cancer, 2 prostatic cancers, 5 breast cancers, 2 parotids cancers and 7 thyroid cancers. Thyroid and parotids cancer occurred mostly in children (respectively 2/2 and 6/7).
Conclusions: This retrospective study confirms the need for long-term follow-up in patients undergoing TBI, principally in children. Nevertheless, young age seems to be a risk factor after TBI regimen irradiation, in particular for parotid and thyroid second cancers).

2029 POSTER

Noninvasive detection of tumour's oxygen status using diffuse optical tomography

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Hypoxia is a key factor of tumor progression and resistance to therapy due to its effects on various metabolic processes. Growing comprehension of its importance in cancer progression and therapy, gave an essential impetus to develop imaging methods to detect and assess tumor oxygen status. Diffuse optical tomography (DOT) is an imaging modality with potential to provide information related to tissue oxygenation. The study objective was to test this approach for tumor's hypoxia identifying and to check its validity by immunohistochemical analysis.
Experiments were performed using white outbreed male rats. Rat's breast cancer-1 and Pliss's lymph sarcoma (6 animals for every tumor model) were transplanted subcutaneously into the right hind-leg of the rats. The tumor sizes at the start of monitoring were about 12 mm. DOT was carried out on the experimental setup with three laser fibers coupled in a single bundle. They scan the studied volume at 684 nm, 794 nm, and 850 nm and provided information about oxygenated hemoglobin and deoxygenated hemoglobin concentrations. Distribution of HbO_2, HHb, total Hb and oxygen saturation was reconstructed numerically. Immunohistochemical analysis with Hypoxyprobe™-1 kit was carried out under Natural Pharmacia International recommendations. Histological material was collected from the centre and periphery of the tumors. The cross-sections were scanned for the FITC (green) fluorescence signal using LSM 510 META. The determined by DOT distribution of the hypoxic areas within the tumor was compared with allocation of pimonidazole positive zones.
Pliss's lymph sarcoma is characterized by rapid growth and early occurrence of necrotic areas. DOT images of this tumor demonstrated the increased concentration of deoxygenated hemoglobin in the centre and the increased concentration of oxygenated hemoglobin at the periphery. The substantial decrease of oxygen saturation was observed in the centre of Plisse's lymph sarcoma as compared with periphery. On the contrary, DOT images of rat's breast cancer-1, which is noted for the rather slow growth and satisfactory oxygenation, showed relatively uniform and high oxygen saturation of the tumor tissue. Immunohistochemial analysis confirmed the distribution of hypoxic and oxygenated areas in both tumor models.
Diffuse optical tomography represents a useful tool for detection and monitoring of oxygen status of the tumors. Its validity was confirmed by the distribution of pimonidazole-positive zones on two different tumor models.

2030 POSTER

Experimental study of a new enzyme-targeting radiosensitizer containing hydrogen peroxide & sodium hyaluronate for intra-tumoral injection using mice transplanted with SCCVII tumor

