**ORIGINAL ARTICLE**

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# Monitoring of response to radiation therapy for human tumor xenografts using $^{99m}$Tc-HL91 (4,9-diaza-3,3,10,10-tetramethyldodecan-2,11-dione dioxime)

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***Purpose:*** Oxygenation status of tumor tissue is an important factor to discriminate it with respect to its radiosensitivity. $^{99m}$Tc-4,9-diaza-3,3,10,10-tetramethyldodecan-2,11-dione dioxime ($^{99m}$Tc-HL91) is retained in hypoxic tissues, making it possible to use it as hypoxic imaging agent. We evaluated if the accumulation of $^{99m}$Tc-HL91 in tumors could aid in the prediction of sensitivity of radiation therapy of cancers. ***Methods:*** Human tumors (the gastric cancer cell line: MKN45, the epidermoid carcinoma cell line: KB-31, and the lung adenocarcinoma cell line: HLC) were xenografted into the thigh of athymic mice and irradiated with a 4 MV linear accelerator. Tumor growth was measured and $^{99m}$Tc-HL91 uptakes in tumors were determined by serial imaging, biodistribution, and autoradiography. ***Results:*** $^{99m}$Tc-HL91 uptake (ratio of $ROI_{tumor}$ to $ROI_{whole\ body}$) in HLC ranged from 1.1 to 8.0%, and it did not show any response to radiation therapy. Major variations were observed in $^{99m}$Tc-HL91 accumulation in MKN45 and KB-31; from 0.7 to 4.7%, and from 1.0 to 7.3%, respectively. Some tumors responded to radiotherapy, while others did not. Tumor response was not dependent on the $^{99m}$Tc-HL91 uptake, tumor size or radiation dose. Comparing $^{99m}$Tc-HL91 uptake in tumors before (B) and after (A) their radiation, uptake (B) was always smaller than uptake (A) for HLC, and they did not respond to irradiation at all. For MKN45 and KB-31, tumors responded to radiation when their uptake (A) was not higher than uptake (B). In contrast, the tumors continued to grow when their uptake (A) was higher than uptake (B). Sequential $^{99m}$Tc-HL91 imaging of KB-31 and their autoradiography indicated that tumors whose $^{99m}$Tc-HL91 uptakes was increased post irradiation were composed of mainly hypoxic cells. On the other hand, many viable areas were observed in tumors when the increase in $^{99m}$Tc-HL91 uptake was relatively small. ***Conclusion:*** $^{99m}$Tc-HL91 uptake in tumors did not always relate to their sensitivities to radiation therapy. Sequential $^{99m}$Tc-HL91 imagings post irradiation showed that the increase in $^{99m}$Tc-HL91 uptake in tumors predicted a poor response to radiation therapy, and that a decrease or no change suggested that radiation therapy would be effective. Monitoring by $^{99m}$Tc-HL91 imaging is a good tool to predict the radiosentivities of tumors.

**Key words:** $^{99m}$Tc-HL91, tumor hypoxia, radiation therapy, prediction, radiosensitivity