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INCREASE IN X-RAY SENSITIVITY OF CANCER AFTER EXPOSURE TO 434 MHz ELECTROMAGNETIC RADIATION

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Summary

The proportion of cancer cells killed by using H-wave polarized 434 MHz electromagnetic radiation (Erbotherm UHF 69 generator) applied fifteen minutes before low doses (50 to 80 rads) of X-radiation (140, 220, 330 KV, 4 MeV and CO^{60} sources) is between three and over one hundred times better than X-radiation alone. This increased sensitivity to X-radiation varies with the cancer's site, with physical features of host and cancer, with the cancer growth rate, with the 434 MHz dose, with the nonthermic X-radiation sensitivity and other as yet unknown factors. Fifty-two patients with ear, nose, and throat cancer treated by combined therapy, compared with similar retrospective series treated at normothermic levels, and a series treated under three atmospheres hyperbaric oxygenation, show primary tumor clearance rates of 81%, 32%, and 61% respectively. Survival is correspondingly improved.

The increased radiation sensitivity is partly thermal but also apparently nonthermal in origin. In vivo temperature measurements reveal a maximum differential rise of over 3.0°C in large avascular cancers. X-radiation sensitivity of some cancers after 434 MHz radiation remains enhanced for approximately thirty minutes even when the cancer is cooled to pre-434 MHz treatment temperatures.

Methods and Equipment

Radio frequency energy at 434 MHz has been delivered using standard radiation antennas, coaxial cables and 200 watt 433.69 MHz generators manufactured in West Germany (1). Curved dipole antennas ("mould" radiators), longer straight dipole antennas, and small circular antennas have been used in various situations. A unit of twelve generators and antennas produced by W. Guettner in West Germany under the trade name "Tronado" is used for whole-body therapy (2). Depth dose (3), energy absorption (4) and reflection patterns were established in the early 1960's using animal tissues (Fig. 1). The radiating antenna is designed to produce a maximum H-wave component because this decreases skin heating, increases the depth dose, and produces the most uniform tissue field strengths (5). It is unknown whether these parameters apply to living tissue.

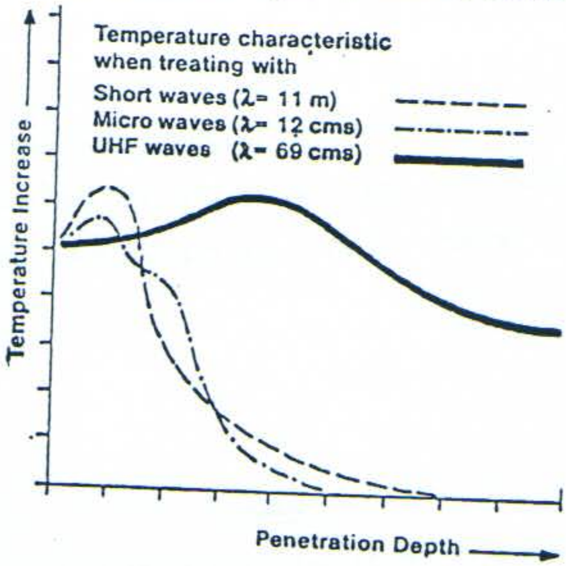

Figure 1. These curves were plotted from measurements in dead tissues which did not contain cancer. There appears to be reasonable penetration of 434 MHz radiation to 10 cm or more depth. (From Erbe Elektromedizin publications).

The output power from each individual radiator was consistently kept at 200 watts. The line voltages used to drive the generator were stabilized to within two percent by a 50 Hz voltage regulator, and the "antenna" current meter, proportional to power output, was calibrated regularly. On a weekly basis the power output was monitored by an in-line watt meter and confirmed to be 200 watts. Also, field strengths near the radiator were checked by a field probe. Our experience has been that the output power over many months of operation has been very stable.

Temperatures in superficial cancers have been monitored using infrared thermography or thermocouples inserted into nylon sheaths preplaced in the cancer. Temperature versus time are recorded starting one-half minute after cessation of 434 MHz radiation and extrapolated back to the time of cessation of irradiation to estimate final tumor temperature. Data from 52 patients have been obtained by the cooling-curve extrapolation technique, and maximal final tumor temperature was approximately 41°. There was considerable variation in final tumor temperature, all the way from only slightly above normal to 41°C. The maximal measured rise of temperature has been 3.5°C in large avascular masses; the typical rise of temperature recorded in normal tissue outside the cancer was about 1°C. This indicates that at this frequency differential heating of cancer tissue can be achieved. At 27 MHz differential heating of cancer occurs, but the effect on cancer differs from that at 434 MHz.

