

LE Magazine November 2001

ABSTRACTS

Page 1 of 4

Scans

Estimated risks of radiation-induced fatal cancer from pediatric CT.

OBJECTIVE: In light of the rapidly increasing frequency of pediatric CT examinations, the purpose of our study was to assess the lifetime cancer mortality risks attributable to radiation from pediatric CT. **MATERIALS AND METHODS:** Organ doses as a function of age-at-diagnosis were estimated for common CT examinations, and estimated attributable lifetime cancer mortality risks (per unit dose) for different organ sites were applied. Standard models that assume a linear extrapolation of risks from intermediate to low doses were applied. On the basis of current standard practice, the same exposures (milliamperere-seconds) were assumed, independent of age. **RESULTS:** The larger doses and increased lifetime radiation risks in children produce a sharp increase, relative to adults, in estimated risk from CT. Estimated lifetime cancer mortality risks attributable to the radiation exposure from a CT in a 1-year-old are 0.18% (abdominal) and 0.07% (head)-an order of magnitude higher than for adults-although those figures still represent a small increase in cancer mortality over the natural background rate. In the United States, of approximately 600,000 abdominal and head CT examinations annually performed in children under the age of 15 years, a rough estimate is that 500 of these individuals might ultimately die from cancer attributable to the CT radiation. **CONCLUSION:** The best available risk estimates suggest that pediatric CT will result in significantly increased lifetime radiation risk over adult CT, both because of the increased dose per milliamperere-second, and the increased lifetime risk per unit dose. Lower milliamperere-second settings can be used for children without significant loss of information. Although the risk-benefit balance is still strongly tilted toward benefit, because the frequency of pediatric CT examinations is rapidly increasing, estimates that quantitative lifetime radiation risks for children undergoing CT are not negligible may stimulate more active reduction of CT exposure settings in pediatric patients.

Am J Roentgenol 2001 Feb;176(2):289-296

Radiation exposure and image quality in chest CT examinations.

OBJECTIVE: The purpose of this study was to determine how changes in radiographic tube current affect patient dose and image quality in unenhanced chest CT examinations. **SUBJECTS AND METHODS:** Ten sets of CT images were obtained from patients undergoing CT-guided chest biopsies. For each patient, six images of the same region were obtained at settings between 40 and 280 mAs. CT data were used to reconstruct tomographic sections with a field of view limited to the normal contralateral lung. Images were printed using lung and mediastinal image display settings. Image quality was determined by asking radiologists to assess the perceived level of mottle in CT images. Five chest radiologists ranked the relative image quality of six images. Patient effective doses were computed for chest CT examinations performed at each milliamperere-second setting. Radiologists indicated whether any perceived improvement of image quality at the higher radiation exposures was worth the additional radiation dose. **RESULTS:** The differences in quality of chest CT images generated at greater than or equal to 160 mAs were negligible. Reducing the radiographic technique factor below 160 mAs resulted in a perceptible reduction in image quality. Differences in CT image quality for radiographic techniques between 120 and 280 mAs were deemed to be insufficient to justify any additional patient exposure. However, the use of 40 mAs results in an inferior image quality that would justify increased patient exposure. **CONCLUSION:** Radiographic techniques for unenhanced chest CT examinations can be reduced from 280 to 120 mAs without compromising image quality.

AJR Am J Roentgenol 2001 Aug;177(2):279-284

Paranasal sinuses: low-dose CT.

While computed tomography (CT) has become an important imaging modality in the evaluation of the paranasal sinuses, the radiation dose remains higher than is necessary. With use of a head phantom and constant kilovolt peak setting, axial and coronal CT scans of the paranasal sinuses were obtained at each of six successively lower milliamperere second settings than are commonly used in clinical practice. Although noise, as measured by the standard deviation of the CT numbers, did increase, images were of diagnostic quality even when dose levels were reduced by a factor of 28. In the same incremental manner, the

milliamperere second settings used in scanning 90 patients were reduced, with no loss of diagnostic quality. The authors discuss the methods of analysis and the advantages of use of lower milliamperere second settings at CT scanning of the sinuses.

Radiology 1991 Dec;181(3):689-691

Ankle/arm pressure index in asymptomatic middle-aged males: an independent predictor of ten-year coronary heart disease mortality.

PURPOSE OF THE STUDY: To evaluate the predictive power of a reduced ankle/brachial pressure index (ABPI) ($< \text{or} = .90$) in an asymptomatic middle-aged male working population free of coronary heart disease. **MATERIALS AND METHODS:** 2023 subjects forty to fifty-five years old were screened at their work place. Standard techniques were used. Blood was drawn in the fasting state. Ankle and brachial blood pressures were measured by Doppler signals and all measures were done by one observer, duly trained in epidemiologic methodology. **RESULTS:** In univariate analysis, an ABPI $< \text{or} = .90$ was significantly associated with age, total serum cholesterol, body mass index, smoking, and awareness of diabetes. In multivariate analysis, it was associated with awareness of diabetes, age, Ln triglycerides ($P = .073$), and smoking ($P = .088$). Relative risks for reduced versus normal ABPI are 2.77 ($P = .010$), 4.16 ($P = .011$) and 4.97 ($P = .006$) for ten-year all causes, cardiovascular, and coronary mortality, respectively. In a multiple logistic regression analysis, the following variables were significant independent predictors of coronary mortality: smoking (odds ratio [OR] = 4.84), reduced ABPI (OR = 3.63), and low density lipoprotein cholesterol (OR for 1 SD = 1.69). Reduced ABPI is also an independent predictor of cardiovascular mortality. **CONCLUSION:** a reduced ABPI is an independent risk factor for coronary and cardiovascular mortality in asymptomatic middle-aged Belgian males.

Angiology 1995 Mar;46(3):211-219

Protective effects of melatonin against oxidation of guanine bases in DNA and decreased microsomal membrane fluidity in rat liver induced by whole body ionizing radiation.

The aim of the study was to examine the potential protective effect of melatonin against whole body ionizing radiation (800 cGy). Changes in 8-hydroxy-2'-deoxyguanosine (8-OH-dG) levels, an index of DNA damage, and alterations in membrane fluidity (the inverse of membrane rigidity) and lipid peroxidation in microsomal membranes, as indices of damage to lipid and protein molecules in membranes, were estimated. Measurements were made in rat liver, 12 h after their exposure to radiation. To test the potential protective effects of melatonin, the indole was injected (i.p. 50 mg/kg b.w.) at 120, 90, 60 and 30 min prior to radiation exposure. Both 8-OH-dG levels and microsomal membrane rigidity increased significantly 12 h after radiation exposure. Melatonin completely counteracted the effects of ionizing radiation. Changes in 8-OH-dG levels and membrane fluidity are early sensitive parameters of DNA and microsomal membrane damage, respectively, induced by ionizing radiation and our findings document the protective effects of melatonin against ionizing radiation.

