

WEB-RAD-TRAIN

Web-Based Educational Program for Diagnostic and Interventional Radiologists: Radiobiology, Radiation Protection, and Risks vs. Benefits

<http://www.web-rad-train.org>

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The WEB-RAD-TRAIN is a web-based training course in radiation biology, radiation protection, and risk/benefit analysis, conceived and targeted primarily for radiologists, specifically radiologists in training who elect to study the biological foundations of radiology. This web-based teaching site is starting its second year in operation and currently presents eight topics. Within each topic there is a review of the pertinent material and links to books, articles, and other web sites for more in-depth coverage of the background information.

The centerpiece of this web-based training course is a series of review questions. Each topic contains five questions, typically framed in terms of an incident or situation in a radiology department. Once the student selects an answer, correct or incorrect, an explanation popup window appears to review the information needed or missed, succinctly, so that the correct answer is justified and the incorrect answers are eliminated.

Ultimately the WEB-RAD-TRAIN will present twelve topics, covering all aspects of radiation biology. The twelve Review Topics in the order in which they will be presented are:

- I. Interactions of Radiation with Matter
- II. DNA Damage / Chromosomal Aberrations / Cellular Response
- III. Tissue Response to Radiation, Including Local Injury (Direct Effects)

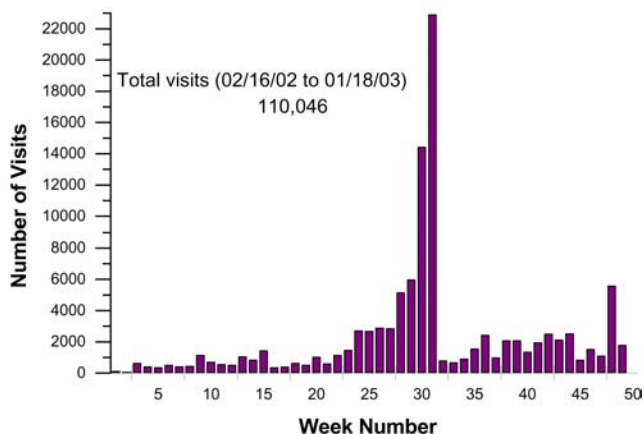



Fig. 1. The weekly number of files accessed on the WEB-RAD-TRAIN since its inception. Usage peaked just before the Board exams. (Courtesy of Richard Miller of the Radiological Society of North America).

- IV. Factors Affecting Radiation Response
- V. Whole-Body Radiation Effects
- VI. Effects on the Developing Embryo and Fetus
- VII. Hereditary Effects & Fertility
- VIII. Radiation Carcinogenesis
- IX. Radiation Cataractogenesis
- X. Radiation Exposure to the Human Population
- XI. Patient/Personnel Exposure; Risk-Benefit in Radiology
- XII. Radiation Protection

An important aspect of the WEB-RAD-TRAIN is the acquisition of feedback from users. To achieve this, after a user has accessed the material for the first of the twelve topics, in order to access the remaining eleven topics, he/she is required to register and fill out a survey regarding the web site's structure and utility. We have documented the number of individuals who have thus far visited the site as a function of age, occupation, and education (M.D., Ph.D., etc.). In addition we have monitored the weekly number of visits to the site (Fig. 1). To date there have been over 100,000 visits to the WEB-RAD-TRAIN. Ride the WEB-RAD-TRAIN by visiting our web site: <http://www.web-rad-train.org> 

Screening Mammography: How Important is the Radiation-Risk Side of the Benefit-Risk Equation?

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There has been much recent debate about the benefits of routine screening mammography. However there has been rather less discussion regarding possible radiation-related risks associated with these examinations, specifically the risk of radiation-induced breast cancer, although some risk-benefit analyses have been reported.

Glandular examination doses for screening mammography are small, typically around 3 mGy of 26-30 kVp low-energy x-rays. A particular issue here, however, is that these very low-energy x-rays are expected to be more hazardous, per unit dose, than higher-energy x or gamma rays (i.e., those on which radiation risk estimates are based, such as from the Japanese A-bombs). The underlying biophysical reason for the expected increase in biological effectiveness for these lower-energy x-rays is that they set in motion slower secondary electrons, with correspondingly higher LET.