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Background: In radiation therapy (RT), it is known that low oxygen environment decreases effect of RT. We have developed a new enzyme-targeted radiosensitization treatment named KORTUC I using a hydrogen peroxide (H_2O_2) solution (Oxydol) for superficially exposed & unresectable neoplasms (Ogawa Y et al. Oncol Rep 19: 1389–1394, 2008), based on our experimental results demonstrating H_2O_2 as a strong radiosensitizer (Ogawa Y et al. Int J Mol Med 12: 453–458, 845–850, 2003, 14: 845–850, 2004). When H_2O_2 is injected into tumor tissue, anti-oxidative enzymes such as peroxidase/catalase is inactivated. Moreover, oxygen is generated from degradation of H_2O_2 by peroxidase/catalase, and hypoxic tumors can be reoxygenated. In our previous study, it was concluded that the most suitable combination of drugs for preserving high intra-tumoral oxygen concentration is sodium hyaluronate & H_2O_2 (Tokuhiro S et al. Radiother Oncol 90: S84, 2009). In this study, the effect of radiosensitization treatment using H_2O_2 & sodium hyaluronate was studied on the transplanted SCCVII tumor of female C3H/He mice following RT.
Materials and Methods: For the experiment, PBS alone (control), PBS containing 0.5 w/v% H_2O_2 (PBS-H_2O_2), and 0.8 w/v% sodium hyaluronate containing 0.5 w/v% H_2O_2 (hyaluronate-H_2O_2), were prepared just prior to the injection, respectively. First of all, approximately 10^5 cells of SCCVII tumor were inoculated into right hind thigh of each of C3H/He mice. And when each tumor grew up to approximately 10 mm in diameter, RT of 30 Gy of 6 MeV electron beam following injection of 0.25 ml of the each combination of drugs mentioned above were performed. For irradiation, mice were anesthetized, and were fixed on an apparatus specially developed for local irradiation of mice (Ogawa Y et al. Int J Raidat Oncol Biol Phys 9: 533–537, 1983).
Results & Conclusions: The growth of the tumors in the group that had been given RT combined with intratumoral injection of hyaluronate-H_2O_2 was remarkably inhibited, and there was a statistically significant difference between the group and another groups receiving RT alone or RT combined with intratumoral injection of PBS-H_2O_2. Moreover, in the group receiving RT combined with intratumoral injection of hyaluronate-H_2O_2, the tumors in three mice disappeared macroscopically. In this experimental study, it was concluded that radiosensitizing effect was achieved by adding sodium hyaluronate to H_2O_2 as has already been shown clinically in our recent paper (Ogawa Y et al. Int J Oncol 34: 609–618, 2009, Radiother Oncol 90: S73, 2009).

2031 POSTER

Potential biomarkers of a complete response and local control for definitive chemoradiotherapy in resectable esophageal squamous cell carcinoma

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Background: Definitive chemoradiotherapy (CRT) has curative potential for patients with esophageal squamous cell carcinoma (ESCC), especially at a resectable stage. However, there is considerable locally persistent/recurrent disease after definitive CRT and salvage esophagectomy may increase morbidity and mortality. The ability to predict CRT outcomes in individual patients would greatly aid therapeutic planning. This study sought to identify molecular markers that predict the response to CRT for resectable ESCC.
Materials and Methods: Tumor biopsy specimens were taken from 38 patients with ESCC who had received definitive CRT between October 2001 and January 2005. All tumors were considered resectable, but the patients chose CRT as the initial treatment and were recruited in a phase II clinical trial at our hospital that consisted of two cycles of cisplatin and fluorouracil with split-course concurrent radiotherapy of 60 Gy in 30 fractions. The patient characteristics were as follows: median age 63.5 (range 45–79) years, 35 males and 5 females, and Stage I, IIA, IIB, and III in 8, 7, 8, and 15, respectively. The expression of cyclin D1, cyclin A, p21, vascular endothelial growth factor (VEGF), epidermal growth factor receptor (EGFR), urokinase-type plasminogen activator (uPA), and plasminogen activator inhibitor type-1 (PAI-1), the microvascular density (CD34), and cell proliferation activity (Ki-67 labeling index) were evaluated immunohistochemically, and the complete response and local control rates of the patients were analyzed.
Results: At a median follow-up of 47.8 months, the 3- and 5-year overall survival was 65.8 and 63.2%, respectively. Eleven patients underwent salvage esophagectomy. A complete clinical response at the conclusion of CRT was achieved in 29 patients (76.3%) and local control in 17 (44.7%). Univariate analysis showed that the Ki-67 labeling index ($p = 0.038$) was significantly higher in the patients who achieved a CR, and that over-expression of uPA ($p = 0.030$) and VEGF ($p = 0.114$) were unfavorable prognostic factors for local control. Logistic regression analysis showed that uPA and VEGF were independent predictors of local control.
Conclusions: We found that the Ki-67 labeling index and the expression of uPA and VEGF were potential predictive biomarkers of the CRT outcome in ESCC, and we are now investigating these factors in another population as part of the same clinical trial to confirm the results.