Mol Cell Biochem 2000 Aug;211(1-2):137-144

Melatonin reduces X-ray irradiation-induced oxidative damages in cultured human skin fibroblasts.

Melatonin is a hormone with multiple functions in humans, produced by the pineal gland and stimulated by beta-adrenergic receptors. Melatonin has been shown to have radioprotection properties, but there has been little progress toward identifying the specific mechanisms of its action. To clarify the role of melatonin as a radioprotective compound, in response to X-ray irradiation, we investigated the effects of X-ray irradiation and melatonin on cytotoxicity, lipid peroxidation and alteration of the cell cycle in cultured skin fibroblast. An 8 Gy dose of X radiation resulted in cell death in 63% of irradiated cells, i.e. the cell viability was 37%. The damage was associated with lipid peroxidation of the cell membrane, as shown by the accumulation of malondialdehyde (MDA). By pre-incubation with melatonin (10^{-5} M), a significant preventive effect was noted on the increase in the absolute number of surviving cells (up to 68% of cells were survived), and the levels of MDA were markedly decreased. These findings suggest a close correlation between an increase of lipid peroxidation and a rate of cell death. Morphological changes associated with apoptotic cell death were demonstrated by TEM. DNA flow-cytometry analysis revealed that X radiation increased pre-G1 apoptotic population by 7.6% compared to a very low level (1.3%) of non-irradiated cells. However, in the presence of melatonin, this apoptotic population decreased up to 4.5% at 10^{-5} M. The p53 and p21 protein levels of skin fibroblasts increased 4 h after 8 Gy irradiation, but melatonin pretreatment did not change those levels. This study suggests that melatonin pretreatment inhibits radiation-induced apoptosis, and melatonin exerts its radioprotective effect by inhibition of lipid peroxidation and without any involvement of the p53/p21 pathway.

J Dermatol Sci 2001 Jul;26(3):194-200

Mechanism of protection against radiation-induced DNA damage in plasmid pBR322 by caffeine.

PURPOSE: Caffeine (1,3,7-trimethyl xanthine), a dietary component, has been shown to have widely varying effects on DNA

damage induced by UV and ionizing radiation, depending upon pre- or post-irradiation administration and its concentration. Caffeine administered post-UV irradiation is known to inhibit enzymatic repair of DNA lesions, leading to potentiation of damage, whereas its presence before or during irradiation elicits protection in a wide range of test systems: bacteria, cultured human cells, plant seeds and mouse. The purpose of this study is to test whether caffeine present during gamma-irradiation of plasmid DNA, a system devoid of replication and repair, could elicit protection by scavenging free radicals. MATERIALS AND METHODS: Plasmid pBR322 DNA was exposed to gamma-radiation in the presence or absence of caffeine at a dose-rate of 1.20 Gy min⁻¹ and damage measured as single-strand breaks. To understand the mechanisms of the observed protection, especially under oxic conditions, reaction of caffeine with superoxide radical (O₂⁻), hydrogen peroxide (H₂O₂) and the deoxyribose peroxy radical (ROO^{*}) were studied. RESULTS: Irradiation of pBR322 was observed to induce a dose-dependent increase in single-strand breaks. Caffeine itself did not induce strand breaks but reduced radiation-induced strand breaks at micromolar to millimolar concentrations. Caffeine has been shown to react with the radiation-derived oxidants. The reaction rate constants observed were 7.5x10¹¹ M⁻¹ s⁻¹ with O₂⁻, 1.05x10⁸ M⁻¹ s⁻¹ with ROO^{*} and 8.8x10¹¹ M⁻¹ s⁻¹ with H₂O₂. CONCLUSIONS: Caffeine effectively protects DNA against ionizing radiation in a system devoid of repair and replication machinery. Thus, DNA protection shown by caffeine is possibly due to the scavenging of radiation-derived primary as well as secondary reactive oxygen species, and this physicochemical protective pathway possibly pre-empts any subsequent inhibitory effect of caffeine on the enzymatic repair of DNA.

Int J Radiat Biol 2001 May;77(5):617-623

Induction of nuclear factor kappa B after low-dose ionizing radiation involves a reactive oxygen intermediate signaling pathway.

Reactive oxygen intermediates (ROIs) have been found to be the messengers in the activation of the kappa B transcription regulator in mitogen- or cytokine-stimulated cells, operating in conjunction with or independently of various other mechanisms; these include Ca⁺⁺-dependent and PKC-dependent cytoplasmic signaling pathways. We have recently reported that low-dose ionizing radiation induces NF-kappa B in human lymphoblastoid 244B cells. Since ionizing radiation generates free radicals in cells, we have investigated whether the ROIs generated by ionizing radiation induce NF-kappa B activity, and also whether they do so by a similar mechanism as in cells treated with PMA or H₂O₂. The results not only confirm a previous observation from our laboratory that low-dose ionizing radiation (0.1-2.0 Gy) activates kappa B transcription factor transiently with a maximal induction at 0.5 Gy exposure, but also demonstrate mechanistically that the activation of NF-kappa B by low-dose ionizing radiation can be inhibited considerably by the antioxidant N-acetyl-L-cysteine, indicating that at least the major part of the activation process is mediated by ROIs. These findings support the idea that ROIs can regulate the kappa B elements which in turn can serve as response elements for oxidant stress.

Radiat Res 1994 Oct;140(1):97-104

Influence of clinically used antioxidants on radiation-induced expression of intercellular cell adhesion molecule-1 on HUVEC.

PURPOSE: The effects of antioxidants (N-acetyl-L-cysteine [NAC] and pyrrolidine dithiocarbamate [PDTC]) on radiation-induced ICAM-1 expression on human umbilical vein endothelial cells (HUVEC) were investigated. MATERIALS AND METHODS: The expression of ICAM-1 on HUVEC was determined by flow cytometry up to 72 h after X-irradiation. Functional competence of induced ICAM-1 was assessed by adhesion experiments with human polymorphonuclear neutrophils on irradiated HUVEC. RESULTS: Preincubation of cells with both or either NAC and PDTC was unable to reduce radiation-induced ICAM-1 expression on HUVEC. In fact, by themselves, these antioxidants induced a significant increase of ICAM-1 expression, which in comparison with a radiation dose of 7 Gy after 24h was nine times higher for PDTC, and more than double for NAC. Treatment with NAC clearly restrained TNF-alpha-induced ICAM expression on HUVEC, while preincubation of cells with PDTC showed synergistic effects. CONCLUSIONS: The role of reactive oxygen intermediates in signal transduction pathways leading to ICAM-1 expression should be investigated further. Furthermore, antioxidants may exert a pro-inflammatory role, as revealed by the induction of ICAM-1 expression on endothelial cells. The inhibition of TNF-alpha-induced ICAM-1 expression by NAC might have clinical implications because this substance is used as a radioprotector in radiotherapy.

