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POTENTIAL TREATMENT OF INFLAMMATORY AND PROLIFERATIVE DISEASES BY ULTRA-LOW DOSES OF IONIZING RADIATIONS

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□ Ultra-low doses and dose- rates of ionizing radiation are effective in preventing disease which suggests that they also may be effective in treating disease. Limited experimental and anecdotal evidence indicates that low radiation doses from radon in mines and spas, thorium-bearing monazite sands and enhanced radioactive uranium ore obtained from a natural geological reactor may be useful in treating many inflammatory conditions and proliferative disorders, including cancer. Optimal therapeutic applications were identified via a literature survey as dose-rates ranging from 7 to 11μGy/hr or 28 to 44 times world average background rates. Rocks from an abandoned uranium mine in Utah were considered for therapeutic application and were examined by γ-ray and laser-induced breakdown fluorescence spectroscopy. The rocks showed the presence of transuranics and fission products with a γ-ray energy profile similar to aged spent uranium nuclear fuel (93% dose due to β particles and 7% due to γ rays). Mud packs of pulverized uranium ore rock dust in sealed plastic bags delivering bag surface β,γ dose-rates of 10-450 μGy/h were used with apparent success to treat several inflammatory and proliferative conditions in humans.

Keywords: Hormesis, Therapy, Radioactive, Rocks

INTRODUCTION

Radiation standards in 1934 were 1 mSv/day for the NCRP [National Council of Radiation Protection & Measurements] and 2 mSv/day for the ICRP [International Commission on Radiological Protection]. Neither dose limit was associated with a measurable increased risk of cancer or any other disease (Taylor 1980). Low doses of γ-and x-rays and low dose-rates from β- and γ-rays exhibit significant hormetic effects based on many observations in epidemiological and experimental studies (Luckey 2008a; Sanders 2010). Protective adaptive response mechanisms are activated by low linear-energy-transfer (LET) radiation doses < 100 mSv (or combined low- and high-LET doses in the indicated range) that can result in reduction in the level of inflammatory and proliferative diseases (Dauer *et al.* 2010). Low doses of ionizing radiation may be useful in preventing cancers in high-risk populations, such as in heavy cigarette smokers, as well as in curing early stage cancers (Scott and Di Palma 2006; Sanders 2008).

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Natural radiation sources are available that may have therapeutic application. A natural nuclear reactor was revealed in Oklo in Gabon, Africa in an area containing a 70% uranium oxide ore seam up to meter(s) thick. Both fission products and transuranic radionuclides were found at this site. Overall, the isotopic composition of the Gabon uranium ore resembled that of aged spent nuclear fuel (Cowan 1976; Meshik 2004). A natural nuclear reactor(s) appears also to have been operational in a high uranium sandstone formation of the Colorado Plateau.

A variety of developing, but rudimentary, low-dose radiation therapy strategies have been evaluated with respect to treating chronic inflammatory and proliferative diseases using natural radiation sources (Yamaoka *et al.* 2004;Falkenbach *et al.* 2005; Takatori *et al.* 2010; Lewis 2011). These include radon therapy in abandoned mines and spas, therapy using thorium-bearing monazite sand, ultra-low doses of x-ray and γ-ray exposures and β/γ exposures from uranium-bearing rocks resembling aged spent nuclear fuel.

METHODS AND RESULTS

Radioactive sandstone rocks for use in low-dose radiation therapy were obtained from an abandoned uranium mine near Monticello in San Juan County, UT. Ore from this mine contained the highest concentration of uranium (up to 87% U_3O_8). The ore was contained within a matrix of calcareous sandstones (filling interstices in the sandstone) and conglomerates colored dark gray to black. Small flat rocks from the mine were examined separately or were pulverized into a fine dust placed in heavy plastic bags as 'mud packs' of sizes that ranged from about 10 to 30 cm square. The packs helped to minimized dose in-homogeneity.

