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Intraoperative radiation therapy (IORT) and chemotherapy in treatment of urinary bladder cancer

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Purpose: Elucidate the role of (IORT) as bladder boost in definitive treatment of bladder cancer

Methods: 18 patients with muscle invasive bladder cancer (T_2- T_3) were subjected to combined modality treatment using cisplatin + radiotherapy. The radiation treatment was performed in (2) phases *Phase I* external beam 44 Gray. *Phase II* IORT 8–15 Mev electrons delivering 12–22 Gray, to the exposed primary site at the time of cystostomy.

Results: 12 out of 18 cases attained complete remission (66.7%). Disease free survival & overall survival rates were 44.4% & 61.1% respectively.

Conclusion: (IORT) bladder boost + chemotherapy attained good response in definitive treatment of bladder cancer as an alternative modality of cystectomy

347 PUBLICATION

Preoperative radiotherapy of schistosomal bladder cancer. Prospective randomised study

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Purpose: To elucidate the impact of preoperative radiation therapy on response rate;recurnce & survival of cancer bladder in Egypt.

Methods: 52 patients "21" received preopeative radiotherapy 44 Gray and "31" cases subjected to cystectomy.

Results: Down staging of cases received radiotherapy T_3 more than T_2 (45% versus 40%). Treatment failure was significantly higher in cystectomy alone group if compared with preoperative radiotherapy group (29% versus 4.7%). The recurrence rate was higher in T_3 than T_2 tumors this was statisticaly significant.

Conclusion: Preoperative radiotherapy significantly improve response & survival in schistosomal bladder cancer

348 PUBLICATION

High-dose-rate brachytherapy after exernal beam irradiation in palliative treatment of squamous cell carcinoma of the esophagus

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Purpose: After external beam irradiation in patients with inoperable squamous cell carcinoma of the esophageus most patients die because of local recurrence of the tumor. In a retrospective study the value of High-dose rate intraluminal brachytherapy to reduce incidence of local tumor recurrence and improve local-tumor-control was evaluated.

Methods: Between 1983 and 1997, 147 patients with inoperable esophageal cancer were treated with external radiotherapy of 50–60 Gy in fractions of 1.8–2.0 Gy per day. Treatment planning was performed individually in various planes by TPS and OSS. 37 patients received a simultaneous chemotherapy with 5-FU and Mitomycin C. 25 patients followed a intraluminal boost therapy in 2–4 fractions with a single dose of 4–8 Gy two weeks after external radiation.

Results: Overall survival after one year was 28% for the whole group (median 10.5 month). Patients with intraluminal brachytherapy showed significant ($p < 0.05$) improvement in survival versus external irradiation alone (1-year-survival 66% vs. 20%, median survival 16 month vs. 9 month). Local disease free survival after one year was 36% in the combination group vs. 12% in external-beam irradiation group ($p < 0.05$). Locai control improved not significantly from 42% in external therapy to 58% in combination group.

Conclusions: Fractionated high-dose-rate brachytherapy performed after external irradiation is a feasible modality in treatment of inoperable esophageal squamous cell carcinoma. We believe it is highly effective to reduce local-tumor-recurrence as well as improve local-tumor-control. Further studies will be needed.

349 PUBLICATION

Dose optimisation of boost irradiation using electron beam in breast carcinoma

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Purpose: The study has been designed to compare the difference between two types of boost treatment planning methods and to obtain optimum dose distrubution.

Method: Ten patients (pts) who had surgical clips placed in the tumor bed at the time of tumor excision were evaluated. At first, treatment field and treatment depth of this pts. were defined according to clinical parameters of the pts. before surgery and incision scars. In the first type of treatment planning since the tumor bed depth was can not be determined, CT scan were done and inner surface of the thorasic wall were covered by 85% reference isodose on the central slice. In the second one, it's aimed that all clips which were within 1 cm in 85% reference dose of each slice encompased in the treatment plan. The changes in field, energy, gantry angle, collimator angle, and field center displacement were evaluated.

Results: It has been shown that in 50% of pts. the energy, in 90% pts. the fields, in 50% of pts. the gantry angles, in 40% of pts. the collimator angles and in 50% of pts. the field centers should have been corrected when the clips were taken in consideration. In the pts. in whom the boost dose planning were done according to the incision scars and clinical findings and the homogeneity correction was not done, dose-volume that took the 75%, 50% and 25% of the target dose were 0–2%, 0–4%, 0–9% respectively. But if the clips were considered and the homogeneity was corrected the volumes were 0–5%, 2–11%, 6–32% respectively.