Int J Radiat Biol 1999 Oct;75(10):1317-1325

Continued on Page 2 of 4

[Back to the Magazine Forum](#)

ABSTRACTS

Page 2 of 4

A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps.

BACKGROUND: Virtual colonoscopy is a new method of imaging the colon in which thin-section, helical computed tomography (CT) is used to generate high-resolution, two-dimensional axial images. Three-dimensional images of the colon simulating those obtained with conventional colonoscopy are then reconstructed off-line. We compared the performance of virtual and conventional colonoscopy for the detection of colorectal polyps. **METHODS:** We prospectively studied 100 patients at high risk for colorectal neoplasia (60 men and 40 women; mean age, 62 years). We performed virtual colonoscopy immediately before conventional colonoscopy. We inserted a rectal tube and insufflated the colon with air to the maximal level that the patient could tolerate. We administered 1 mg of glucagon intravenously immediately before CT scanning to minimize the degree of smooth-muscle spasm and peristalsis and to reduce the patient's discomfort. **RESULTS:** The entire colon was clearly seen by virtual colonoscopy in 87 patients and by conventional colonoscopy in 89. Fifty-one patients had normal findings on conventional colonoscopy. In the other 49, we identified a total of 115 polyps and 3 carcinomas. Virtual colonoscopy identified all 3 cancers, 20 of 22 polyps that were 10 mm or more in diameter (91 percent), 33 of 40 that were 6 to 9 mm (82 percent), and 29 of 53 that were 5 mm or smaller (55 percent). There were 19 false positive findings of polyps and no false positive findings of cancer. Of the 69 adenomatous polyps, 46 of the 51 that were 6 mm or more in diameter (90 percent) and 12 of the 18 that were 5 mm or smaller (67 percent) were correctly identified by virtual colonoscopy. Although discomfort was not specifically recorded, none of the patients requested that virtual colonoscopy be stopped because of discomfort or pain. **CONCLUSIONS:** In a group of patients at high risk for colorectal neoplasia, virtual and conventional colonoscopy had similar efficacy for the detection of polyps that were 6 mm or more in diameter.

N Engl J Med 1999 Nov 11;341(20):1496-1503

Technique factors and image quality as functions of patient weight at abdominal CT.

PURPOSE: To investigate how changes in kilovolt peak and milliamperere second settings, and patient weight affect transmitted x-ray energy fluence and the image contrast-to-noise ratio (CNR) at abdominal computed tomography (CT). **MATERIALS AND METHODS:** Cylinders of water were used as patient models, and x-ray spectra, including x-ray tube potentials of 80-140 kVp, were investigated. The mean photon energy and energy fluence transmitted through water cylinders with varying diameters and the image contrast for fat, muscle, bone, and iodine relative to water were determined. The effect of changing the x-ray tube potential on CNR also was investigated. **RESULTS:** At a constant kVp, increasing patient weight from 10 kg to 120 kg reduced the transmitted energy fluence by two orders of magnitude. Changing the x-ray tube potential from 80 kVp to 140 kVp increased the mean photon energy from approximately 52 keV to approximately 72 keV and thus reduced the image contrast relative to water by 12% for muscle, 21% for fat, 39% for bone, and 50% for iodine (approximate reduction values). Increasing the x-ray tube potential from 80 kVp to 140 kVp increased the CNR by a factor of 2.6 for muscle and by a factor of 1.4 for iodine. **CONCLUSION:** With changes in patient weight at abdominal CT, x-ray tube potentials must be varied to maintain a constant detector energy fluence. Increasing the x-ray tube potential generally improves CNR.

Radiology 2000 Nov;217(2):430-435

Use of colonoscopy to screen asymptomatic adults for colorectal cancer.

BACKGROUND AND METHODS: The role of colonoscopy in screening for colorectal cancer is uncertain. At 13 Veterans Affairs Medical Centers, we performed colonoscopy to determine the prevalence and location of advanced colonic neoplasms and the risk of advanced proximal neoplasia in asymptomatic patients (age range, 50 to 75 years) with or without distal neoplasia. Advanced colonic neoplasia was defined as an adenoma that was 10 mm or more in diameter, a villous adenoma, an adenoma with high-grade dysplasia, or invasive cancer. In patients with more than one neoplastic lesion, classification was based on the most advanced lesion. **RESULTS:** Of 17,732 patients screened for enrollment, 3196 were enrolled; 3121 of the enrolled patients (97.7 percent) underwent complete examination of the colon. The mean age of the patients was 62.9 years, and 96.8 percent were men. Colonoscopic examination showed one or more neoplastic lesions in 37.5 percent of the patients, an adenoma with a diameter of at least 10 mm or a villous adenoma in 7.9 percent, an adenoma with high-grade dysplasia in 1.6 percent, and invasive cancer in 1.0 percent. Of the 1765 patients with no polyps in the portion of the colon that was distal to the splenic flexure, 48 (2.7 percent) had advanced proximal neoplasms. Patients with large adenomas (\geq 10 mm) or small adenomas ($<$ 10 mm) in the distal colon were more likely to have advanced proximal neoplasia than were patients with no distal adenomas (odds ratios, 3.4 [95 percent confidence interval, 1.8 to 6.5] and 2.6 [95 percent confidence interval, 1.7 to 4.1], respectively). However, 52 percent of the 128

patients with advanced proximal neoplasia had no distal adenomas. CONCLUSIONS: Colonoscopic screening can detect advanced colonic neoplasms in asymptomatic adults. Many of these neoplasms would not be detected with sigmoidoscopy.

N Engl J Med 2000 Jul 20;343(3):162-168

Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) Study.