Beta/gamma dose-rates for the radiation sources were measured in Pritchett, Colorado with an 'Inspector Alert' nuclear radiation monitor manufactured by International Medcom (United States) and differential γ-ray dose-rates were measured in Korea with a γ-detector which had a photon energy range of 30 keV to 1.2 meV. The natural background γ dose-rate at 91 cm above the ground was 0.28 μGy/h in Daejeon, Korea and 0.55 μGy/h in Pritchett, Colorado. Gamma-ray spectroscopy was performed on the surface area of a small flat rock (8 x 5 x 0.6 cm) that had a surface γ-dose-rate of 11μGy/h. The spectrum was quite different from that seen with typical uranium ore samples (Figure 1). Presumptive radionuclides detected in the Utah rock included ^{214}Bi, ^{214}Pb, ^{125}Xe, ^{226}Ra, ^{133}Ba, ^{196}Au, ^{111m}Cd, ^{114}In, ^{237}Pu and ^{242}Am. This made the rocks considerably more radioactive than typical uranium-bearing mine samples. Laser-induced breakdown fluorescence spectroscopy was used for elemental analysis on a small flat rock (7 x 5 x 1 cm) that had a dose rate of 9.8 μGy/h. The entire rock had a high vanadium content. One circular area had a high uranium content which was associated with a small

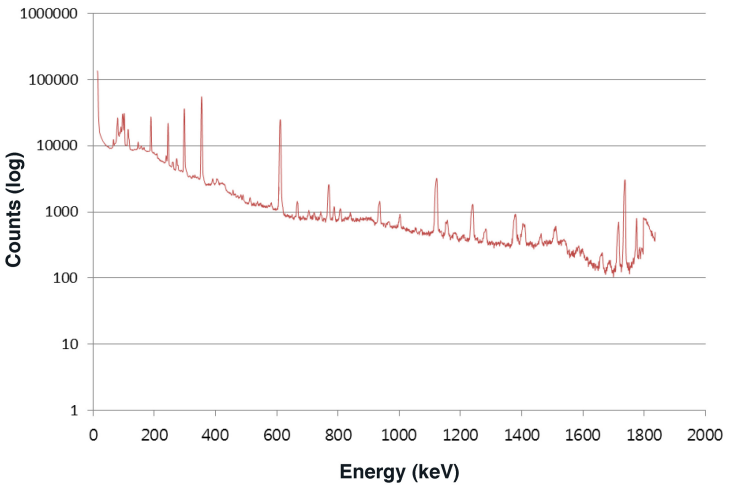

FIGURE 1. Surface γ-ray spectroscopy of a small flat rock from a uranium mine in Utah; the surface γ-dose-rate was 11μGy/h.

amount of americium (spectral lines 356.916 nm, 367.312 nm, and 466.279 nm).

Beta/gamma dose-rates for the surface of rocks and mud packs ranged from ~10 to 500 μGy/hr. The γ-ray surface dose-rates ranged from ~1 to 70μGy/h. The γ-ray dose rate in air was determined at intervals up to 28 cm from the rock surface for six rocks which had surface dose-rates of 9.8 to 43 μGy/hr. The mean half-value distance for γ-rays in air was about 1.5 cm with 10% of surface dose-rate found at about 8.5 cm and 2.5% of the surface dose found at 20-28 cm from the rock surface. The dose-rate distribution with increasing distance from the rock surface is not what one would expect from a single γ-ray photon because it represents a composite of hundreds of different γ-ray energies.

The differential air dose contribution by radiation types for rocks and mud packs were 93% β and 7% γ at their surface. No significant differences were noted in β/γ differential air dose contributions among the rocks or packs. The maximum range of β-particles, with energies > 0.8 MeV, in soft tissue is about 1/2 their energy in MeV given as range in cm. Thus, a 2.3 MeV β-particle has a range of about 1.1 cm and a 1.1 MeV β-particle has a range of about 0.5 cm in soft tissue. The vast majority of β-energy from the rock samples would be absorbed by the first cm of skin.

