Einige Kooperationsveranstaltung für die Hyperthermie in Deutschland
Local hyperthermia in the complex treatment of patients with malignant tumors

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It is generally accepted that hyperthermia is the most powerful modifier of chemo- and radiotherapy. However, hyperthermia in cancer treatment is not widely available. Classical concept of hyperthermia is simple and based on the ability of elevated temperature to enhance cell metabolism, on the one hand, and on the characteristics of tumor blood flow, on the other hand. The blood flow in healthy tissues continuously and significantly increases (approximately 10-fold) as the temperature gets higher (up to 44-45 °C). Compared to the normal tissue blood flow, the tumor blood flow increases slightly (1.5 to 2-fold), and drops sharply if the temperature reaches 42-43°C. The decreased blood flow under conditions of the maximum tumor tissue metabolism leads to the development of hypoxia, acidosis and ultimately to the death of the tumor cells.

**Purpose:** To conduct clinical testing of local hyperthermia Celsius TCS to install in combination with radiation therapy in the combined treatment of patients with malignant tumors of various localizations.

**Materials and methods:** The Tomsk Cancer Research Institute in 2013, a study on the use of local hyperthermia in combination with radiation therapy in patients with malignant tumors of the larynx / hypopharynx, brain, lung, soft tissue, cervical cancer. For two years (2013-2014) treated more than 160 patients. Local hyperthermia was administered to the tumor with 2-3 days from the start of radiotherapy. Duration: 60 minutes at a temperature of 42-45 ° C. The multiplicity: 2-3 times a week. The number of sessions: 8 sessions using hyperthermia to radiotherapy (40-44 Gy) in the preoperative mode and 10-12 sessions at radical course of irradiation (60-70 Gy). The effect of treatment was assessed 3-4 weeks. Methods: diagnostic ultrasound, CT and MRI.
The greatest number of patients treated with local hyperthermia: patients with cancer of the larynx / hypopharynx (n- 46) and soft tissue sarcomas (n-32).

**Results:** The preliminary treatment outcomes were analyzed for 40 patients with laryngeal cancer and 6 patients with laryngopharyngeal cancer (T1-3N0-2M0). Out of these patients, 26 received 40 Gy preoperative radiation therapy and 20 patients received 60 Gy radiotherapy. Local hyperthermia (8-10 sessions) resulted no in radiation-induced skin damage. Preventive tracheostoma was not an obstacle for the treatment. Laryngeal and laryngopharyngeal cancer patients with tumor regression < 50% or stable disease underwent surgery. The extent of surgery depended on the location of the primary tumor and its size. Resection of the larynx was performed in 10 patients, laryngectomy combined with lymphodissection in 8 patients, laryngectomy in 6 patients and resection of the pharynx with plastic repair of the defect by musculocutaneous flap in 2 patients. Histological examination of surgical specimens revealed that complete pathological response was achieved in all patients who received combined modality treatment. Patients with laryngeal and laryngopharyngeal cancer, having tumor regression > 50% received radiotherapy combined with local hyperthermia.

Patients with soft tissue sarcomas (n-32) represented another large group of patients who received preoperative radiation therapy in combination with local hyperthermia. Local hyperthermia applied to a tumor resulted no in serious complications. Radiotherapy was well tolerated by patients and none of the patients showed any markedly pronounced radiation-induced reactions. Soft tissue edema was observed in 6 patients (19%), requiring no further treatment. Only 1 patient (3%) experienced radiation-induced dermatitis resulting in the interval prolongation before surgery. External beam radiotherapy did not affect the postoperative period. Purulent necrotic complications were observed in 3 patients (9%). None of the patients had disease progression.
Partial tumor regression was observed in 19 (59 %) patients. The remaining patients had stable disease. Pathological tumor response of grade 3 was noted in 22 (69 %) patients, of grade 2 in 6 (19 %) patients and of grade 1 in 4 (12 %) patients. In addition to the above cancer localizations, local hyperthermia combined with radiation therapy was used for glioblastoma, locally advanced cervical cancer and lung cancer. In all cases, tumor regression or stable disease were achieved.

**Conclusion:** Local hyperthermia was shown to be a promising treatment modality, which is capable of increasing the sensitivity of cancer cells to radiation therapy, thus reducing the recurrence rate and improving long-term survival rates.
Presentation of a prospective Phase II Study with hyperthermia and radiation
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Purpose: To evaluate the objective response and toxicity of transcatheter arterial Chemoembolization (TACE) followed by radiotherapy and hyperthermia (CERT) in hepatocellular carcinoma patients with portal vein tumor thrombosis.