The resting ankle-brachial index (ABI) is a non-invasive method to assess the patency of the lower extremity arterial system and to screen for the presence of peripheral occlusive arterial disease. To determine how the ABI is associated with clinical coronary heart disease (CHD), stroke, preclinical carotid plaque and far wall intimal-medial thickness (IMT) of the carotid and popliteal arteries, we conducted analyses in 15 106 middle-aged adults from the baseline examination (1987-1989) of the Atherosclerosis Risk in Communities (ARIC) Study. The prevalence of clinical CHD, stroke/transient ischemic attack (TIA) and preclinical carotid plaque increased with decreasing ABI levels, particularly at those of < 0.90. Individuals with ABI < 0.90 were twice as likely to have prevalent CHD as those with ABI > 0.90 (age-adjusted odds ratio (OR) ranging from 2.2 (95% CI: 1.0-5.1) in African-American men to 3.3 (95% CI: 2.1-5.0) in white men). Men with ABI < 0.90 were more than four times as likely to have stroke/TIA as those with ABI > 0.90 (age-adjusted OR: 4.2 (95% CI: 1.8-9.5) in African-American men and 4.9 (95% CI: 2.6-9.0) in white men). In women the association was weaker and not statistically significant. Among those free of clinical cardiovascular disease, individuals with ABI < or = 0.90 had statistically significantly higher prevalence of preclinical carotid plaque compared to those with ABI > 0.90 (age-adjusted ORs ranging from 1.5 (95% CI: 1.0-1.9) in white women to 2.6 (95% CI: 1.0-6.6) in african-american men). The ABI was also inversely associated with far wall IMT of the carotid arteries (in both men and women) and the popliteal arteries (in men only). The associations of ABI with clinical CHD, stroke, preclinical carotid plaque and IMT of the carotid and popliteal arteries were attenuated and often not statistically significant after further adjustment for LDL cholesterol, cigarette smoking, hypertension and diabetes. These data demonstrate that low ABI levels, particularly those of < 0.90, are indicative of generalized atherosclerosis.

Atherosclerosis 1997 May;131(1):115-125

Correlation of homocysteine levels with the extent of coronary atherosclerosis in patients with low cardiovascular risk profiles.

Elevation of homocysteine is now known as an independent risk factor for vascular diseases. However, influences of homocysteine to the extent of coronary atherosclerosis in patients with different coronary risk profiles have not been studied. In this study, we used angiographic "diffuse score" and "clinical vessel score" to evaluate the extent of coronary atherosclerosis, and examined the correlation between levels of serum total homocysteine and angiographic scores among patients with high- and low-risk profiles. Seventy consecutive patients (58 men and 12 women, mean age 50 years) undergoing selective coronary angiography for the first time were recruited for this study. Patients were divided into high-risk (risk factor > or =3, n = 35) and low-risk (risk factor <3, n = 35) groups. Linear regression analysis revealed that levels of serum homocysteine were only significantly correlated with diffuse (r = 0.217, p = 0.007) and clinical vessel (r = 0.078, p = 0.037) scores in low-risk patients. These correlations could not be observed in diffuse (r = 0.070, p = 0.319) and clinical vessel (r = -0.001, p = 0.970) scores in the high-risk group. In conclusion, levels of homocysteine correlated with the extent of coronary atherosclerosis only among patients with low cardiovascular risk profiles.

Am J Cardiol 2000 Jan 1;85(1):49-52

Effect of plasma homocysteine concentration on early and late events in patients with acute coronary syndromes.

BACKGROUND: Although a raised plasma homocysteine is a risk factor for vascular disease, it is not known whether it is associated with an adverse cardiac outcome in patients admitted with acute coronary syndromes. We evaluated the relationship between plasma homocysteine and short-term (28 days) and long-term (median 2.5 years) prognosis in acute coronary syndromes. **METHODS AND RESULTS:** We evaluated the relationship of quintiles of homocysteine to fatal and nonfatal coronary disease early (28 days) and late (29 days to a median of 2.5 years) after admission to a single unit of patients with unstable angina (n=204) and myocardial infarction (n=236). The end points studied were cardiac death (n=67) and/or myocardial (re) infarction (n=30). Cox regression and logistic regression were used to estimate the relationship of homocysteine to coronary events. The event rate within the first 28 days (22 cardiac deaths and 5 nonfatal infarctions) was not related to the admission homocysteine level. In the 203 unstable angina and 214 myocardial infarction survivors, an apparent threshold effect was seen on long-term follow-up, with a significant step-up in the frequency of events between the lowest 3 quintiles (14 cardiac deaths and 11 nonfatal infarctions) and the upper 2 quintiles (31 fatal and 12 nonfatal events). Patients in the upper 2 quintiles (>12.2 micromol/L) had a 2.6-fold increase in the risk of a cardiac event (95% CI, 1.5 to 4.3, P<0.001). **CONCLUSIONS:** Elevated total homocysteine levels on admission strongly predict late cardiac events in acute coronary syndromes.

Circulation 2000 Aug 8;102(6):605-610

Computed tomographic colonography and conventional colonoscopy for colon diseases: a prospective, blinded study.

OBJECTIVES: Computed tomographic (CT) colonography or virtual colonoscopy is a new diagnostic method for the colon and rectum, developed on the basis of spiral computed axial tomography and employing virtual reality technology. The aim of this study was to determine the sensitivity, specificity, and diagnostic accuracy of CT colonography compared with colonoscopy in a prospective, blinded study in one single institution in Italy. **METHODS:** Ninety-nine patients randomly selected among those attending the open-access endoscopy unit for diagnostic colonoscopy underwent colonoscopy and spiral CT. The images obtained were transmitted to generate the virtual colonoscopy pictures. A supervisor compared the results with the findings of conventional colonoscopy. **RESULTS:** CT colonography diagnosed seven of eight tumors, one being missed because the patient had been inadequately prepared. In 28 patients, CT colonography identified 26 polyps of 45 (57.8% sensitivity, 92.6% specificity, 86.7% positive predictive value), regardless of their size. The sensitivity in detecting colonic polyps was 31.8% (7/22) in the first 25 cases and 91.6% (11/12) in the last 20 patients. CT colonography missed one flat adenoma, some angioectasias and colonic lesions because of portal hypertension in one patient, Crohn's disease ulcers in two patients, and ulcerative colitis lesions in three. **CONCLUSIONS:** CT colonography shows poor sensitivity for identifying colonic polyps and does not always detect neoplastic lesions. Flat lesions are impossible to see by this method.

Am J Gastroenterol 2001 Feb;96(2):394-400

An initial experience with screening for colon polyps using spiral CT with and without CT colography (virtual colonoscopy).