All experimental dose-rates from the rocks or mud packs were taken at their surface or at intervals of distance in air from their surface. Dose-rates were either combined β + γ radiation or γ radiation alone. Dose was determined as a simple measure of dose-rate in μGy/h x time in hours.

Two cases closely observed by the author were successfully treated (with their consent) by uranium ore mud packs:

Case 1: A dozen 3-7 mm warts on a 5 x 8 cm skin patch near the knee, had been repeatedly treated about every six months, with cryosurgery for the last 10 years. The warts were treated with a 12 cm square mud pack for a few hours a day for six continuous weeks; the dose-rate was 70 μGy/hr and the total dose was 15 mGy. The warts and cryosurgical scars disappeared by 6 weeks and have not returned after 24 months. The skin was healthy and normal following treatment. Treatment was not been repeated.

Case 2: Two raised lesions of seborrheic keratoses on the left shoulder about 5 cm apart were treated with a 1cm thick 7 x 15 cm flat radioactive rock for a few hours a day for four consecutive weeks; the dose-rate was 250 μGy/h and the total dose was 19 mGy. The lesions disappeared and have not returned after 44 months. The skin was healthy and normal following treatment. Treatment was not repeated.

A more recent case is presented of a 50 year-old woman who was diagnosed with adenocarcinoma of the left breast by needle biopsy on September 2011. A PET scan showed no metastatic disease and no lymph node involvement. She declined chemotherapy, radiation therapy or surgery. In the spring of 2012, the patient developed a cough and breathing difficulty that was evaluated by x-ray, showing multiple nodules in both lungs consistent with metastatic disease. The primary tumor size at this time was a firm mobile mass of 10 cm in diameter. She went to Pritchett, Colorado in early April 2012 where she received near continuous exposures to the front and back of the chest from mud packs delivering an average of about 100 μGy/hr at the pack surface. Total dose to the chest after 7 weeks of continuous therapy was ~150 mGy. The size of the primary tumor decreased about 40% in diameter at this time with improvement in breathing and cough. Observations a few weeks later by a different physician indicated that the primary tumor was 'dead' being comprised of necrotic tissue. The patient subsequently received high dose radiotherapy to the head for brain metastases and is currently receiving low dose iv chemotherapy along with near continuous treatment with mud packs.

Case studies have also been provided by Jay Gutierrez (personal communication, 2012) from individuals seen at his radon clinic in Pritchett, Colorado. A medical doctor (MD) is also associated with the clinic. Among medical conditions claimed by Gutierrez to have positive responses to low-dose radiation therapy using radioactive rocks/packs are cancer, ragweed allergy, Dupuytren's contracture, Meniere's disease, wet retinopathy, rheumatoid arthritis and circulatory failure associated with diabetes. Total doses used were estimated to be in the range 10-500 mGy, chronically given over weeks to months. Sufficient medical records and dose details are not available to adequately document these cases.

DISCUSSION

Cellular Mechanisms of Radiation Hormesis

Early 20th century radioprotection limits were based on the maximum permissible dose that implied the existence of a threshold. The LNT assumption was introduced later as a substitute and applies to stochastic effects such as cancer and genetic changes. The LNT assumption suggests that carcinogenic and other stochastic health effects, do not exhibit a threshold, and are cumulative over a lifetime. A single-hit (to cell nucleus) model of radiation-induced mutations (which can lead to cancer) provided the rationale for the LNT assumption, based initially on observations of mutations in fruit fly germ cells (Muller 1927). Muller's work involved very high X-ray doses so that no conclusive results could be obtained related to low radiation doses and he ignored data that showed a threshold at what was then considered low doses (Calabrese 2011), but were quite high compared to today's definition of low dose (< 100 mGy). Koana et al. (2004) found a threshold at about 1000 mGy for somatic mutations in fruit flies. In a later study, the frequency of sex-linked recessive lethal mutations in fruit fly germ cells was significantly lowered from the un-irradiated control group by a γ-ray dose of only 500 μGy (Ogura 2009). This observation can be considered to be a protective bystander effect, since at the indicated dose fewer than one electron track (from ionizing events) per cell would be expected. The protection relates to an adaptive response occurring as a result of the mild radiation stress imposed.