An increase in the relative biological effectiveness (RBE) of low-energy vs. high-energy photons is of relevance in assessing the risk side of the benefit-risk equation for mammography, in that the radiation-related risks are calculated based on studies of populations (A-bomb survivors and women who received multiple fluoroscopies) exposed to higher-energy photons.

We have measured *in-vitro* oncogenic transformation frequencies in C₃H10T $\frac{1}{2}$ cells, induced by monoenergetic x-rays in the 15 to 25 keV range, produced at the Brookhaven National Synchrotron Light Source (NSLS). Transformation data for 15.2 keV monoenergetic x-rays are shown in Fig. 1. Using linear-quadratic fits (see Fig. 1) to the low-dose data, we estimate a low-dose RBE (ratio of alpha terms) of 1.96 ± 0.78 for 15.2-keV x-rays vs. 662-keV ¹³⁷Cs gamma rays. While these experiments are still in progress, in no case have we estimated a low dose RBE (defined, as above, as the ratio of alpha terms) of greater than 1.5 relative to 250-kVp x-rays (0.2 mm Cu, 1 mm Al external filtration), or greater than 2.5 relative to ¹³⁷Cs gamma rays.

These fairly modest RBE estimates are consistent with the earlier experimental data, as well as theoretical estimates (1) of 1.3 (vs. 250-kVp x-rays) and 2.0 (vs. gamma rays at Hiroshima and Nagasaki), for the low-dose RBE of 23-kVp filtered x-rays. The reason for the comparatively small predicted enhancements in effectiveness at mammographic x-ray energies is that the differences in energy deposition patterns between the higher and the lower-energy photons are

relatively subtle.

We stress, however, that even if the risks per unit dose of mammographic x-rays are just twice as large as those from the radiations at Hiroshima and Nagasaki, this would be of some significance. For example, Fig. 2 shows the age-dependent risk-benefit ratio, as estimated in NCRP Report 85 (1986) for 5 annual mammograms, each producing a glandular dose of 2 mGy. Here the “benefit” is assumed to be a 10% decrease in mortality, and the excess relative risk of radiation-related breast cancer was appropriately derived from studies of the Japanese A-bomb survivors. Now if it is assumed that mammographic x-rays are twice as hazardous, per unit dose, than the radiations at Hiroshima and Nagasaki, the benefit-risk ratio would also be decreased, by this same factor of 2.

As illustrated in Fig. 2, such a reduction in the benefit-risk ratio would be reflected in the age at which commencement of annual breast screening is recommended. For example, the American Cancer Society recommendation to begin annual screening at age 40 corresponds to the age when the estimated benefit-risk ratio reaches an acceptable value (numerically equal to 7 in Fig. 2). If the benefit-risk ratio were halved, because the radiation risk was twice that previously estimated, then the age above which this same benefit-risk ratio is reached would be increased (see Fig. 2), in this case from age 40 to 47. Similarly, if annual screening were recommended from age 50 (NIH consensus panel, 1997),