BACKGROUND: Computed tomographic (CT) colography (virtual colonoscopy) is a new imaging method for detection of colon polyps and cancer. **OBJECTIVE:** To evaluate the sensitivity of CT colography for polyp detection in a population without symptoms that included persons without colon neoplasia and with radiologists blinded to colonoscopic findings. **METHODS:** Forty-six persons without symptoms underwent spiral CT followed by same-day colonoscopy with subsequent inspection of two-dimensional axial CT images, interactive multiplanar images, and surfaced and volume-rendered images of the colon (three-dimensional CT colography). **RESULTS:** Three-dimensional CT colography was superior to two-dimensional axial imaging for detection of colon polyps. Three-dimensional CT colography depicted 1 of 4 (25%) adenomas 2 cm in diameter or larger, 6 of 10 (60%) adenomas 1 to 1.9 cm, 6 of 14 (43%) 6 to 9 mm, and 7 of 65 (11%) 5 mm in diameter or smaller. Three-dimensional CT colography showed a polyp that might have led to colonoscopy in 3 of 4 (75%) patients whose largest adenoma was 2 cm or larger, 5 of 6 (83%) patients with largest adenoma 1 to 1.9 cm, 3 of 7 (43%) patients with largest adenoma 6 to 9 mm, and 4 of 16 patients (25%) with largest adenoma 5 mm or smaller. Large, flat adenomas of the right colon were difficult to identify with three-dimensional CT colography. The specificity of three-dimensional CT colography for patients with adenomas 1 cm in diameter or larger was 89%. Examination of patients with missed adenomas after unblinding indicated that meticulous bowel preparation and adequate distention are critical to accurate interpretation. Perceptual errors were common. **CONCLUSIONS:** CT colography as performed in this study is not adequate as a colorectal cancer screening test. Several technical factors that appear critical to accurate performance of CT colography are defined.

Gastrointest Endosc 1999 Sep;50(3):309-313

Increased plasma homocysteine is an independent predictor of new coronary events in older persons.

A prospective study investigated the association of plasma homocysteine and other risk factors with the incidence of new coronary events at 31 +/- 9 month follow-up in 153 men and 347 women, mean age 81 +/- 9 years. The stepwise Cox regression model showed that significant independent predictors of new coronary events in older persons were age (risk ratio 1.041), plasma homocysteine (risk ratio 1.073), current cigarette smoking (risk ratio 2.524), hypertension (risk ratio 2.032), diabetes mellitus (risk ratio 2.022), serum total cholesterol (risk ratio 1.013), serum high-density lipoprotein cholesterol (risk ratio 0.925), and serum triglycerides (risk ratio 1.004).

Am J Cardiol 2000 Aug 1;86(3):346-347

Mammograms obtained with rhodium vs molybdenum anodes: contrast and dose differences.

OBJECTIVE: A mammography unit with both a molybdenum anode and a rhodium anode, filtered with molybdenum and rhodium, respectively, was evaluated to determine which types of women would benefit from the dose savings of the rhodium combination despite some loss of contrast. **SUBJECTS AND MATERIALS:** In 100 women, the molybdenum anode and molybdenum filtration (Mo/Mo) were used to obtain mammograms of the right breast, and the rhodium anode and rhodium filtration (Rh/Rh) were used for mammograms of the left breast. All mammograms were obtained at 26 kVp. All milliampere-second values used to radiograph the breasts of these women were recorded. Mammograms of 54 women (30 with previous mammograms available), representing the four types of breasts as defined by the American College of Radiology, were interpreted by three radiologists. Each mammogram was assigned a grade for breast type, preference (Rh/Rh, Mo/Mo, or previous mammograms), contrast, and sharpness. **RESULTS:** Overall, mammograms obtained by using the Mo/Mo combination were preferred. However, for images of types 3 and 4 breasts, Rh/Rh was preferred twice as often as it had been for mammograms of types 1 and 2 breasts. The mean glandular dose for all breast types when the Rh/Rh combination was used was 42% of the dose used for the Mo/Mo combination. For a 6-cm-thick dense breast, the Rh/Rh combination required 40% of the dose required for the Mo/Mo combination. **CONCLUSION:** Mammograms

obtained with the Rh/Rh combination carried an overall decrease in contrast and mean glandular dose. However, for young women and some women with large dense breasts, the Rh/Rh mammograms were equivalent to or better than the mammograms obtained with the Mo/Mo combination. Effective use of Rh/Rh units requires careful selection of women based on age or the amount of glandular tissue seen on previous mammograms.

AJR Am J Roentgenol 1994 Jun;162(6):1313-1317

Continued on Page 3 of 4

[Back to the Magazine Forum](#)

ABSTRACTS

Page 3 of 4

Radiation

Management of radiation-induced accelerated carotid atherosclerosis.

Patients with long survival following cervical irradiation are at risk for accelerated carotid atherosclerosis. The neurologic presentation in these patients mimics naturally occurring atheromatous disease, but patients often present at younger ages and with less concurrent coronary or systemic vascular disease. Hypercholesterolemia also contributes to this accelerated arteriosclerosis. Angiographic findings in this disorder include disproportionate involvement of the distal common carotid artery and unusually long carotid lesions. Pathologic findings include destruction of the internal elastic lamina and replacement of the normal intima and media with fibrous tissue. This article describes two surgical patients with radiation-induced accelerated carotid atherosclerosis who typify the presentation and characteristics of this disease.

Arch Neurol 1987 Jul;44(7):711-714

Differential radiation response of cultured endothelial cells and smooth myocytes.

In vivo observations have suggested that endothelial cells are the most radiosensitive elements of the vascular wall. To test whether this represents an intrinsic differential sensitivity, the response of bovine aortic endothelial cells and smooth myocytes was investigated in confluent cell cultures exposed to single doses of gamma radiation (250, 500, 1,000 or 2,000 rad). Both cell types showed a dose-dependent decrease in attachment efficiency when dissociated and replated at six hours after radiation. However, the attachment efficiency in both cell types was similar when a 72-hour postirradiation incubation period was used prior to dissociation of the cells. Growth inhibition was significantly greater (7- to 10-fold) in endothelial cells than in myocytes when examined four days after attachment. Confluent endothelial monolayers showed a dose-dependent, progressive cell loss during the 72-hour postirradiation period (70% after 1,000 rad); the myocyte cultures showed no radiation effect on the cell numbers. In spite of the reduction in number, the endothelial cells maintained the continuity of their monolayer by compensation with an increase in mean cell size. Endothelial cells developed multiple structural lesions, including an increase in the number and size of residual and lysosomal bodies, electron-lucent cytoplasmic defects, interruptions in the plasma membrane and irregular aggregation of chromatin, causing electron-lucent nuclei. These changes increased in severity with time and dose and were most pronounced 24 to 72 hours after 1,000 rad. No significant ultrastructural alterations were detected in myocytes four days after 2,000 rad.