Conclusion: This study demonstrates that surgical clips and CT scan usage are important to correct the lung tissue volume doses and to do optimum boost treatment planning.

350 PUBLICATION

Re-evaluation of the study design of the phase I clinical trial with BNCT for patients with glioblastoma at the High Flux Reactor Petten (EORTC protocol 11961)

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A radiation dose escalation study on Boron Neutron Capture Therapy (BNCT) was started in 1997 at the Petten epithermal neutron facility, using BSH as boron carrier with 10 glioblastoma patients/cohort in 4 steps, escalating the boron dose defined in the point of the maximal thermal neutron fluence in the head. The other component of this binary system, the 10B content is kept constant in the blood. The systemic toxicity due to BSH was reported during the BNCT and in 3 months thereafter. Acute radiation toxicity is recorded within 90 days after BNCT and late radiation morbidity is detected in a minimum of 6 months. After the treatment of the first ten patients the study design was re-evaluated. The definitions of goals, end points, trial termination, recruitment, unacceptable toxic events and how to interpret the detected toxicity have been stated more precisely, separating the investigation of the feasibility using BSH and the establishment of the qualitative and quantitative radiation Dose Limiting Toxicity (DLT) and the Maximum Tolerated radiation Dose (MTD) under the defined conditions. In addition to the defined quality management of the trial further steps were introduced in order to achieve the maximal unbiased objectivity in the evaluation and interpretation of the detected toxicity.

351 PUBLICATION

Comparative study between respiratory gated conventional 2-D plan and 3-D conformal plan for predicting radiation hepatitis

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Purpose: To evaluate influences associated with radiation treatment planning obtained with the patient breathing freely.

Methods: We compared reduction or elimination of planning target volume (PTV) margins with 2-D conventional plan with inclusion of PTV margins associated with breathing with 3-D conformal therapy. The respiratory non gated 3-D conformal treatment plans were compared with respiratory gated conventional 2-D plans in 4 patients with hepatocellular carcinomas. Iso-

dose distribution, dose statistics, and dose volume histogram (DVH) of PTVs were used to evaluate differences between respiratory gated conventional 2-D plans and respiratory non gated 3-D conformal treatment plans. In addition, the risk of radiation exposure of surrounding normal liver and organs are evaluated by means of DVH and normal tissue complication probabilities (NTCPs).

Results: The vertical movement of liver ranged 2–3 cm in all patients. We found no difference between respiratory gated 2-D plans and 3-D conformal treatment plans with the patients breathing freely. Treatment planning using DVH analysis of PTV and the normal liver was used for all patients. DVH and calculated NTCP showed no difference in respiratory gated 2-D plans and respiratory non gated 3-D conformal treatment plans.

Conclusion: Respiratory gated radiation therapy was very important in hepatic tumors because radiation induced hepatitis was dependent on remaining normal liver volume. Further investigational studies for respiratory gated radiation treatment combined with 3-D conformal treatment are required.

352 PUBLICATION

Measurement of patient entry and exit doses during total body irradiation

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Purpose: There is no standard algorithm to calculate the dose distribution for TBI under translation conditions with commercial treatment planning systems. Therefore it is necessary to observe the applied dose which has to be calculated by hand for several points with in vivo measurements.

Methods: The doses at relevant points of the body are calculated using the beam-zone method and data from systematical phantom measurements. To verify these calculations we use a set of at least 6 up to 12 semiconductor probes which are attached to the patients skin to measure the entrance and exit doses. The dose at body-center can be calculated from these values. The results are corrected for varying patient geometries.

Results: Dose measurements for actual 35 patients show a correspondence between calculated and applied doses in the range of ±10% for the center of the lung and in the range of ±5% for a reference point in the middle of the body.

Conclusion: In the clinical routine the use of semiconductor probes provides an easy and fast way to measure point doses during TBI. This method allows an online verification of calculated doses.

353 PUBLICATION

Intraoperative high dose rate interstitial irradiation of hepatic metastases

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Resection of hepatic metastases offers long-term survival (25–30% 5-year), and possibly cure for selected patients. Thirty per cent of patients undergoing laparotomy for possible resection have unresectable metastatic disease confined only to the liver. Irradiation might provide benefit in median survival if a tumoricidal dose could be administered to the hepatic metastases.