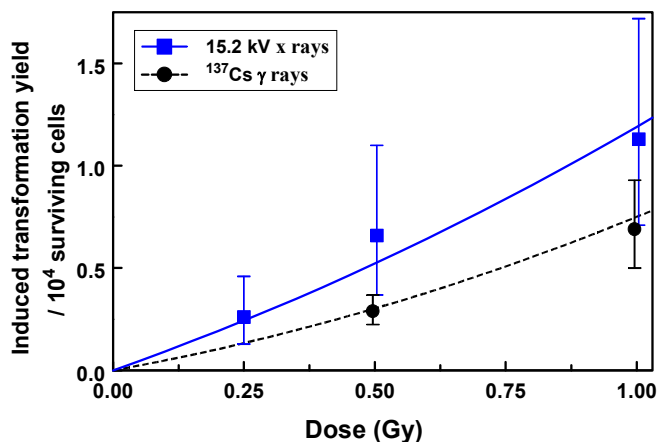


Fig. 1. Measured induced oncogenic transformation frequencies per 10⁴ surviving C₃H10T $\frac{1}{2}$ cells, as a function of the dose of 15.2-kV monoenergetic x-rays and 662-keV ¹³⁷Cs gamma rays. Estimated 68% confidence limits are shown. For clarity, only low-dose data points are shown. Curves represent fits to the full data set using the model $TF_{15keV} = \alpha_{15keV}D + \beta D^2$ and $TF_{662keV} = \alpha_{662keV}D + \beta D^2$, where $\alpha_{15keV} = 0.90 \pm 0.15 \text{ Gy}^{-1}$, and $\alpha_{662keV} = 0.46 \pm 0.11 \text{ Gy}^{-1}$.

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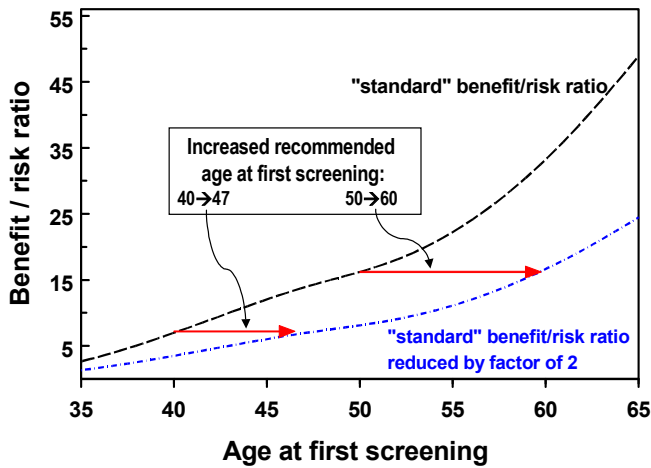


Fig. 2. Dash curve: Estimated benefit-risk ratio for yearly mammographic screening examinations for 5 years, assuming a total glandular dose of 2 mGy per exam (NCRP Report 85, 1986). The benefit is assumed to be a 10% reduction in breast cancer mortality, and the excess relative risk for radiation-induced breast cancer was assumed to be $2.2 \times 10^{-4}/\text{mGy}$.

Dot-dash curve: Corresponding benefit-risk ratio in which the estimated radiation risk is doubled, to account for an increased risk per unit dose of about 2 for low-energy mammographic x-rays

Arrows indicate the increase in age at which a given benefit-risk ratio would be achieved, assuming the radiation risk were doubled; these suggest that recommended starting ages for routine mammography might reasonably be increased, if the radiation risk from mammographic x-rays was larger than that previously assumed.

doubling the radiation risk, while keeping fixed the benefit-risk ratio for commencement of screening, would imply an increase in the recommended age to begin screening, from age 50 to about 60 (Fig. 2). Similar quantitative conclusions are obtained if other estimates of the age-dependent benefit-risk ratio for mammographic screening are re-analyzed by doubling the radiation risk.

In summary, there is evidence that low-energy x-rays as used in mammography have an increased biological risk relative to higher-energy photons. However the RBE values are not large, probably less than a factor two. Thus it is extremely unlikely that the radiation risk alone could prove to be a “show stopper” regarding screening mammography because, for older women, the benefit is still likely to considerably outweigh the radiation risk. For women below 50, however, this increase in the estimated radiation risk might suggest a somewhat later age than currently suggested, by about 5 to 10 years, at which to recommend commencement of routine breast screening.

References

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The Impact of IMRT on the Incidence of Radiation-Induced Second Cancers

Eric J. Hall and Cheng-Shie Wu¹

Intensity Modulated Radiotherapy (IMRT) represents the latest effort to tailor dose distribution to conform more closely to the tumor outline and so to minimize the volume of normal tissue receiving the higher doses. It typically employs a larger number of fields, and the use of multi-leaf collimators allow field sizes to be shaped and changed over time. This complex plan replaces the relatively simple four-field box technique used in the past. The hope is that tumor control will be increased because doses can be escalated, and normal tissue morbidity decreased. The expected gains remain an expectation but have not yet been proven in practice. Meanwhile, there is some concern that IMRT may have a down-side in terms of an increase in the incidence of radiation induced cancers. This may result from two sources.