DNA damage and other stresses can trigger a highly conserved, anti-cancer, anti-aging survival response (adaptation) that suppresses metabolism and growth and boosts defenses that maintain the integrity of the cell (Hoeijmakers 2009). Protective cellular responses to ionizing radiation include DNA repair, intracellular metabolic redox reactions, cell cycle checkpoint controls, intra- and inter-cellular signaling cascades, apoptosis and mitotic linked cell death. These mechanisms are activated by low radiation doses that result in non-linear responses, producing an adaptive response that reduces the spontaneous or background level of cell transformations, cancer, heart disease or other diseases (Dauer *et al.* 2010).

Thresholds and Hormesis in Radiation Carcinogenesis

Natural background radiation varies by geographic location up to nearly three orders of magnitude (0.5 to 300mSv/y). No increase in mortality from diseases has been observed for people living in high background dose regions (Mortazavi and Karam 2005). Data on deaths from all causes and cancers among workers in the nuclear industry were evaluated by the International Agency for Research on Cancer (Vrijheid *et al.* 2007). The low SMRs for all-cancer mortality (0.74) and all-cause mortal-

ity (0.62) are examples of radiation hormesis rather than a HWE (Healthy Worker Effect) (Kojiro 1999; Fornalski and Dobrzynski 2009, 2010). These data are consistent with the earlier findings (Luckey 2007; 2008b; Rockwell and Muckerheide, 2008) that workers chronically exposed to low dose radiation exhibit significantly lower SMRs for all mortality and cancer mortality than in unexposed control groups. A study of 250,000 nuclear workers found an average mortality of 67 ± 13% compared to the control group (Luckey 2007, 2008a). A decreased cancer mortality was also observed in radiotherapy patients in organs outside high dose therapy regions of the body (Luckey 2008b). An environmental survey of the US indicates that overall cancer mortality would be negligible at an annual whole-body, presumably low LET radiation dose of 7 mGy (Frigerio *et al.* 1973).

Cancer was significantly reduced (SMR ~0.80) in 240,000 Chernobyl emergency workers who received a dose of 100 mSv (Jaworowski 2010). Several ^{60}Co orphan sources were inadvertently recycled into 20,000 tons of structural steel which was used to construct about 200 residential, industrial and school buildings in 1982 housing 10,000 residents of Taiwan. The average cumulative dose for the exposed residential population was about 50 mSv (Chang *et al.* 1997); the average dose-rate was estimated at11 μSv/h. Only seven fatal cancers were observed out of an expected 232 (SMR = 0.03) (Chen *et al.* 2004). A latter paper showed an observed cancer incidence of 95 out of an expected 115 (SIR = 0.8) which was significantly less than expected (Hwang *et al.* 2006); this paper used 10 year lagging (throwing away radiation dose) for solid cancers, resulting in a misrepresentation of the true dose and cancer risk and also did not provide any SMR values. SIR values that are considerably higher than SMR values for cancer may represent, in part, a therapeutic effect of low dose radiation on cancer progression.

Young adult beagle dogs have been exposed to a variety of α, β, γ radionuclides by ingestion and inhalation, thresholds from 0.5 to 20 Gy were found for leukemia, bone tumor and lung tumor formation in lifespan studies carried out during the last fifty years (Raabe 2010). The threshold dose for bone cancer in radium dial painters was 10 Gy; a large majority of painters received less dose and ended up living longer than the unexposed control population (Sanders 2010). The threshold for lung tumors in rats, dogs and Mayak workers exposed to alpha radiation plutonium-239 aerosols ranged from 0.4 to 0.8 Gy (Sanders and Lundgren 1995; Sanders 2008; Tokarskaya *et al.* 1997) when combined with chronic gamma irradiation. Low LET gamma rays appear to activate natural protection against high-LET alpha-radiation-induced lung cancer from plutonium-239 and also radon-progeny. Greater than 80% of plutonium-239 alpha-radiation-induced rat lung cancers were prevented by chronic, low dose-rate gamma-ray exposure. Interestingly, lifetime expo-

sure to residential radon at the Environmental Protection Agency's action level of 4 pCi L^{-1} appears to be associated with on average a > 60% reduction in lung cancer cases from associated low LET radiations (Cohen 1995, 1997). The threshold for lung cancer in humans exposed to low LET radiation ranges from 1-2 Gy (Sanders and Scott 2008).

