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学位論文の題名	<p>Biological effects of hydrogen peroxide administered intratumorally with or without irradiation in murine tumors. (過酸化水素水腫瘍内投与単独あるいは放射線照射の併用によるマウス腫瘍における生物学的効果)</p> <p>Cancer Science. 108(9): 1787-1792, 2017</p>
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## Abstract

**Purpose:** Despite insufficient laboratory data, radiotherapy after intratumoral injection of hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) is increasingly being used clinically for radioresistant tumors. Especially, this treatment might become an alternative definitive treatment for early and advanced breast cancer in patients who refuse any type of surgery. The purpose of this study was to investigate the biological effects and appropriate combination methods of irradiation and  $\text{H}_2\text{O}_2$  *in vivo*.

**Materials and Methods:** SCCVII tumor cells transplanted into the legs of C3H/HeN mice were used. Chronological changes of intratumoral distribution of oxygen bubbles after injection of  $\text{H}_2\text{O}_2$  were investigated using computed tomography. The effects of  $\text{H}_2\text{O}_2$  alone and in combination with single or five-fraction irradiation were investigated using a growth delay assay. The optimal timing of  $\text{H}_2\text{O}_2$  injection was investigated. Immunostaining of tumors was performed using the hypoxia marker pimonidazole.

**Results:** Oxygen bubbles decreased gradually and almost disappeared after 24 h. Administration of  $\text{H}_2\text{O}_2$  produced 2–3 days' tumor growth delay. Tumor regrowth was slowed further when  $\text{H}_2\text{O}_2$  was injected before irradiation. The group irradiated immediately after  $\text{H}_2\text{O}_2$  injection showed the longest tumor growth delay. Dose-modifying factors were 1.7–2.0 when combined with single irradiation and 1.3–1.5 with fractionated irradiation. Pimonidazole staining was weaker in tumors injected with  $\text{H}_2\text{O}_2$ .  $\text{H}_2\text{O}_2$  injection alone had modest antitumor effects. Greater tumor growth delays were demonstrated by combining irradiation and  $\text{H}_2\text{O}_2$  injection.

**Conclusions:** The results of the present study could serve as a basis for evaluating results of various clinical studies on this treatment.