First, delivery of a specified dose to the isocenter from a


modulated field, delivered by IMRT, will require the accelerator to be energized for longer by a factor of 2 to 3 (hence more monitor units are needed) compared with delivering the same dose from an unmodulated field. The total body dose due to leakage radiation will therefore be at least doubled. This may result in a doubling of the incidence of second cancers from 0.25% to 0.5% (assuming a risk estimate for fatal cancer of 1%/Sv in elderly patients).

Second, there is likely to be an increased incidence of radiation induced cancers for IMRT compared with conventional techniques due to the different dose distribution. IMRT exposes a larger volume of normal tissue to lower doses which might be expected to result in more radiation-induced tumors. The impact of this change is difficult to assess since it depends on the shape of the dose response relationship for radiation induced carcinomas in the dose range from 10 to 70 Gy. At doses of a few Gy, good esti-

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mates are available from the Japanese survivors, but data for higher doses are uncertain. The best estimate is that IMRT will result in a 0.5% increase in second cancers due to this cause.

In summary, the increased monitor units and the modified dose distribution may result in an extra 0.75% of surviv-

ing patients developing a radiation induced malignancy. This approximately doubles the rate seen in patients treated by conventional techniques. This is the price which must be offset against the gains expected from improved tumor control. 

Radiation Risks Associated with CT Screening of Smokers for Lung Cancer

David J. Brenner

There is increasing interest in the possibility of using low-dose computed tomography (CT) scans for annual screening of smokers and former smokers for early-stage lung cancer. Several pilot studies have already taken place, showing an increased capability for detecting small malignant nodules, and a National Lung Screening Trial is now underway.

Whilst the potential benefits of lung cancer screening have been much debated, less attention has been paid to the potential risks, specifically radiation-induced lung cancer, associated with the radiation from these CT scans. In part this is because the screening technique involves “low dose,” rather than standard, CT lung scans, and in part this is because excess relative risks (ERR) of radiation-induced cancer generally decrease markedly with increasing age. There are, however, several indications that the radiation risk to the lung associated with this screening technique may not be insignificant: Cancer risks from radiation are generally multiplicative of the background cancer risk, which is, by definition, high for lung cancer in the target population here. In addition, while radiation-related cancer risks do generally decrease markedly with increasing age at exposure, the ERR for radiation-induced lung cancer does not follow this pattern, and does not decrease significantly through adulthood.

These considerations suggest that risk of radiation-induced lung cancer associated with the radiation from repeated CT scans of the lung may not be negligible. We report here on estimates of these risks, and use these to define the minimum benefits from annual CT screening which will be necessary to outweigh these potential radiation risks.

These estimated radiation dose- (D), gender- (G), and smoking-status- (S) dependent low-dose / low-dose-rate excess relative risks (ERR) of lung cancer in a US population were used to calculate the excess lung cancer risk, R_{CT} , associated with a single individual CT lung scan at a given age (A):

$R_{CT}(A, G, S) = ERR(D, G, S) \times D_{CT} \times B(A+10, G, S) \times P_{10}(A)$, where D_{CT} is the lung dose for a single CT scan (see below), $B(A, S, G)$ is the lifetime lung-cancer risk for an in-

dividual alive at aged A (US tumor registries data with adjustments for smoking status), and $P_{10}(A)$ is the probability of living at least 10 years from age A . This approach essentially assumes a latency period of 10 years after each radiation exposure before any risk is manifest. 95% credibility intervals associated with these risk estimates were also estimated, combining estimates of the various individual sources of uncertainty (such as in the risk transfer from Japanese to U.S. populations, and in dose-fractionation effects) that contribute to the overall credibility limits.