Optimal Beneficial Doses and Dose-Rates

Very small doses and dose-rates of radiation often exhibit significant health hormetic effects based on observations in epidemiological and experimental studies (Sanders 2010). Low doses and dose rates of ionizing radiation have been defined by UNSCEAR and BEIR VII as those below 100-200 mGy and below 50-100 mGy/min, respectively. Uniform, whole-body, continuous, low-LET radiation exposure was estimated to cause no excess risk of radiation-induced cancer at dose-rates < 150 mSv/y in humans (Keirim-Markus 2002). For the system studied, the adaptive response operates within these dose and dose-rate limits.

An inverse dose-rate effect has been observed with low LET radiations for radioadaptive cellular and therapy mechanisms (Gridley *et al.* 2005; Leonard 2007). A low dose/dose-rate microdosimetry model for radiation hormesis has been proposed (Feinendegen 2003) based on observations in mammalian cells. Cellular lesions are eliminated by the disappearance of genomically damaged cells at doses < 10 mGy while repair systems are activated at > 10 mGy. An adaptive response is seen in mammalian cells between a dose range of < 1 mGy and 100 mGy for a single low-LET exposure (Mitchel 2010). The consequences of oxyradical-caused cell damage is reduced once a cell has sensed the radiation by an electron or photon traversal.

The adaptive response causes genomic instability related outcomes, such as cell transformation and chromosomal aberration formation, to decrease below the normal background or spontaneous levels following exposure to ultra-low doses and dose-rates. Cellular hormesis responses from natural and anthropogenic sources of radiation are similar (Pollycove and Feinendegen 2003). However, dose-rates from anthropogenic radiation sources are typically much higher than from natural sources (Ulsh 2010).

Bio-positive effects were estimated to be between 1 mSv and 1000 mSv/y (Luckey, 2008a; Gregoire and Cleland, 2006). Radiation protocols showing evidence of radiation hormesis for γ-dose-rates are found in the 1-50 μSv/hr dose-rate range. Optimal bio-positive effects were estimated to be at a dose-rate of 100 mGy/yr or 11 μGy/hr given as a continuous exposure (Cuttler and Pollycove 2009). Luckey (2008a) estimated the optimal radiation level as 60 mGy/yr or 6.9 μGy /hr. Luckey (2008b) also estimated that 50 mSv/y would reduce cancer mortality to near zero and

that the elimination of cancer deaths would increase lifespan by about 10 years.

Are there optimal photon energies that stimulate hormetic reactions? A few studies have examined the role of photon energy. Experimental evidence is limited. Lower energy x-rays were more efficient in inducing genomic instability than γ-rays while higher energy γ-rays and 60 kvp x-rays were more efficient in activating the Protective Apoptosis Mediated (PAM) response than 28 kvp x-rays (Scott 2005). If you could chronically deliver the right gamma ray energy spectrum to critical cellular sites at the same time, then you might expect to see more significant positive biomedical effects, both in prevention and in therapy for inflammatory and proliferative diseases, at ultra-low dose- rates.