Anal Quant Cytol 1982 Sep;4(3):188-198

Resonant formation of DNA strand breaks by low-energy (3 to 20 eV) electrons.

Most of the energy deposited in cells by ionizing radiation is channeled into the production of abundant free secondary electrons with ballistic energies between 1 and 20 electron volts. Here it is shown that reactions of such electrons, even at energies well below ionization thresholds, induce substantial yields of single- and double-strand breaks in DNA, which are caused by rapid decays of transient molecular resonances localized on the DNA's basic components. This finding presents a fundamental challenge to the traditional notion that genotoxic damage by secondary electrons can only occur at energies above the onset of ionization, or upon solvation when they become a slowly reacting chemical species.

Science 2000 Mar 3;287(5458):1658-1660

Establishment of a radiation- and estrogen-induced breast cancer model.

It is well accepted that cancer arises in a multistep fashion in which exposure to environmental carcinogens is a major etiological factor. The aim of this work was to establish an experimental breast cancer model in order to understand the mechanism of neoplastic transformation induced by high LET radiation in the presence of 17beta-estradiol (E). Immortalized human breast cells (MCF-10F) were exposed to low doses of high LET alpha particles (150 keV/microm) and subsequently cultured in the presence or absence of E for periods of up to 10 months post-irradiation. MCF-10F cells irradiated with either a single 60 cGy dose or 60/60 cGy doses of alpha particles showed gradual phenotypic changes including altered morphology, increase in cell proliferation relative to the control, anchorage-independent growth and invasive capability before becoming tumorigenic in nude mice. In alpha

particle-irradiated cells and in those cells subsequently cultured in the presence of E, increased BRCA1, BRCA2 and RAD51 expression were detected by immunofluorescence staining and quantified by confocal microscopy. These studies showed that high LET radiation such as that emitted by radon progeny, in the presence of estrogen, induced a cascade of events indicative of cell transformation and tumorigenicity in human breast epithelial cells.

Carcinogenesis 2000 Apr;21(4):769-776

Induction of a bystander mutagenic effect of alpha particles in mammalian cells.

Ever since the discovery of X-rays was made by Rontgen more than a hundred years ago, it has always been accepted that the deleterious effects of ionizing radiation such as mutation and carcinogenesis are attributable mainly to direct damage to DNA. Although evidence based on microdosimetric estimation in support of a bystander effect appears to be consistent, direct proof of such extranuclear/extracellular effects are limited. Using a precision charged particle microbeam, we show here that irradiation of 20% of randomly selected A(L) cells with 20 alpha particles each results in a mutant fraction that is 3-fold higher than expected, assuming no bystander modulation effect. Furthermore, analysis by multiplex PCR shows that the types of mutants induced are significantly different from those of spontaneous origin. Pretreatment of cells with the radical scavenger DMSO had no effect on the mutagenic incidence. In contrast, cells pretreated with a 40 microM dose of lindane, which inhibits cell-cell communication, significantly decreased the mutant yield. The doses of DMSO and lindane used in these experiments are nontoxic and nonmutagenic. We further examined the mutagenic yield when 5-10% of randomly selected cells were irradiated with 20 alpha particles each. Results showed, likewise, a higher mutant yield than expected assuming no bystander effects. Our studies provide clear evidence that irradiated cells can induce a bystander mutagenic response in neighboring cells not directly traversed by alpha particles and that cell-cell communication process play a critical role in mediating the bystander phenomenon.

Proc Natl Acad Sci U S A 2000 Feb 29;97(5):2099-2104

Clustered DNA damages induced in isolated DNA and in human cells by low doses of ionizing radiation.

Clustered DNA damages-two or more closely spaced damages (strand breaks, abasic sites, or oxidized bases) on opposing strands-are suspects as critical lesions producing lethal and mutagenic effects of ionizing radiation. However, as a result of the lack of methods for measuring damage clusters induced by ionizing radiation in genomic DNA, neither the frequencies of their production by physiological doses of radiation, nor their reparability, nor their biological effects are known. On the basis of methods that we developed for quantitating damages in large DNAs, we have devised and validated a way of measuring ionizing radiation-induced clustered lesions in genomic DNA, including DNA from human cells. DNA is treated with an endonuclease that induces a single-strand cleavage at an oxidized base or abasic site. If there are two closely spaced damages on opposing strands, such cleavage will reduce the size of the DNA on a non-denaturing gel. We show that ionizing radiation does induce clustered DNA damages containing abasic sites, oxidized purines, or oxidized pyrimidines. Further, the frequency of each of these cluster classes is comparable to that of frank double-strand breaks; among all complex damages induced by ionizing radiation, double-strand breaks are only about 20%, with other clustered damage constituting some 80%. We also show that even low doses (0.1-1 Gy) of high linear energy transfer ionizing radiation induce clustered damages in human cells.

Proc Natl Acad Sci U S A 2000 Jan 4;97(1):103-108

Induction of a senescence-like phenotype in bovine aortic endothelial cells by ionizing radiation.

Treatment of confluent monolayers of bovine aortic endothelial cells (BAEC) with gamma rays resulted in the delayed appearance of cells with an enlarged surface area that were morphologically similar to senescent cells. The majority of these cells stained positively for senescence-associated beta-galactosidase (SA-beta-gal), indicating that these cells are biochemically similar to senescent cells. The incidence of the senescence-like phenotype increased with dose (5-15 Gy) and time after irradiation. Cells with a senescence-like phenotype began to appear in the monolayer several days after irradiation. The onset of the appearance of this phenotype was accelerated by subculturing 24 h after irradiation. This acceleration was not entirely due to stimulation of progression through the cell cycle, since a high percentage of the senescent-like cells that appeared after subculture were not labeled with BrdUrd during the period after subculture. Prolonged up-regulation of expression of CDKN1A (also known as p21 (CIP1/WAF1)) after irradiation was noted by Western blot analysis, again suggesting a similarity to natural senescence. Phenotypically altered endothelial cells were present in the irradiated monolayers as long as 20 weeks after irradiation, suggesting that a subpopulation of altered endothelial cells that might be functionally deficient could persist in the vasculature of irradiated tissue for a prolonged period after irradiation.

Radiat Res 2001 Sep;156(3):232-240

Ionizing radiation accelerates aortic lesion formation in fat-fed mice via SOD-inhibitable processes.