Low dose CT lung scans use an exposure setting in the range from 30 to 100 mAs, with the National Lung Screening Trial recommending 60 mAs. We have used a direct measurement by Nishizawa et al (1) scaled to a 60 mAs setting, yielding a dose to the lung of 5.2 ± 0.9 Sv.

Fig. 1 shows the estimated lifetime radiation-related lung-cancer risks, R_{CT} , summed for a series of annual low-dose CT scans starting at age A and ending at age 75. For example, a 50 year old female current smoker who plans annual low-dose screening CT lung scans starting in 2002, would accrue an estimated excess lung cancer risk, associated with the total radiation exposure, of about 0.72% [95% C.I. 0.24 – 1.9%]; this is in addition to her otherwise expected lung cancer risk of about 11.5%. The corresponding estimated radiation-related excess lung cancer risk for 50 year old male smoker currently planning annual low-dose CT screens is 0.24% [95% C.I. 0.06 – 0.66%], in addition to his expected lung cancer risk of about 16%.

Fig. 2 shows the predicted numbers of radiation-related lung cancers in the population, assuming that 50% of the current smoking and former-smoking US population above a given age receive annual low-dose lung CT scans, starting in 2002, until age 75. Thus, for example, if the entire ever-smoking current population US population aged between 50 and 75 (about 39,000,000 individuals) were offered annual CT screens up to age 75, with a 50% compliance rate the estimated number of lung cancers associated with the radiation from these scans would be about 14,000 [95% C.I.: 4,400 – 36,400].

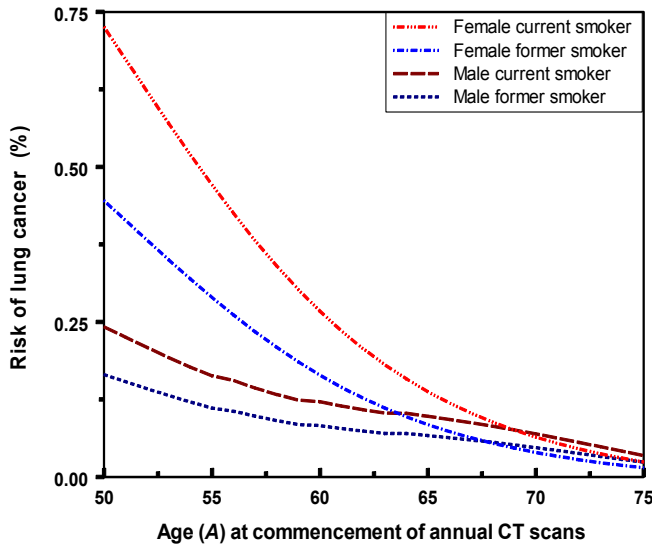


Fig. 1. Estimated risks of lung cancer associated with the radiation from annual low-dose CT lung scans. Annual scans are assumed to commence in 2002 at age *A* and continue till age 75. Estimated 95% credibility limits are approximately a factor of 3 in either direction. Risks were estimated using a lung dose of 5.2 mSv; risks for other doses can be proportionately scaled according to the dose.

While baseline screening would result in fairly small radiation risks, yearly screening from aged 50 would add about 0.5% to the ~14% lung cancer risk faced by a 50 year old ever smoker. The estimated radiation-associated risks can, of course, only be assessed in the context of the potential benefits of CT lung cancer screening. Of the 50% of the current 50 to 75 year old ever-smoking US population who are assumed here to undergo annual CT lung scans, about 1,300,000 would be expected to develop lung cancer, independent of the radiation. An additional 14,000 radiation-associated lung cancer cases thus represents about a 1.1% [95% C.I.: 0.4% - 2.8%] increase. At this time, the magnitude of the potential mortality benefit from screening adult ever smokers with CT is not yet established, but a mortality