Tumor Cell Response at Low Doses

Low dose radiation-induced enhancement of apoptosis and self-destruction of transformed or pre-cancerous cells represents a potential control system during carcinogenesis (Bauer, 2007). Tumor cell apoptosis is stimulated by < 10 mGy of low-LET radiation (Cotter 2009).Very low priming doses increase latency for cancer induction in experimental animals (Wolff 1996; Tapio and Jacob 2007).Very low dose-rates cause cell transformation at 2 mGy/day (Elmore *et al.* 2009), simulate apoptosis in mice with knock-out gene at 1.2 mGy/hr (Ina and Sakai 2005), suppress thymic lymphoma at 1.2 mGy/hr (Ina *et al.* 2005), increase lifespan at 25-50 x background dose (Caratero *et al.* 1998), and suppress methylcholanthrene-induced skin tumors at 1.2 mGy/hr (Sakai *et al.* 2003).

Low dose radiotherapy modulates the immune-inflammatory response (Rodel *et al.* 2007). A dose of 200 mGy enhanced phagocytosis by macrophages and increased $CD8^+$ T cell production in mice (Pandey *et al.* 2005). LDR (Low Dose Radiotherapy) up-regulated genes that encode cytokines at doses as low as 100 mGy (Barcellos-Hoff 1998). Continuous gamma ray exposure (100 mGy per year) prolonged lifespan, suppressed B-cell lymphoma formation and increased $CD49^+$ cell production in mice (Lacoste-Collin *et al.* 2007). A single dose of 100-200 mGy x-rays to mice reduced lung metastases from implanted syngeneic L1 sarcoma cells, while also increasing NK cell numbers (Cheda *et al.* 2004).

Single daily doses of 330 μGy at 700 μGy/hr in mice to a total dose of 146 mGy delivered over a period of 90 weeks inhibited tumorigenesis (Mitchel *et al.* 2008). A dose of 10 mGy increased cancer latency and decreased cancer incidence in cancer prone mice (Mitchel *et al.* 2003). Low doses of TBI (Total Body Irradiation) significantly delayed SaI tumor cell growth in mice (Anderson *et al.* 1982). Lower doses delivered over an extended period of time may preferentially sensitize tumor cells, while inducing radio-resistance in normal cells due to the radio-adaptive response. Continuous administration of ultra-low level radiation with

either ^{125}I seeds or whole body exposure to ^{137}Cs γ-rays significantly increased the efficacy of HDR (High Dose Radiotherapy) for implanted human malignant glioma cells in athymic mice (Williams *et al.* 1998). Low dose TBI reduced the incidence of spontaneous lymphoma in mice (Ishii *et al.* 1996).

A threshold dose-rate effect was seen for skin tumor by localized β-irradiation (Ootsuyama and Tanooka 1991). Exposure of mouse skin to 500 mGy β-irradiation at 24 hr before treatment with methyl-nitro-nitroso guanidine, reduced papilloma formation by five-fold but had no significant effect on carcinoma formation (Mitchel *et al.* 1999). Administration of tritium to mice in drinking water protected against thymic lymphoma formation up to a dose-rate of 900 mGy/day (Yamamoto *et al.* 1998). A dose of 100 mGy of 6 MeV x-rays given 24 hours before start of radiotherapy with 48 Gy in 16 x 3 Gy fractions to dogs with oral cancer caused a cytoprotective effect to surrounding normal tissues (Blankenbecler 2010).

Geology and Radioactivity of Uranium-Bearing Sandstone

Uranium mine tailings are not considered to be significantly radioactive. However, there are exceptions (McLeary 2004; Chareyron 2008; Sengiyumva 2010). Uraniferous mineralization consists primarily of the oxides, uraninite and pitchblende (Augustithis, 1995).The ^{238}U/^{235}U ratio has generally been considered invariant in nature with a value of 137.8. However, two modal values of the isotopic ratio exist with a significant relative difference of 0.03% in uranium ores with the lower mode being found in some mines of the Colorado Plateau. This could be attributed to separation from ^{238}U and depletion of ^{235}U by *in situ* geological nuclear reactions (Cowan and Adler 1976). Uranium deposits form when groundwater with leached uranium is reduced to precipitate uraninite. This is a possible mechanism by which ^{235}U can be fractionated from ^{238}U in ground waters at low temperature in the redox state transition of uranium ($U^{6+} \leftrightarrow U^{4+}$) (Stirling *et al.* 2007) . Sufficient separation and concentration of ^{235}U to ~3% level required to sustain a nuclear reaction appeared to have occurred in the uranium-bearing rocks examined in this study. Water also serves as a neutron moderator.