Ionizing radiation promotes formation of reactive oxygen species, including the superoxide anion (O₂⁻). To evaluate whether O₂⁻ or

O₂—mediated perturbations may contribute to the known atherogenic effects of radiation, we examined aortic lesion formation in irradiated C57BL/6 mice and evaluated the effects of CuZn-superoxide dismutase (CuZn-SOD) overexpression. Ten-week-old mice were exposed to a 2-, 4-, or 8-Gy dose of 250-keV x-rays to the upper thorax and then placed on a high-fat diet for 18 weeks. Based on quantitative lipid staining of serial sections of the proximal aorta, mean lesion area was increased with increasing radiation dose and was 3-fold greater in 8-Gy-irradiated than sham-irradiated mice (7800±2140 versus 2635±709 micrometer²), P<0.05). These effects were absolutely dependent on a high-fat diet, which had to be introduced within 1 to 2 weeks of the radiation exposure, suggesting the early involvement of atherogenic lipoproteins that were elevated in response to the diet. The importance of radiation-induced oxidative stress was supported by the observation of a 2-fold lower mean lesion area in irradiated CuZn-SOD transgenic mice than in their irradiated, nontransgenic littermates (3026±1590 versus 6102±1834 micrometer²), P<0.05). Lucigenin-enhanced chemiluminescence, used as an index of aortic O₂⁻ concentrations, was significantly elevated in the postradiation period, and this response was reduced in CuZn-SOD transgenics. On the basis of these results, we propose that radiation may be a useful tool for initiating oxidative or redox-regulated events that promote atherogenesis and for testing the antiatherogenic properties of antioxidants.

Arterioscler Thromb Vasc Biol 1999 Jun;19(6):1387-1392

Continued on Page 4 of 4

[Back to the Magazine Forum](#)

ABSTRACTS

Page 4 of 4

Effects of radiation on endothelial function.

PURPOSE: The response of endothelium to ionizing radiation was studied. **METHODS AND MATERIALS:** The abdominal aorta in different experimental groups of rats was irradiated, and the response of arterial rings from the irradiated segments to norepinephrine, acetylcholine (ACh), and nitroglycerin (NTG) was studied. Nonirradiated thoracic segments in the same experimental animals were used as a control for comparisons. Two age-matched nonirradiated control groups were also studied. **RESULTS:** A poor endothelium-dependent vasodilator response was obtained with ACh in the irradiated rings and also in those not directly irradiated; the endothelium-independent vasodilator response to NTG was preserved during the first 3 days after irradiation. By 6 months, both the endothelium-dependent response and endothelium-independent response were impaired. **CONCLUSIONS:** Alterations in nitric oxide synthesis and/or release by the endothelium were observed during the early phase of radiation in irradiated and nonirradiated segments. In the delayed phase of radiation, endothelium-independent muscular relaxation was also affected.

Int J Radiat Oncol Biol Phys 1998 Jul 1;41(4):905-913

Enhancement of prostate cancer xenograft growth with whole-body radiation and vascular endothelial growth factor.

Prostate cancer research has been limited by the slow growth of human prostate tumors in athymic rodent models. This study sought to determine if low-dose radiation and vascular endothelial growth factor (VEGF) could enhance the development of PC-3 human prostate adenocarcinoma xenotransplanted into nude mice. Whole body radiation (2 Gy) was delivered only once, whereas VEGF (39 ng total/mouse) was injected subcutaneously over a 17-day period. The combination of the two agents, compared to nontreated controls, resulted in significantly higher tumor incidence (100% versus 50%) and more-rapid tumor progression (1288 mm³ versus 190 mm³ by day 60). Treatment-associated changes were observed in body weights and assays of blood and spleen cells. In addition, ³H-thymidine uptake by PC-3 cells cultured in the presence of VEGF and transforming growth factor-beta 1 was compared. These results show that low-dose, whole-body radiation and VEGF can be used in concert safely and effectively to facilitate growth of PC-3 prostate tumor and that the mechanisms of interaction may involve leukocyte modulation.

Anticancer Res 1997 Mar;17(2A):923-928

Ionizing radiation enhances platelet adhesion to the extracellular matrix of human endothelial cells by an increase in the release of von Willebrand factor.

The effect of radiation on the secretion of von Willebrand factor by endothelial cells was studied in a three-compartment culture system. The release of von Willebrand factor was significantly increased at 48 h after a single gamma-radiation dose of 20 Gy in both the luminal and abluminal direction by 23 ($P < 0.05$) and 41% ($P < 0.02$), respectively. To establish whether the enhanced production of von Willebrand factor affected the thrombogenicity of the extracellular matrix, platelet adhesion to the matrix produced by a monolayer of cultured endothelial cells during 48 h after irradiation was analyzed in a perfusion chamber at high shear rate (1300 s⁻¹). Platelet adhesion was significantly increased by irradiation both in the presence and in the absence of plasma von Willebrand factor by 65 ($P < 0.05$) and 34.5% ($P < 0.005$), respectively. Incubation of the perfusate with a monoclonal antibody that blocks the binding of von Willebrand factor to platelet GPIb (CLB-RAg 35) resulted in an almost complete inhibition of platelet adhesion. These data indicate that radiation enhances platelet adhesion to the extracellular matrix by an increase in the release of von Willebrand factor by endothelial cells. This event may be important in early radiation-induced vascular pathology.

Radiat Res 1994 Feb;137(2):202-207

Targeted cytoplasmic irradiation with alpha particles induces mutations in mammalian cells.

Ever since x-rays were shown to induce mutation in *Drosophila* more than 70 years ago, prevailing dogma considered the genotoxic effects of ionizing radiation, such as mutations and carcinogenesis, as being due mostly to direct damage to the nucleus. Although there was indication that alpha particle traversal through cellular cytoplasm was innocuous, the full impact remained unknown. The availability of the microbeam at the Radiological Research Accelerator Facility of Columbia University made it possible to target and irradiate the cytoplasm of individual cells in a highly localized spatial region. By using dual

fluorochrome dyes (Hoechst and Nile Red) to locate nucleus and cellular cytoplasm, respectively, thereby avoiding inadvertent traversal of nuclei, we show here that cytoplasmic irradiation is mutagenic at the CD59 (S1) locus of human-hamster hybrid (AL) cells, while inflicting minimal cytotoxicity. The principal class of mutations induced are similar to those of spontaneous origin and are entirely different from those of nuclear irradiation. Furthermore, experiments with radical scavenger and inhibitor of intracellular glutathione indicated that the mutagenicity of cytoplasmic irradiation depends on generation of reactive oxygen species. These findings suggest that cytoplasm is an important target for genotoxic effects of ionizing radiation, particularly radon, the second leading cause of lung cancer in the United States. In addition, cytoplasmic traversal by alpha particles may be more dangerous than nuclear traversal, because the mutagenicity is accomplished by little or no killing of the target cells.