The 434 MHz radiation has not damaged any organ except the skin. A total of 140 hours of irradiation to one patient's skull over six weeks, (three or more hours per day) had no effect on regrowth of hair which was recovering after X-radiation therapy. Healing of wounds, mental or physical activity of the brain, personality and special sense organs were normal. No patient has developed cataract or visual changes. Headaches and eye pains have been noted, but can be avoided by using acetazolamide, one-half gram orally, two hours before treatment, (or by intravenous injection). Three patients have had skin burns; in each case the tumor was very close to the skin and close to the antenna.

A total of nearly one thousand patients has been treated. Erbe generators have been used for twenty years in Europe for physiotherapy without any complications being reported. Skin burning does not occur with careful physiotherapeutic exposures in non-cancerous patients.

Sensitization to X-Irradiation

We desired a technique to quantitate change in radio sensitivity of our cancer patients. Although we recognize that good quantitative estimates of radiosensitivity are difficult to obtain, we nonetheless chose the following formula (which hopefully represents at least in some respects our clinical procedures) as a basis for comparisons of therapy.

$$N_r = N_t[1-(1-e^{-D/D_o})^x]^y$$

N_r is the tumor cell population after treatment, N_t is the tumor cell population before treatment, D is rads per treatment, D_o is the dose required to obtain $N_r = N_t/e$, y is the number of doses of D rads, and x is a constant depending on the cancer type. x can be estimated from data relating cell destruction to x-ray dose.

It is clear that for optimum radiotherapy D_o and x should be small. Hyperbaric oxygen therapy has been used as a radiosensitizer and reported to produce a reduction in D_o by a maximum factor of 2.7. We have conducted extensive tests of x-ray therapy at 41.8°C by simple wax bath hyperthermia and have obtained similar reductions in D_o.

In our calculations for D_o we have assumed x = 2 for a series of 156 treated ear, nose, and throat cancer patients. Most of these cancers were squamous cell cancers for which x is known to be 2. It has been shown that x can be reduced by the application of heat (6).

The observed increase in radiosensitivity (decrease in D_o) after 27 MHz radiation is much poorer than after 434 MHz radiation. It reaches a maximum of about three, coinciding with the maximum temperature, and is approximately the same as that produced from simple whole body hyperthermia by Pettigrew's wax bath method (7) to 41.8°C. Simple experiments using superficial cancers whereby the 434 MHz radiation was delivered and the cancers cooled to their pre-treatment temperature and then given X-ray therapy, show that the radiation sensitivity is not solely dependent upon the temperature. Such sensitivity persists for up to thirty minutes after 434 MHz radiation even when the cancer is at normal temperature. Tests have been performed immediately after the cessation of 434 MHz radiation, 15 minutes after, and 30 minutes after. There is a considerable sensitivity enhancement immediately after irradiation, with a slight further increase in sensitivity 15 minutes after irradiation. At 30 minutes post irradiation the sensitivity is sharply reduced. No such residual sensitivity has been observed at 27 MHz.

Results

The clinical subjects consisted of three groups of 52 patients each, all suffering from ear, nose, or throat cancer. The staging of tumors for the three treatment groups is illustrated in Table I. The three methods of therapy are described: 1) X-irradiation alone at 37°C, 2) X-irradiation under three atmospheres hyperbaric oxygen at 37°C, and 3) X-irradiation combined with 434 MHz radiation.

Patients were selected in late stages with tumor sizes greater than 5 centimeters, in earlier or recurrent stages with tumor sizes less than 5 cm, with histologically positive nodes, and with fixed inoperable nodes. Table II lists the primary site of origin of the tumors in the three treatment groups.

Table III summarizes the methods, results, and calculated D_0 values based on the equation given previously. The x-ray treatment group (1) consisted of 200 rads per day (Monday through Friday) over a six week period maximum, depending on the response to treatment. This constituted a total of 6000 rads maximum in six weeks. The hyperbaric oxygen treatment group(2) received six treatments of 600 rads, or seven treatments of 500 rads, for a total of 3600 or 3500 rads, respectively, one treatment per week. Group (3) was subjected to three treatments per week (Monday, Wednesday, and Friday) with 434 MHz treatments each Monday only. Treatments lasted up to a maximum of nine weeks (5400 rads). These patients received 20 minutes of 434 MHz radiation followed by a 15 minute waiting period prior to x-irradiation.

Note that a calculated D_0 value of 140 rads was obtained for group (1), 51 rads for the hyperbaric group (2), and a significant reduction to eight rads was obtained in response to the 434 MHz radiation, group (3).

In addition to these results, 13 patients received whole-body hyperthermia by the hot wax bath method at 41.8°C. The calculated D_0 value for these 13 patients was 50-60 rads. Finally, four patients were treated with 7 MHz radiation similar to group (3) in Table III, resulting in D_0 values greater than 60 rads.

