Symposium with Proffered Papers: Re-irradiation: Challenges and clinical evidence

SP-0331
Radiobiological basis of retreatment
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Experimental studies on the retreatment tolerance of previously irradiated tissues have generally been performed in the 1980’s and 90’s, and were mostly limited in scope. Generally, the retreatment tolerance of different tissues and organs differ for early and late responding tissues. Early responding tissues are characterized by rapid proliferation and a clearly defined stem cell compartment (epidermis, mucosal lining of GI-tract) with the timing of response related to the turnover times of stem cells. Except after very severe early reactions these tissues show a complete resturation of tolerance. Late tissue reactions in slowly or non-proliferating tissues show a much more limited long term recovery which is also dependent on the dose of the initial treatment. An example of such a tissue is the lung, contrasting with the kidney that does not show any recovery at all.

A paradoxical exception is the central nervous system, which based on its proliferation characteristics is not expected to show any significant recovery. However, extensive studies in several institutions have shown that the spinal cord shows almost complete recovery when the initial dose is approximately 50-75% of full tolerance.

SP-0332
Clinical evidence after re-irradiation using brachytherapy: review of clinical data
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Purpose: Despite aggressive multimodality treatment protocols used in first-line treatment, a significant proportion of patients with different cancer develop locoregional recurrences in previously irradiated area, typically during the first years of follow-up. Compared to salvage external-beam radiation therapy the salvage interstitial brachytherapy offers clearly better possibility to give high doses without inevitably leading to high complication rates.

Methods and results: The authors analyse and review the role of salvage brachytherapy in previously irradiated patients with breast cancer, prostate cancer, head-and-neck malignancies, Gyn tumors, cancer of anorectal region and other tumors.

An overview of selected results of modern image-guided salvage brachytherapy will be given. The analysis makes evident, that re-irradiation with doses in the range of 55-60 Gy (after previous irradiation up to doses of 60-70 Gy) represents very narrow tightrope walk between realistic tumor control probability and an unacceptable incidence of serious side effects. However, a reasonable number of these patients, if selected carefully, may have a chance for long-term disease control. The observed local control rates of salvage brachytherapy for previously irradiated recurrent head and neck cancer vary very widely between 16% and 86% after 2 to 5 years, for previously irradiated recurrent prostate cancer between 30% and 90%, for previously irradiated recurrent breast cancer about 95%, et cetera. The salvage external beam radiation therapy is in these indications mostly not possible and compared with the results of salvage surgery the salvage brachytherapy seems to offer lower toxicities in all indications.

Conclusion: Salvage interstitial brachytherapy in selected patients with locoregional recurrences in previously irradiated area is for a whole range of tumors proven, safe and effective treatment method with very good long-term data and with minimal toxicity.

SP-0333
Clinical evidence after brachytherapy re-irradiation - head and neck cancer
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Purpose: Re-irradiation of the recurrences in the areas of head and neck (h/n) and upper respiratory tract should always be considered as a risky treatment. These cancers quite often need to be radiate the second time because of their relapse and clinical advancement in the primary examination. High dose rate brachytherapy (HDR-BT) is very useful in short time tumor dose delivering when external beam radiotherapy (EBRT) is not possible to depot once more after previous treatment failure. Pulsed dose rate brachytherapy (PDR-BT) is safe but longer method of salvages and according to differences in recovery times allows better sparing healthy tissue during second radiation treatment. The aim of this work was to analyze the results and complications rates of another radiation treatment patients with recurrent tumors in head and neck and upper respiratory tract.

Material and methods: 47 patients with h/n and 22 with larynx/trachea (l/t) recurrent cancers were enrolled to the study. The mean time of the recurrence after diagnosing of the disease and first treatment was 9,7 months. 50 patients were treated by the HDR brachytherapy (5 doses of 4 Gy) and 19 by PDR-BT with total dose ranged between 20-40 Gy (0,8 Gy per pulse) with one or two stage treatments (respectively 9 and 4 doses). HDR-BT and PDR-BT were performed with a remote afterloading microSelectron unit (192Ir source) after planning procedure (Oncentra system). Mean age of patients undergoing observation was 50,1 years.

In three l/t patients, BT procedures were performed in combination with simultaneous chemotherapy. In 16 patients cytoreduction of the tumor preceded interstitial, surgical catheter placement. Local control, survival rates and tolerance of the treatment were discussed.

Results: The remission after 1,3,6 months after treatment and early complication were assessed. In 15% patients complete remission (CR), in 65,9% partial remission (PR) and 10,6 % no response for brachytherapy (NR) were stated; in the other (8,5%) patients there were progression (P) of the tumor. Percentages of remission after 3 and 6 months were:

CR - 10,6 % and 6,4%, PR - 53,2% and 36,2%, NR and P - 36,2% and 57,4%, respectively. For the I/t group complete and partial remissions in 6 months treatment time were achieved in 20% patients, survival rate 24 months after BT were estimated for 22%. Progression of the disease was noted in 60% of cases. The most common side effect was superficial
necrosis - 74.5% in 6 months observation time for each: HDR-BT and PDR-BT method in h/n. Serious late side-effects were seen in two patients (9%) - l/t and PDR-BT group.

Conclusions: 1. HDR and PDR both had similar percentages of side effects. 2. Early complications due to the total radiation dose are frequent and needs to be treated by intensive pharmacology. 3. HDR or PDR are effective tools in tumor recurrence radiation treatment, when surgical procedure is impossible and using another EBRT schedule very dangerous for the patient. 4. Future studies should aim to determine the maximum tolerated dose and appropriate patient selection.