The contribution from actinides and their daughter products to beta decay in CANDU (CANadianDeuteriumUranium) reactor spent fuel becomes significant after 200 years and is dominant at times greater than 300 years, at which time the radiation dose is predominantly from beta decay (Garisto *et al.* 2009). Very low level levels of transuranics were also found in pitchblende and uraninite ores from Canada and Belgium Congo (Levine and Seaborg 1951; Ridenour 1961). The rocks from Utah also exhibit predominantly beta decay. The presence of 'excess' radioactivity, transuranics and fission products and β, γ dose-distribution in the

Utah rocks indicates a probably origin from an *in situ* nuclear reaction hundreds to thousands of years ago.

Low Dose Radiotherapy for Inflammatory and Proliferative Diseases

A pooled analysis of twenty-eight radon epidemiological studies indicates that radon does not cause lung cancer up to a lung dose of 150 mSv (Fornalski and Dobrzynski 2011). The lung cancer rate in the lowest radon states was nearly four times greater than predicted by the LNT while the lung cancer rate in the highest radon states was one-seventh of the LNT prediction (Rockwell and Muckerheide 2008). The low-LET component from radon progeny was probably responsible for the strong hormetic effect described for lung cancer by Cohen (1995) in an ecological radon study and by Thompson *et al* (2008) in a case-control residential radon study.

Radon therapy is widely available in Europe to treat a variety of chronic inflammatory and painful diseases. These include rheumatoid arthritis, lupus, scleroderma, ankylosing spondylitis, asthma, bronchitis and psoriasis (Erickson 2007). Falkenbach *et al* (2005) described five trials of radon therapy for rheumatoid arthritis, three of which were double-blind that showed beneficial effects. Radon therapy was also effective in treating osteoarthritis (Yamaoka *et al.* 2004), bronchial asthma (Mitsunobu *et al.* 2003), and dyslipidemia associated with cardiovascular disease (Iashina *et al.* 2011). The standard uranium mine therapy for the Free Enterprise Radon Health Mine in Boulder, Montana recommends a stay of 40 hours in the mine spread over 10 consecutive days. The average mine radon concentration is 1200 pCi/l. This gives a cumulative lung dose of ~6 mSv (150 μSv/h). The dose schedule in the Free Enterprise mine has been found effective for treating a variety of inflammatory diseases in several thousand people during the last several decades. The bio-positive effects of radon therapy typically last from 6 to 12 months (Lewis 2011). Similar radiation doses are given in European radon therapy protocols. In comparison, the radioactive rocks from Utah gave β/γ–dose-rates that ranged from 21 to 450 μGy/h and γ-dose-rates that ranged from ~1 to 30μGy/h at the source surface.

India has about 30% of the world's thorium reserves including monazite-bearing beach sands. Monazite contains 2-7% thorium by weight with nearly all thorium comprised of ^{232}Th. Thoriated gas mantles are widely used in India for lighting both outdoors and indoors resulting in annual effective doses of 2 and 8 mSv, respectively (Ramachandran 2010). People in parts of Iran use the ash from burned thorium-containing mantles for healing of skin wounds. Radioactive lantern mantle ash enhanced the healing of excision wounds in the skin of rats (Mortazavi *et al.* 2009). The Kerala and Orissa monazite-bearing beach sands of India give

absorbed γ-dose-rates in air that range to over ten times background rate in most other areas of India (Mahur *et al.* 2009; Rao *et al.* 2009).