Proc Natl Acad Sci U S A 1999 Apr 27;96(9):4959-4964

Mutagenic effects of a single and an exact number of alpha particles in mammalian cells.

One of the main uncertainties in risk estimation for environmental radon exposure using lung cancer data from underground miners is the extrapolation from high- to low-dose exposure where multiple traversal is extremely rare. The biological effects of a single alpha particle are currently unknown. Using the recently available microbeam source at the Radiological Research Accelerator Facility at Columbia University, we examined the frequencies and molecular spectrum of S1- mutants induced in human-hamster hybrid (A(L)) cells by either a single or an exact number of alpha particles. Exponentially growing cells were stained briefly with a nontoxic concentration of Hoechst dye for image analysis, and the location of individual cells was computer-monitored. The nucleus of each cell was irradiated with either 1, 2, 4 or 8 alpha particles at a linear energy transfer of 90 keV/microm consistent with the energy spectrum of domestic radon exposure. Although single-particle traversal was only slightly cytotoxic to A(L) cells (survival fraction approximately 0.82), it was highly mutagenic, and the induced mutant fraction averaged 110 mutants per 10⁵ survivors. In addition, both toxicity and mutant induction were dose-dependent. Multiplex PCR analysis of mutant DNA showed that the proportion of mutants with multilocus deletions increased with the number of particle traversals. These data provide direct evidence that a single alpha particle traversing a nucleus will have a high probability of resulting in a mutation and highlight the need for radiation protection at low doses.

Proc Natl Acad Sci U S A 1997 Apr 15;94(8):3765-3770

Direct evidence for the participation of gap junction-mediated intercellular communication in the transmission of damage signals from alpha-particle irradiated to nonirradiated cells.

It has generally been considered that important biological effects of ionizing radiation arise as a direct consequence of DNA damage occurring in irradiated cells. We have examined this hypothesis by exposing cells to very low fluences of alpha-particles, similar to those emitted by radon gas, such that as few as 1% of the cells in a population are traversed by a particle and thus receive any radiation exposure. By using the endpoints of changes in gene expression and induction of DNA damage, we show that nonirradiated "bystander" cells participate in the overall response of confluent density-inhibited populations of cultured fibroblast and epithelial cells. By in situ immunofluorescence techniques and the use of cells genetically compromised in their ability to perform gap junction intercellular communication, we present direct evidence for the involvement of connexin43-mediated intercellular communication in the transmission of damage signals to nonirradiated cells. Induction of the stress-inducible p21 (Waf1) protein in aggregates of neighboring cells far exceeding the fraction of cells whose nucleus has been traversed occurred in gap junction-competent cells only. These changes in p21(Waf1) expression correlated with both the induction of DNA damage (as measured by micronucleus formation) as well as increased Ser-15 phosphorylation of p53.

Proc Natl Acad Sci U S A 2001 Jan 16;98(2):473-478

Differential radiation response of cultured endothelial cells and smooth myocytes.

In vivo observations have suggested that endothelial cells are the most radiosensitive elements of the vascular wall. To test whether this represents an intrinsic differential sensitivity, the response of bovine aortic endothelial cells and smooth myocytes was investigated in confluent cell cultures exposed to single doses of gamma radiation (250, 500, 1,000 or 2,000 rad). Both cell types showed a dose-dependent decrease in attachment efficiency when dissociated and replated at six hours after radiation. However, the attachment efficiency in both cell types was similar when a 72-hour postirradiation incubation period was used prior to dissociation of the cells. Growth inhibition was significantly greater (7- to 10-fold) in endothelial cells than in myocytes when examined four days after attachment. Confluent endothelial monolayers showed a dose-dependent, progressive cell loss during the 72-hour postirradiation period (70% after 1,000 rad); the myocyte cultures showed no radiation effect on the cell numbers. In spite of the reduction in number, the endothelial cells maintained the continuity of their monolayer by compensation with an increase in mean cell size. Endothelial cells developed multiple structural lesions, including an increase in the number and size of residual and lysosomal bodies, electron-lucent cytoplasmic defects, interruptions in the plasma membrane and irregular aggregation of chromatin, causing electron-lucent nuclei. These changes increased in severity with time and dose and were most pronounced 24 to 72 hours after 1,000 rad. No significant ultrastructural alterations were detected in myocytes four days after 2,000 rad.

Incidence of female breast cancer among atomic bomb survivors, 1950 to 1985.

An incidence survey among atomic bomb survivors identified 807 breast cancer cases, and 20 second breast cancers. As in earlier surveys of the Life Span Study population, a strongly linear radiation dose response was found, with the highest dose-specific excess relative risk (ERR) among survivors under 20 years old at the time of the bombings. Sixty-eight of the cases were under 10 years old at exposure, strengthening earlier reports of a marked excess risk associated with exposure during infancy and childhood. A much lower, but marginally significant, dose response was seen among women exposed at 40 years and older. It was not possible, however, to discriminate statistically between age at exposure and age at observation for risk as the more important determinant of ERR per unit dose. A 13-fold ERR at 1 Sv was found for breast cancer occurring before age 35, compared to a 2-fold excess after age 35, among survivors exposed before age 20. This a posteriori finding, based on 27 exposed, known-dose, early-onset cases, suggests the possible existence of a susceptible genetic subgroup. Further studies, involving family histories of cancer and investigations at the molecular level, are suggested to determine whether such a subgroup exists.

Radiat Res 1994 May;138(2):209-223

Endothelial alkaline phosphatase activity loss as an early stage in the development of radiation-induced heart disease in rats.

Alkaline phosphatase activity of capillary endothelial cells in the heart of Wistar and Sprague-Dawley rats was studied sequentially after single doses of 10, 15, 20 or 25 Gy. Following irradiation capillary density and alkaline phosphatase activity were focally lost before myocardial degeneration or clinical symptoms of heart disease developed. Recovery from both changes took place after doses of 10 or 15 Gy. The decrease in capillary density and enzyme activity showed the same strain difference in latency times and in the extent of the lesions as previously described for pathological and clinical signs of heart disease.

Radiat Res 1987 Apr;110(1):118-128

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

LifeExtension®

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.