Eligibility criteria included only liver disease with the primary tumor controlled and no extrahepatic involment, no cirrotic liver, acceptable surgical risk, patient life expectancy greater than 3 months and a total volume of potentially unirradiated liver of 30–40% (defined by 3D reconstruction with MRI). All the patients must have been treated at least with a first line of chemotherapy. From July 1998 to February 1999, 7 procedures have been done in our Unit. Patients underwent laparotomy in the operative suite of the Radiotherapy Unit, adjacent to the radiotherapy bunker where the afterloaded high intensity (10 Ci) iridium 192 source is kept. Careful abdominal exploration define both, resectability or implant of hepatic metastases. Liver was mobilized by disecction of the falciform ligament. Patients with resectable lesions underwent lobectomy or wedge resection. Unresectable disease and the scar of resectable metastases are encompassed within a volume implant or implants. Intraoperative ultrasound is employed to confirm diagnosis and for guiding the insertion of the implant covering the area wanted to be irradiated. The dosimetry is done in real time with optimization of the dose to the required volume. After irradiation, the patient is carried back to the operating room, the needles are removed, hemostasis is achieved and abdominal closure is completed. There are not acute or chronic complication referable to irradiation. Hospitalizations were from 8 to 15 days (median 10 days). We will present this early experience and the technical aspects of the Intraoperative radiation therapy technique

354 PUBLICATION

The impact a multileaf collimator (MLC) may have on a departments confidence and quality assurance

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Purpose: To investigate the effect of introducing an MLC into a radiotherapy department. Is confidence affected by the possible 80 variables involved in making a conformal field, compared to none with customised blocks. Can confidence be restored?

Methods: A strict efficient method of Quality Assurance (QA) was employed involving all types and levels of operational staff. Strict protocols and test tools that graphically represented the correct function of the device were used. Methods for physically setting up the MLC during a service or repair that minimised downtime and Physics acceptance were employed.

Results: The MLC specification once proved during acceptance was the base for designing QA tools. Experience using the MLC quickly showed where time was lost and which items or problems most frequently occurred.

Conclusions: The final regimes allow a speedy daily QA and if a problem is detected, is followed by various levels of protocols, and tools, all of which may be carried out efficiently by any trained member of staff. An MLC expert is not required.

355 PUBLICATION

Concurrent radiotherapy and chemotherapy with topotecan and stealth liposomal doxorubicin for the treatment of locally advanced pelvic tumours

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Purpose: Topoisomerases may have an important role in the repair of DNA damages induced by radiotherapy. The feasibility of radiotherapy combination with a topo-I inhibitor (topotecan, Hycamtin®) and a topo-II inhibitor (stealth liposomal formulation of doxorubicin, Caelyx®) was assessed in a pilot study.

Methods: Twelve patients (pts) with locally advanced pelvic tumours were recruited (3 sarcomas, 4 bladder carcinomas, 2 adenocarcinomas of unknown origin and 3 pelvic masses metastatic from cholangiocarcinoma or pancreatic carcinoma). Caelyx was given once every 2 weeks (d1) at a dose of 20 mg/m^2 and, Hycamtin was given 3 times every 2 weeks (d4, 8, 11) at a dose of 1 mg/m^2. Four cycles were given during the course of radiotherapy (64–70 Gy). The regimen was supported with G-CSF 480 μg sc. every Saturday and Sunday. Six received prophylactic use of HuEPO (20.000IU every Saturday and Sunday) and 6 did not.

Results: Complete symptomatic relief was obtained in all pts. Complete response was noted in 6/12 (50%) cases. No severe "in-field" radiation toxicity was observed. None of the pts developed neutropenia. Hemoglobin (Hb) levels were substantially reduced in 6 patients that did not receive HuEPO (mean Hb decrease 1.8 g/dL), while no Hb reduction was noted in pts supported with HuEPO.

Conclusion: Combination of radiotherapy with topotecan and stealth liposomal doxorubicin is feasible, well tolerated and a promising approach for locally advanced inoperable pelvic tumours.

356 PUBLICATION

Subcutaneous administration of Amifostine in patients treated with radiotherapy. A preliminary report

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Purpose: To demonstrate the efficacy of Amifostine (AF) in patients treated with External Beam Radiotherapy (EBRT) plus chemotherapy.

Material and Methods: From January to August 1998 we enrolled in our study 6 patients affected by non small cell lung cancer (NSCLC) at stage IIIb; 6 patients affected by rinoipo-oropharyngeal cancer; 4 affected by cervix cancer. EBRT was delivered with a 6–23 Mv linear accelerator. In all patient treatment doses were >50 Gy. AF was delivered subcutaneously 10 minutes before EBRT with the dosage of 500 mg.