

REFERENCES

Akima R., Tsuzuki K., Tokuhiko S., Ue H., Ogawa Y. Experimental study of a new enzyme-targeting radiosensitizer (KORTUC) containing hydrogen peroxide & sodium hyaluronate for intra-tumoral injection using mice transplanted with SCCVII tumor. *Jpn J Clin Radiol.* 2009; 54: 1683–88. (In Japanese).

Aoyama N, Ogawa Y, Yasuoka M, et al. Therapeutic response to a novel enzyme-targeting radiosensitization treatment (Kochi Oxydol-Radiation Therapy for Unresectable Carcinomas) in patients with recurrent breast cancer. *Oncol Lett.* 2016; 12(1): 29-34.

Aoyama N, Ogawa Y, Yasuoka M, et al. Therapeutic response to a novel enzyme-targeting radiosensitization treatment (KORTUC II) for residual lesions in patients with stage IV primary breast cancer, following induction chemotherapy with epirubicin and cyclophosphamide or taxane. *Oncol Lett.* 2017a; 13(1): 69-76.

Aoyama N, Ogawa Y, Yasuoka M, et al. Therapeutic results of a novel enzyme-targeting radiosensitization treatment, Kochi Oxydol-Radiation Therapy for Unresectable Carcinomas II, in patients with stage I primary breast cancer. *Oncol Lett.* 2017b; 13(6):4741-7.

Arriagada R, Mouriessse H, Sarrazin D, Clark RM, Deboer G. Radiotherapy alone in breast cancer. I. Analysis of tumor parameters, tumor dose and local control: the experience of the Gustave-Roussy Institute and the Princess Margaret Hospital. *Int J Radiat Oncol Biol Phys.* 1985; 11(10): 1751-7.

Baskar R, Lee KA, Yeo R, Yeoh KW. Cancer and radiation therapy: current advances and future directions. *Int J Med Sci.* 2012; 9(3): 193-9.

Brown JM. The hypoxic cell: a target for selective cancer therapy—eighteenth Bruce F. Cain Memorial Award lecture. *Cancer Res.* 1999; 59(23): 5863-70.

Dalton TP, Shertzer HG, Puga A. Regulation of gene expression by reactive oxygen. *Annu Rev Pharmacol Toxicol.* 1999; 39:67-101.

Demaria S, Pilonis KA, Vanpouille-Box C, Golden EB, Formenti SC. The optimal partnership of radiation and immunotherapy: from preclinical studies to clinical translation. *Radiat Res.* 2014; 182(2): 170-81.

Fang Y, Moore BJ, Bai Q, et al. Hydrogen peroxide enhances radiation-induced apoptosis and inhibition of melanoma cell proliferation. *Anticancer Res.* 2013; 33(5): 1799-807.

Fujita S, Hosokawa Y, Saga R, et al. Apoptotic induction mechanism of X-ray irradiation combined with hydrogen peroxide. *Radiat Environ Med.* 2019 8(2): 85-93.

Griendling KK, Harrison DG. Dual role of reactive oxygen species in vascular growth. *Circ Res.* 1999; 85(6):562-3.

Hammond EM, Asselin MC, Forster D, O'Connor JP, Senra JM, Williams KJ. The meaning, measurement and modification of hypoxia in the laboratory and the clinic. *Clin Oncol (R Coll Radiol).* 2014; 26(5):277-88.

Hayashi N, Ogawa Y, Kubota K, et al. Computed tomography demonstration of the production and distribution of oxygen gas following intratumoral injection of a new radiosensitizer (KORTUC) for patients with breast cancer-Is intratumoral injection not an ideal approach to solve the major problem of tumor hypoxia in radiotherapy? *Cancers (Basel).* 2016; 8(4): 43.

Hitomi J, Kubota K, Ogawa Y, Hamada N, Murata Y, Nishioka A. Non-surgical therapy and radiologic assessment of stage I breast cancer treatment with novel enzyme-targeting radiosensitization: Kochi Oxydol-Radiation Therapy for Unresectable Carcinomas, type II (KORTUC II). *Exp Ther Med.* 2010;1(5):769-75.

Kariya S, Sawada K, Kobayashi T, et al. Combination treatment of hydrogen peroxide and X-rays induces apoptosis in human prostate cancer PC-3 cells. *Int J Radiat Oncol Biol Phys.* 2009; 75(2): 449-54.

Ko EC, Formenti SC. Radiation therapy to enhance tumor immunotherapy: a novel application for an established modality. *Int J Radiat Biol.* 2019; 95(7): 936-39.

Miyatake K, Kubota K, Ogawa Y, Hamada N, Murata Y, Nishioka A. Non-surgical care for locally advanced breast cancer: radiologically assessed therapeutic outcome of a new enzyme-targeting radiosensitization treatment, Kochi Oxydol-Radiation Therapy for Unresectable Carcinomas, Type II (KORTUC II) with systemic chemotherapy. *Oncol Rep.* 2010; 24(5):1161-8.

Morita-Tokuhiro S, Ogawa Y, Yokota N, et al. Development of a novel enzyme-targeting radiosensitizer (New KORTUC) using a gelatin-based hydrogel instead of a sodium hyaluronate. *Cancers (Basel).* 2016;8(1): 10.