TABLE I

Staging

Group	1	2	3
	Megavoltage x-ray; 37°C	Megavoltage x-ray under 3 Atmosphrs. Hyperbaric Oxygen; 37°C	Megavoltage x-rays combined with 434 MHz radiation
T3 or T4 (late stage >5 cm diameter)	26	23	26
T2 or recurrent (< 5 cm diameter)	23	26	23
N+ (histologically positive nodes)	31	37	28
N_2 or N_3 (fixed inoperable nodes)	23	26	20
Total	52	52	52

The percent of patients without cancer over a three-year period after treatment for the three groups is illustrated in Fig. 2.

TABLE II

Primary Site of Origin

Group	1	2	3
	Megavoltage x-ray; 37°C	Megavoltage x-ray under 3 atmosphrs. Hyperbaric Oxygen; 37°C	Megavoltage x-rays combined with 434 MHz radiation
Salivary carcinomata	2	4	1
Sinuses, ear	2	0	5
Nose, nasopharynx	4	3	2
Palate	2	6	6
Tonsil	9	5	9
Tongue	6	10	5
Mouth	4	4	5
Pharynx	8	6	10
Larynx	6	7	7
Pyriform fossa	9	7	2
Total	52	52	52

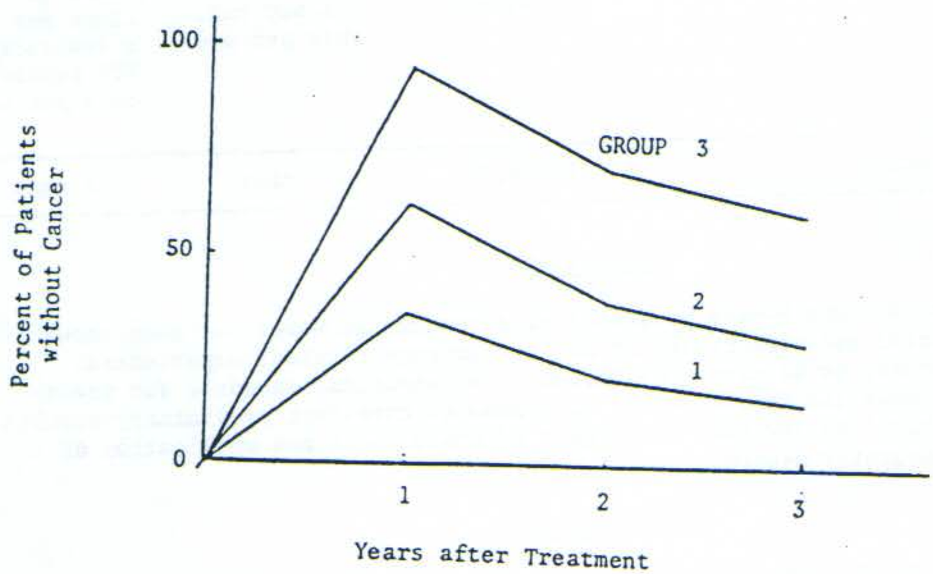

Figure 2. Comparative data of patient response to the three treatment regimens three years past treatment.

TABLE III

Methods, results and radiosensivity (D_0) values

Group	1	2	3
	Megavoltage x-rays; 37°C	Megavoltage x-rays under 3 Atmosphrs. Hyperbaric Oxygen; 37°C.	Megavoltage x-rays combined with 434 MHz radiation
Clinical clearance of primary (T) and nodes (N)	17 (32%)	32 (61%)	42 (81%)
Limited radioactive implant to residual primary and/or nodes	2	0	7
Complete clinical control by above 2 procedures	19 (36%)	32 (61%)	49 (94%)
Recurrences at one year	8/19 (42%)	12/32 (37%)	9/49 (18%)
Subsequent recurrences during second year	3/19	5/32	4/40
Dead, cancer free; during three years after treatment	1	2	3
Treatment Regimine	6000 rads (30 x 200 rads over six weeks)	3500-3600 rads (7 x 500 rads or 6 x 600 rads once per week)	5400 rads. max over 9 weeks (3 times per work x 200 rads) 434 exposure once per week
Calculated D_0 value	140 rads	51 rads	8 rads

Conclusions

The use of 434 MHz H-wave polarized electromagnetic waves has been shown to be an exquisite radiosensitizer in our preliminary clinical experiences. This effect appears to be partly nonthermal. An empirical schedule for treating human ear, nose and throat cancer has produced excellent preliminary results. Further development of physical techniques of measurement and application of such waves is urgently needed.

Acknowledgements

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