Methods: This study was designed as a single-center, prospective phase II trial. Patients were first treated with TACE by simulation, with the first session of hyperthermia one week later. Ten fractions of 35 gray respiration-gated radiotherapy (RT) started after another week. Six sessions of hyperthermia were delivered twice a week according to an energy escalation protocol. Response evaluation was planned at one month after RT completion using the modified Response Evaluation Criteria in Solid Tumors. Toxicity was determined using the Common Terminology Criteria for Adverse Events Version 4.0.

Results: This interim analysis was conducted on patients enrolled from October 2013 to November 2014. During the study period, 46 patients (90.2 %) who received at least one hyperthermia session were eligible and enrolled. Median follow-up was 6.7 months (range, 2.0 to 15.0 months). Complete response was observed in 10 (21.7 %) patients and partial response in 27 (47.8 %). Most toxicities were grade I or II. One death was related to severe pneumonia of unknown cause in the left lung and one patient could not complete planned treatment because of continuous elevation of bilirubin after TACE. Late, asymptomatic gastroduodenal toxicities were noticed in 13 (28.3 %) patients.

Conclusions: Preliminary evaluation of CERT showed a promising response rate with acceptable toxicities.
Chemoradiotherapy with local hyperthermia vs. chemoradiotherapy alone in locally adv. cervix cancer patients
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Introduction: Among all the patients with newly diagnosed cervix cancer more than a half have locally advanced tumors and most of them are suitable for chemoradiotherapy (CRT) as a definitive treatment. Local radiofrequency hyperthermia (LRH) is known to be a potent chemo- and radiosensitizer, that is why we wished to combine it with CRT for locally advanced cervix cancer (LACC) patients for whom this combination appeared to be the only appropriate method of curative treatment in most of cases. So far there has never been a trial comparing the results of CRT with or without heat in LACC patients. The main aims of the study were to evaluate the feasibility of LRH and CRT, the complications rate and the efficacy of such combination in the definitive treatment of LACC patients including local control rate, disease free survival and event free survival.

Methods: Between October 2012 and November 2014, 37 patients with LACC were treated with CRT in combination with LRH. Twenty nine of them had stage IIb and 8 – stage III according to FIGO staging system. The total dose of radiotherapy given to the point A varied between 74 and 80 Gy. All the patients received cisplatin 40 mg/m2 weekly within the whole course of radiotherapy (4-6 i.v. infusions). LRH was delivered two or three times per week within 1 hour prior to radiotherapy, the median number of sessions – 8 (range 5-10).

Results: All 37 patients completed the treatment planned. Average follow up period was 17.6 months (range from 10 to 27 months).The major acute complications registered were: skin reaction grade I-II (6 pts), vaginal mucositis grade I-II (16 pts), leucopenia grade I-II (4 pts), bladder toxicity grade I-II (3 pts), and bowel toxicity grade I-II (8 pts).
One patient revealed grade III skin toxicity, and 1 experienced grade III leucopenia but this was considered as acceptable. Eleven women did not demonstrate any acute complication at all. Three cases of late toxicity (ulceration of rectum and erosive sigmoiditis or proctitis) were detected within the follow-up period without signs of local progression. The objective clinical response evaluation was performed minimum in two months after the treatment course completion and included physical examination, pelvic and abdominal ultrasound or computed tomography. Clinical complete response was registered in 30 (81.1 %) patients; 13.5 % showed partial response and all of them (as well as the majority of patients with stage III LACC) proceeded for further chemotherapy. Two patients (both young women, about 30 years old) showed local progression and metastatic disease at 2 months follow up. Six patients progressed afterwards, however only 2 of them revealed local relapse, while the other 4 demonstrated distant metastases (liver, bones, lungs or paraaortic lymphnodes) within 5-13 months after treatment completion. Two patients died, one in 5 months after the treatment completion, the second survived within 23 months. Local control at one year was 89.2 %, 1-year event-free survival – 83.8 %, and overall survival at one year was 97.3 %. There were no episodes of profuse bleeding during the treatment period. The majority of patients noted fast pain relief onset after the first LRH sessions.

**Conclusions**: The combination of LRH and CRT is well tolerated without increase in typical acute and late complications rate and can be safely applied for the curative treatment of LACC patients. The treatment leads to positive clinical response development in an absolute majority of patients with good local control and overall survival rates at one year. The first comparison results with chemoradiotherapy of LACC alone will be presented at symposium session.
VORANKÜNDIGUNG

JUBILÄUMSKONGRESS 2016

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Die Deutsche Gesellschaft für Hyperthermie e.V. lädt zu ihrem 20-jährigen Bestehen in die Hauptstadt ein.

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