Mukai H, Watanabe T, Mitsumori M, et al. Final results of a safety and efficacy trial of preoperative sequential chemoradiation therapy for the nonsurgical treatment of early breast cancer: Japan Clinical Oncology Group Study JCOG0306. *Oncology*. 2013; 85(6): 336-41.

Nishioka A, Ogawa Y, Miyatake K, et al. Safety and efficacy of image-guided enzyme-targeting radiosensitization and intraoperative radiotherapy for locally advanced unresectable pancreatic cancer. *Oncol Lett*. 2014; 8(1): 404-8.

Obata S, et al. Possibility of a "Sentinel Effect" in Chemo-Radiotherapy and a New Radio-Sensitizer Injection (KORTUC). *Jpn J Clin Radiol*. 2018; 63: 317-27 (in Japanese).

Ogawa Y, Kubota K, Ue H, et al. Phase I study of a new radiosensitizer containing hydrogen peroxide and sodium hyaluronate for topical tumor injection: a new enzyme-targeting radiosensitization treatment, Kochi Oxydol-Radiation Therapy for Unresectable Carcinomas, Type II (KORTUC II). *Int J Oncol*. 2009; 34(3): 609-18.

Ogawa Y, Kubota K, Ue H, et al. Safety and effectiveness of a new enzyme-targeting radiosensitization treatment (KORTUC II) for intratumoral injection for low-LET radioresistant tumors. *Int J Oncol*. 2011; 39(3): 553-60.

Ogawa Y, Kubota K, Aoyama N, et al. Non-surgical breast-conserving treatment (KORTUC-BCT) using a new radiosensitization method (KORTUC II) for patients with Stage I or II breast cancer. *Cancers (Basel)*. 2015;7(4):2277-89.

Ogawa Y et al. Basic and Clinical Research of KORTUC. Tokyo: Shinoharashinsha Publishers; 2015 (in Japanese).

Overgaard J. Hypoxic radiosensitization: adored and ignored. *J Clin Oncol*. 2007; 25(26): 4066-74.

Pollack A, Zagars GK, Starkschall G, et al. Prostate cancer radiation dose response: results of the M. D. Anderson phase III randomized trial. *Int J Radiat Oncol Biol Phys*. 2002; 53(5): 1097-105.

Schreck R, Rieber P, Baeuerle PA. Reactive oxygen intermediates as apparently widely used messengers in the activation of the NF-kappa B transcription factor and HIV-1. *EMBO J*. 1991; 10(8):2247-58.

Shibamoto Y, Murai T, Suzuki K, et al. Definitive radiotherapy with SBRT or IMRT boost for breast cancer: excellent local control and cosmetic outcome. *Technol Cancer Res Treat*. 2018;17:1533033818799355.

Sundaresan M, Yu ZX, Ferrans VJ, Irani K, Finkel T. Requirement for generation of H₂O₂ for platelet-derived growth factor signal transduction. *Science*. 1995; 270(5234):296-9.

Tokuhiro S, Ogawa Y, Tsuzuki K, et al. Development of a novel enzyme-targeting radiosensitizer (KORTUC) containing hydrogen peroxide for intratumoral injection for patients with low linear energy transfer-radioresistant neoplasms. *Oncol Lett*. 2010; 1(6):1025-8.

Tsuzuki A, Ogawa Y, Kubota K, et al. Evaluation of changes in tumor shadows and microcalcifications on mammography following KORTUC II, a new radiosensitization treatment without any surgical procedure for elderly patients with stage I and II breast cancer. *Cancers (Basel)*. 2011; 3(3): 3496-505.

Yaogawa S, Ogawa Y, Morita-Tokuhiro S, et al. Serial assessment of therapeutic response to a new radiosensitization treatment, Kochi Oxydol-Radiation Therapy for Unresectable Carcinomas, Type II (KORTUC II), in patients with stage I/II breast cancer using breast contrast-enhanced magnetic resonance imaging. *Cancers (Basel)*. 2015; 8(1): 1.

Ye JC, Formenti SC. Integration of radiation and immunotherapy in breast cancer – Treatment implications. *Breast*. 2018; 38: 66-74.

Samantha Nimalasena , Lone Gothard , et al. Intratumoral Hydrogen Peroxide With Radiation Therapy in Locally Advanced Breast Cancer: Results From a Phase 1 Clinical Trial. *Int J Radiat Oncol Biol Phys*. 2020 Nov 15;108(4):1019-1029. doi: 10.1016/j.ijrobp.2020.06.022

Mio Nakata, Ken Yoshida, Taiju Shimbo, et al. High-dose-rate interstitial brachytherapy with hypoxic radiosensitizer KORTUC II for unresectable pelvic sidewall recurrence of uterine cervical cancer: a case report. *J Contemp Brachytherapy*. 2020 Dec;12(6):606-611. DOI: 10.5114/jcb.2020.101695

Shiro Obata, Yutaka Ishimaru, et al. Actual practice of Kochi oxydol radiation therapy for unresectable carcinomas by intra-tumoral administration of hydrogen peroxide as a radiosensitizer. *Mol Clin Oncol*. 2022 Mar;16(3):68.