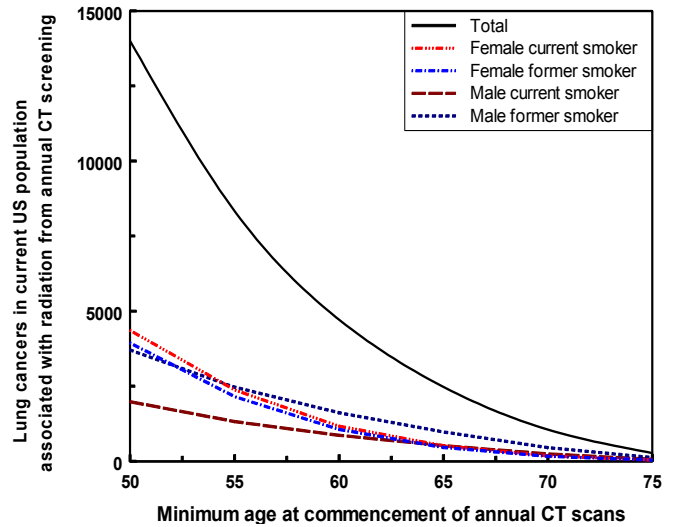



Fig. 2. Predicted numbers of lung cancers in the current US population associated with the radiation from annual low-dose CT lung scans. Assumed is that 50% of the current smoking and former-smoking population received annual low-dose CT scans at the given age until age 75. These results can be linearly scaled for different doses, different compliance rates and, approximately in North American and Western European populations, different population numbers in the four smoking categories here.

benefit of considerably greater than 3% in the screened population would potentially be necessary to appropriately outweigh these estimated radiation risks.

References

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What Protocols are Appropriate for Clinical Trials of Hypofractionated Prostate Radiotherapy?

David J. Brenner, Jack F. Fowler,¹ Mark A. Ritter¹ and Rick J. Chappell¹

Motivated by radiobiological concepts originating *in vitro*, recent analyses of clinical results have suggested that the fractionation sensitivity of prostate tumors is remarkably high; corresponding point estimates of the α/β ratio for pros-

tate cancer are around 1.5 Gy, much lower than the typical value of 10 Gy for most other tumors. This low α/β value is comparable to the nominal α/β value of 3 Gy for surrounding late-responding tissues, suggesting that logistically-convenient hypofractionated schemes could be designed for prostate cancer with no loss in tumor control or increase in


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late effects. An even more advantageous scenario arises if the α/β ratio for prostate tumors was actually significantly less than that for late rectal complications; in fact there is credible evidence that α/β for late rectal complications might actually be somewhat higher – in the 4-5 Gy range, due to contributions from “consequential” late effects which originate from tissue with high α/β values. If the α/β value for prostate is really less than for late-responding rectal damage, hypofractionated regimens could be designed with fewer but larger dose fractions (and, of course, a lower total dose), to maintain equivalent late sequelae whilst yielding improved tumor control. One would also expect less acute sequelae and less “consequential” late effects, provided that overall time is not shortened too drastically.

The low α/β ratio for prostate relative to that for the surrounding late-responding normal tissue gives the potential for therapeutic gain, and we analyze here possible protocols for prostate cancer to test this suggestion. Using standard linear-quadratic (LQ) modeling, a set of high-gain/low-risk hypofractionated protocols can be designed in which a series of dose steps is given, each step of which keeps the late complications constant in rectal tissues. This is done by adjusting the dose per fraction and total dose to maintain a constant level of late effects. The effect on tumor control is then investigated.

If the α/β value for prostate is less than that for the surrounding late-responding normal tissue, the clinical gains can be rather large. For example, 10 fractions, each of 4.4

Gy, are predicted to give about the same tumor control as 75 Gy in 2 Gy fractions, *but with the same late complications as 66 Gy in 2 Gy fractions*; in this case, the estimated bNED for tumors has increased from 51.6% (with 33F \times 2 Gy) to 77.1% (with 10F \times 4.44 Gy), so the therapeutic ratio has been increased substantially. This possible increase in bNED would require a clinical trial with two arms of 72 patients in each, to have a 90% power of demonstrating the difference. In this particular protocol, one-third of the number of fractions would have to be delivered, no increase in late complications would be expected, and the early sequelae rate would be expected to decrease. An overall time not shorter than 5 weeks appears advisable, at least initially, for the hypofractionation schedules considered, because of a possible risk of acute or consequential late reactions in the rectum. Sensitivity tests suggest that, even if the prostate tumor α/β ratio turns out to be the same (or even slightly larger than) the surrounding late-responding normal tissue, these hypofractionated regimens would be very unlikely to result in significantly increased late effects.