A group of four patients with advanced cancer and two patients with severe rheumatoid arthritis and dermatomyositis were exposed to radon and γ-rays from monazite sand for one hour, three times weekly, for a period of 3 to 36 consecutive months. Radon (200 pCi/l) delivered a dose to the lung of 25 μSv/h while monazite delivered 40 μSv/hr from γ-rays. The weekly dose was ~200 μSv and the monthly dose was ~1 mSv. All patients had failed orthodox therapy. In each case bio-positive changes were noted, including a decrease in tumor marker antigens, improved tumor control, and improved appetite, muscle strength and exercise ability (Takatori *et al.* 2010). Advanced cancer patients are currently being treated using thin silicon plates (50 X 50 cm) containing concentrated monazite which give about 2000μSv/h from beta and gamma radiations (Takatori, personal communication).

Prior to and into World War II, Roentgen radiation was used to treated a variety of infections (Kelley 1942). Single and fractionated doses of x-rays of less than 1 Gy were successfully used to cure diphtheria, tuberculosis and gas gangrene, and limit inflammation of arthritis, rheumatism and bronchitis (Cuttler 2004, 2008; Calabrese and Dhawan, 2012) and ulcerative dermatitis (Mitchel *et al.* 2007). Radiotherapy with fractions of mostly 0.3-1.0 Gy and a total dose of 3-12 Gy exerted anti-inflammatory and analgesic effects for painful degenerative disorders. Relatively low dose radiotherapy for joint inflammation was an effective and less toxic alternative to steroids and low dose chemotherapy drugs in treating arthritis (von Pannewitz 1933; Seegenschmiedt *et al.* 2000; Micke and Seegenschmiedt 2002; Niewald *et al.* 2008). Low doses of radiation were effective in treating ulcerative colitis if given chronically over a longer period of time (Mitchel *et al.* 2007). Low dose TBI may control or even cure AIDS (Shen *et al.* 1989, 1997)

Low dose radiation alone or in combination with other agents [e.g., agents that shut down cancer cell survival signaling pathways] has potential use in cancer therapy. Patients with multiple myeloma, lymphoma and nasal carcinoma underwent tumor regression after receiving LDI radiotherapy to a total dose of 1.5 Gy (Cuttler and Polycove 2009). Implanted ^{125}I seeds giving 40-70 mGy/hr, significantly improved survival in glioblastoma patients also given external beam radiotherapy (Scharfen *et al.* 1992). Fractionated whole-body doses (TBI) of 100 mSv or half-body doses (HBI) of 150 mSv delivered three times or two times a week, respectively, for a total dose of 1.5 Sv, significantly improved survival of patients with non-Hodgkin's lymphoma (Choi *et al.* 1979; Sakamoto 2004). Low dose TBI decreased lung metastases (Hosoi and Sakomato 1993). Radiation doses delivered in this study are one to two orders of magnitude lower than those used to treat cancer patients with TBI or HBI, given

at dose-rates that are lower by four orders of magnitude. Low LET radiation inhibits the development of spontaneous and artificial metastases in humans and laboratory animals. This suggests that γ-irradiation may be used to treat and cure cancer and prevent cancer metastases (Nowosielska *et al.* 2010).

Evidence obtained from the review of low dose radiobiological studies in this paper and limited anecdotal observations in individuals given low dose exposure to enhanced radioactive uranium ore, radon and monazite sands should provide motivation to pursue controlled experimental studies in animals and humans to evaluate their possible therapeutic utilization in treating a wide variety of conditions associated with inflammation and cell proliferation. Low-dose radiation was successful in treating warts, a model of virus-induced benign tumor, and seborrheic keratosis, a model of squamous metaplasia. A small dose of radiation may be administered in a continuous fashion or at regular intervals for a long time. However, radiation protocols currently lack any standard dose quantization, dose fractionation and duration of a treatment course. Mathematical models, computer simulations and clinical trials are warranted to exploit the potential of low dose radiation therapy to control and cure chronic and complicated diseases. It appears that low-dose radiation therapy may have far reaching effects in controlling and curing many diseases throughout the world. The application of 'natural' low dose sources of ionizing radiation may be a particularly low cost, common sense method for treating inflammatory and proliferative diseases without apparent side-effects.

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