

BIOMEDICAL EVALUATION OF THE SIMULTANEOUS EXTERNAL RADIATION AND HYPERTHERMIA INDUCED BY A MINIATURE EM APPLICATOR (434 MHz)

Osinsky S.*,¹ Bubnovskaya L.,¹ Sergienko T.,¹ Mazokhin V.,² Gelvich E.²

¹*Inst. exp. Pathol. Oncol. Radiobiol., NASU, Kiev, Ukraine,*

²*State Res. Product. Co., "Istok", Fryazino, Russia.*

Purpose: to evaluate the antitumor efficacy of simultaneous application of radiation (RT) and local hyperthermia (LHT) applied with a radio-resistant miniature contact microstrip applicator (MCMA), operating at the frequency of 434 MHz.

Materials and methods: Female rats (strain IEPOR bred, with a body weight of 220-250g) bearing subcutaneous Guerin carcinoma were used. Tumors were transplanted into the right flank. All experiments had been approved by the regional animal ethics committee. Treatments were performed when tumors reached a volume of 0.7-0.9 cm³. LHT was administered using a new radio-resistant contact microstrip applicator MCMA, operating at the frequency of 434 MHz (Istok Ltd., Russia). Tumor temperature (⁰T) was measured by means of semiconductor thermoprobes (0.7 mm diameter). One hyperthermic session per treatment was conducted (43⁰C, 45 min). Irradiation was carried out using a γ -rays (⁶⁰Co unit, ROCUS-AM, Russia). The dose rate was 0.83 Gy/min. The total doses of RT were 15 Gy and 20 Gy as a single exposure. RT was commenced on the 15th min of LHT (⁰T under the tumor 43⁰C, usually). The antitumor effect of TRT was evaluated by means of standard criterias. The bioenergetic status of tumor was assessed by ³¹P NMR spectroscopy, tumor choline-containing substances were registered using ¹H NMR. Each treatment group have 3-5 animals, experiments were repeated 2 times. Statistical methods included t-tests and correlation analysis.

Results: The combined RT and LHT treatment was feasible, any kind of serious complications were not registered. It was shown the significant deterioration of tumor bioenergetic under radiation that was accompanied by increase of hypoxic fraction in the tumor. Application of HT in combination with radiation enhances these effects, especially in "simultaneous" group. Cho/Cr ratio was decreased after radiation and not returned to the initial level after 24 and 48 h, thus indicating the significant damage of tumor cells as well as inhibition of their restoration after combined treatment.

Table. Combined treatment of Guerin carcinoma bearing rats (TGD – tumor growth delay, CR – cured rats, SR - skin response, Fowler scoring)

Treatment	TGD (day)	CR (%)	SR (scores)
15 Gy	20	0	3.0
20 Gy	28	0	4.5
15 Gy, in 1.0 h HT (43 ⁰ C, 45 min)	22	40	4.0
20 Gy, in 1.0 h HT (43 ⁰ C, 45 min)	34	50	5.0
15 Gy, simultaneously HT (43 ⁰ C, 45 min)	27	50	5.0
20 Gy, simultaneously HT (43 ⁰ C, 45 min)	32	70	6.0

Above mentioned data have shown that LHT combined with RT both in "sequential" and, especially, "simultaneous" regimes displays significant radiosensitizing effect. TER was calculated as 1.3 for the "simultaneous" schedule. At the same time, TGF value was obtained as 1.2 under these conditions due to the increase of the skin response to radiation simultaneously combined with LHT.

Conclusion:

- 1) Simultaneous EM LHT and RT is feasible and leads to an increase of TER and TGF, though further investigations are warranted.
- 2) Obtained results allow recommend the new miniature contact microstrip applicator (MCMA) for the exploitation in the simultaneous application of radiation and local microwave hyperthermia in biomedical HT experiments.

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