The hypofractionated regimens that we suggest be tested for prostate-cancer radiotherapy have high potential therapeutic gain as well as economic and logistic advantages. They appear to have little potential risk and considerable potential for therapeutic gain, as long as excessively short overall times (<5 weeks) and very small fraction numbers (<5) are avoided. 

Dietary Supplements and Radiation Therapy: Effects of Lycopene and Vitamin E on Prostate Cancer Cells

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Lycopene and alpha-tocopherol (Vitamin E) are both among the potent dietary antioxidants being investigated for their potentially protective role against the formation of free radical-induced mutagenesis involved in the development of cancer. In particular, lycopene – a biological carotenoid found in high concentration in tomatoes, watermelon, apricots, guava, rosehips and pink grapefruit – has been shown to be an extremely efficient quencher of singlet oxygen radicals, with a quenching rate of more than double that of beta-carotene.

Studies investigating the correlation between lycopene intake and prostate cancer have shown that increased dietary intake of tomato-based products increases serum levels of

lycopene, and that healthy men with elevated serum lycopene have a decreased risk of developing prostate cancer, particularly aggressive, extraprostatic tumors.

These findings have led to brand name vitamin manufacturers promoting products that are supplemented with lycopene and other antioxidants, including Vitamin E, selenium and zinc, in an effort to advance prostate health in their consumers.

However, in men already diagnosed with prostate cancer who are being treated with radiation therapy, the effect of dietary antioxidants is unclear. Because the effectiveness of radiotherapy is believed to depend upon radiation-induced free radical formation and the subsequent oxidative damage caused to cancer cell DNA, dietary antioxidants taken during radiation therapy may decrease this therapy's potency and ability to kill malignant cells.

Studies investigating the effect of lycopene on cells have

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been somewhat variable, showing it to have both anti-oxidant and pro-oxidant properties. In contrast with the variable effects observed with lycopene in vitro, Vitamin E demonstrates more consistent trends, appearing to be harmful to cancer cells, but protective of normal cells.

In this study, a clonogenic survival assay and micronucleus assay were performed on DU-145, PC3, and LNCaP prostate cancer cell lines in vitro to determine the effect that lycopene and Vitamin E may have on survival and DNA damage in gamma-irradiated prostate cancer cells.

DU-145 cells were grown in DMEM, and PC-3 and LNCaP cells were grown in RPMI, all containing 1% streptomycin-penicillin and 15% FBS. Cells were seeded into 4 cm petri dishes, and were incubated at 37°C for 24 hours. Dishes were then treated with lycopene at 4.0 µM and 7.2 µM, Vitamin E at 50 µM, and a combination of Vitamin E (50 µM) and lycopene (4.0 µM for PC3 cells; 7.2 µM for DU-145 and LNCaP cells). Controls were done for untreated media, 0.4 % THF (corresponding to lycopene of 4.0 µM), 0.7% THF (corresponding to lycopene of 7.2 µM) and 0.05% ethanol (corresponding to Vitamin E of 50 µM). Once treated, cells were incubated for three hours before irradiation with 137Cs gamma rays (1.1 Gy/min) at doses of 0, 0.5, 1, 2, 4, 6 and 8 Gy. DU-145 cells were then incubated for 9 days, LNCaP cells for 18 days, and PC3 cells for 21 days at 37°C, allowing colonies to become large enough to be counted without magnification. Colonies were then fixed with 70% ethanol, stained with crystal violet, and counted. All dishes were done in triplicate for each cell line.