Key words: head and neck cancer, HDR brachytherapy, PDR, recurrence, salvage treatment.

OC-0334
Reirradiation plus hyperthermia for irresectable recurrent breast cancer; size matters
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Purpose/Objective: Irresectable locoregional recurrent breast cancer in previously irradiated area is a life threatening disease and optimal treatment is still a matter of debate. Re-irradiation combined with hyperthermia (reRT+HT) is a valid treatment option. Four hundred and fourteen patients were treated with reRT+HT in the AMC (n=301) and the BVI (n=113), from January 1982 up to January 2006. We calculated response rates and local control (LC). Prognostic factors for tumor control were analysed in a multivariable analysis, with special emphasis on tumor size.

Materials and Methods: All patients previously received radiation, overlapping the current reRT field, to a median dose of 50Gy with or without boost. Median interval between initial treatment and reRT+HT was 54 months (range, 3-469). Most patients (80%) received one or more courses of systemic therapy in the past. The median age was 57 years at start of reRT+HT. The estimated tumour size was >10cm in 48% of patients (range 0.2 - 26 cm). Distant metastases (DM) were present in 36% of patients and 74% had experienced previous recurrence episodes (range, 1-13). ReRT consisted typically of 8x4Gy, twice a week (AMC) or 12x3Gy, four times a week (BVI). Superficial hyperthermia was added once (ACM)/twice (BVI) a week using 434MHz Contact Flexible Microstrip Applicators. Treatment quality was monitored by 60 minutes, or later 75 minutes, depending on patients’ tolerance using the HYPERcollar, aimed at achieving 43°C in the target region. Treatment quality was monitored by patient specific hyperthermia pre-treatment planning alone. RT was given using either external beam irradiation (Cyberknife or IMRT) or interstitial patient specific hyperthermia pre-treatment planning. Re-irradiation combined with hyperthermia (reRT+HT) is a valid treatment option. Four hundred and twenty-two episodes (range, 1-13). ReRT consisted typically of 8x4Gy, twice a week (AMC) or 12x3Gy, four times a week (BVI). Superficial hyperthermia was added once (ACM)/twice (BVI) a week using 434MHz Contact Flexible Microstrip Applicators. Treatment quality was monitored by 60 minutes, or later 75 minutes, depending on patients’ tolerance using the HYPERcollar, aimed at achieving 43°C in the target region. Treatment quality was monitored by patient specific hyperthermia pre-treatment planning alone. RT was given using either external beam irradiation (Cyberknife or IMRT) or interstitial irradiation.

Results: Applying hyperthermia in the very well perfused head and neck region proved to be challenging and high power levels were required (median 543W). 13% of the hyperthermia treatments were not fully completed, mostly due to pain (5%), which we allocated to hyperthermia treatment and dyspnoea (2%) caused by sticky saliva, associated with irradiation. Mean hyperthermia treatment time was 94% of planned duration. No severe complications or enhanced thermal or mucosal toxicities were observed. Preferably, metal implants (>1cm) should be removed to minimize the risk of toxicity, and prevent any unpredictable resonances reducing the predictive value of treatment.

Table 1.

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>Without DM</th>
<th>With DM</th>
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<tbody>
<tr>
<td>&lt;3 cm</td>
<td>a (CR,%)</td>
<td>2-y LC (%)</td>
</tr>
<tr>
<td>3-5 cm</td>
<td>27</td>
<td>90</td>
</tr>
<tr>
<td>&gt;5 cm</td>
<td>81</td>
<td>65</td>
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* data unknown for 5 patients

Conclusions: Re-irradiation combined with hyperthermia for locoregional recurrence after previous irradiation results in high response rates of 86%, despite resistance to previous treatments. Overall long-term LC control was 25%, but up to 47% in smaller tumors (< 5cm.). Tumor size, and absence of DM were positive prognostic factors for LC duration and overall survival.

OC-0335
Feasibility of deep head and neck hyperthermia
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Purpose/Objective: The outcome of current treatment of locally-advanced and recurrent head and neck carcinoma (HNC) in patients treated with radiotherapy alone is disappointing. The combination treatment of radiotherapy (RT) and cisplatin or cetuximab improves survival. Increased toxicity and comorbidity prohibiting combined treatment with cisplatin or cetuximab warrant the need for another radiosensitizer. Stimulated by several randomised studies demonstrating the radio-sensitizing effect of hyperthermia, we developed the HYPERcollar for applying deep hyperthermia in the HNC region. Here, we report the early experience and toxicity of deep hyperthermia treatment combined with radiotherapy in a cohort of patients with advanced HNC.

Materials and Methods: In total, 119 hyperthermia treatments given to 27 patients, treated with advanced HNC, were included in this analysis. Hyperthermia was applied for 60 minutes, or later 75 minutes, depending on patients’ tolerance using the HYPERcollar, aimed at achieving 43°C in the target region. Treatment quality was monitored by patient specific hyperthermia pre-treatment planning combined with real-time invasive thermometry if possible, or pre-treatment planning alone. RT was given using either external beam irradiation (Cyberknife or IMRT) or interstitial irradiation.

Results: Applying hyperthermia in the very well perfused head and neck region proved to be challenging and high power levels were required (median 543W). 13% of the hyperthermia treatments were not fully completed, mostly due to pain (5%), which we allocated to hyperthermia treatment and dyspnoea (2%) caused by sticky saliva, associated with irradiation. Mean hyperthermia treatment time was 94% of planned duration. No severe complications or enhanced thermal or mucosal toxicities were observed. Preferably, metal implants (>1cm) should be removed to minimize the risk of toxicity, and prevent any unpredictable resonances reducing the predictive value of treatment.