSM, he has created a multidisciplinary research group focused on understanding how radiation damages the normal brain, and the application of interventional therapies aimed at preventing this devastating late effect of anticancer therapy. He is an Overseas Editor for the British Journal of Radiology, a member of the Editorial Board of the International Journal of Radiation Biology, and Associate Editor for Radiation Research and PPAR Research.

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Other cases in which I have testified as an expert at trial or by deposition

None

Compensation to be paid for the study and testimony in this case

Compensation is to be paid at the rate of $450 per hour.

Time spent to date on the case is 35.25 h = $14,100

Figure 1 from Bishayee et al Radiat Res, 152:88-97, 1999

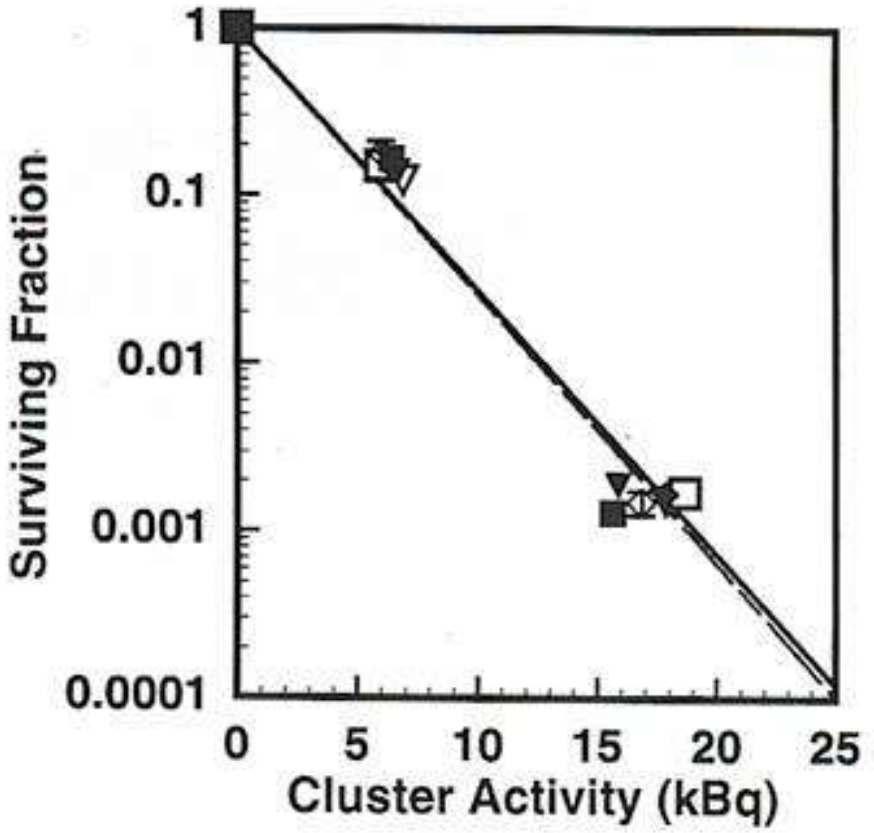

FIG. 7. Survival of V79 cells as a function of cluster activity of [^{3}H]dThd when 100% of the cells were labeled. Multicellular clusters were maintained at 10.5°C for 72 h in the presence of (1) [^{3}H]dThd (▼, ▽); (2) [^{3}H]dThd + 0.58% DMSO (■, □); (3) [^{3}H]dThd + 0.58% DMSO + 100 μ*M* lindane (◆, ◇). Data from two independent experiments are plotted for each treatment condition and are differentiated as open and closed symbols. Representative standard deviations are indicated by the error bars. The short-dashed, long-short dashed, and solid curves represent least-squares fits of the data to Eq. (1) for cases 1, 2 and 3 respectively.