For the micronucleus assay cytochalasin B at a concentration of 3 µg/ml of PBS was added to dishes immediately after irradiation. DU-145 cells were harvested after 30 hours of incubation with cytochalasin B, and PC3 and LNCaP cells after 80 hours of incubation, to allow for the difference in cell cycle timing between cell lines. To prepare the binucleated cells, cells were trypsinized, treated with cold (4°C) hypotonic (0.075 M) KCl, and centrifuged at 800 rpm for 8 minutes, without disturbing the pellet. Leaving only 2.5 ml of supernatant, 7.5 ml of 3:1 methanol: acetic acid fixative and 4 drops of formaldehyde (a preservative) were then added to each tube, drop by drop, and tubes were again centrifuged at 800 rpm for 8 minutes. Tubes were treated with two more cycles of 3:1 methanol: acetic acid fixative and centrifugation at 1000 rpm for 8 minutes, breaking up the pellet. The fixed cell solution was then placed on slides and allowed to air dry before staining with Acridine Orange (0.03 mg/ml in PBS) and scoring via fluorescent microscopy.

Lycopene clearly protects prostate cancer cells against gamma radiation-induced DNA damage in the form of decreased micronuclei formation, resulting in a significant increase in survival in both androgen-sensitive and androgen-insensitive cell lines. In contrast, vitamin E dramatically enhances gamma radiation-induced apoptosis in prostate cancer cells, leading to a significant reduction in survival in both androgen-sensitive and androgen-insensitive cell lines. The impact of these antioxidants on survival was maintained in both non-irradiated cells, and irradiated cells across a broad spectrum of radiation doses which included doses

typically used in radiation therapy.

The inclusion of the micronucleus assay was essential to this study for several reasons. First, the micronucleus assay successfully provided both a mechanism, as well as corroboration, for the results of the survival assay in both Vitamin E- and lycopene-treated cells. While the survival assay clearly showed Vitamin E to significantly decrease survival in all three treated prostate cancer cell lines, this was explained and supported by a dramatic increase in the percentage of apoptotic cells, as well as a modest increase in the percentage of micronucleated cells. Additionally, while lycopene was shown to increase survival in DU-145 and LNCaP cells, this was supported by a significant decrease in the percentage of micronucleated cells seen.

This study's findings, that Vitamin E inhibits growth and induces apoptosis in gamma-irradiated prostate cancer cells, are a consistent addition to the published literature. However, in contrast to previous studies demonstrating lycopene to inhibit growth and survival in cancer cells, the protective effect seen with lycopene in gamma-irradiated prostate cancer cells is unique to this study.

The absolute impact that lycopene and Vitamin E had on survival and DNA damage varied, both among the different cell lines, and with respect to one another. In general, Vitamin E appeared to have a greater impact on decreasing survival than lycopene did on increasing survival. Vitamin E not only decreased survival in all three cell lines (as compared to lycopene increasing survival in only the DU-145 and LNCaP cells), but Vitamin E's effects were greater in each cell line than lycopene.

The findings of this study, that lycopene protects prostate cancer cells in vitro against gamma radiation-induced DNA damage leading to an increase in cell survival at clinically-relevant radiation doses, raises a query at this time about the use of dietary lycopene supplements in men with prostate cancer undergoing radiation therapy. Although it cannot be claimed from these findings that the protective role observed in lycopene-treated cells in vitro would necessarily translate into a survival advantage for prostate cancer cells treated with radiation therapy in human subjects, the deficiency of literature in this area reflects the lack of knowledge regarding the role of dietary antioxidants in this population of patients. In addition, the different effects observed in other studies between purified and oxidized lycopene may have clinical implications, making it important to verify which form of lycopene is present in tomato-based products and vitamin supplements available to consumers.

Conversely, the findings of this study that Vitamin E decreases survival in irradiated prostate cancer cells in vitro by the induction of apoptosis may hold clinical promise in the future for Vitamin E supplementation during radiation therapy. Particularly when considered in the context of the findings of others that such an effect is not seen in normal cells. Additional studies are certainly warranted at this time to more definitively clarify the impact that antioxidant supplementation may have on the effectiveness of radiation therapy for prostate cancer, and to determine whether oncologists should recommend Vitamin E and lycopene supplementation during radiation therapy.

