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 need 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 50 Gy 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 >10 cm 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 8x4 Gy, twice a week (AMC) or 12x3 Gy, four times a week (BVI). Superficial hyperthermia was added once (ACM)/twice (BVI) a week using 434 MHz Contact Flexible Microstrip Applicators. Mean hyperthermia treatment duration was 4.6 ± 3 months, or later 5 months, depending on patients’ experience and toxicity of deep hyperthermia treatment.

Results: Overall clinical response rate was 86% (58% cCR + 28% cPR). Median follow-up (FU) 17 months. Median overall survival was 17 months. The 3-year LC rate was 25%. Tumor size, time interval to recurrence, the number of previous recurrent episodes, and presence of DM were significant prognostic factors for LC. For patients with isolated locoregional recurrences ≤ 5 cm the 3-year LC rate was 47%.

Table 1. Tumor size, Without DM, With DM

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>Without DM</th>
<th>With DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 3 cm</td>
<td>37</td>
<td>90</td>
</tr>
<tr>
<td>3-5 cm</td>
<td>22</td>
<td>77</td>
</tr>
<tr>
<td>5-10 cm</td>
<td>81</td>
<td>65</td>
</tr>
<tr>
<td>&gt;10 cm</td>
<td>122</td>
<td>58</td>
</tr>
</tbody>
</table>

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 (<5 cm). 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 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 543 W). 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 (>1 cm) should be removed to minimize the risk of toxicity, and prevent any unpredictable resonances reducing the predictive value of treatment.
planning. After 3 months a complete response was observed in 46%, and 7% had partial response.

Conclusions: Using the HYPERcollar, deep hyperthermia treatment of HNC was found to be safe, feasible, with good compliance and promising outcome. These promising early clinical results culminated in the use of hyperthermia as a standard addition to reirradiation. We will now embark on a study for (chemo-)irradiation combined with hyperthermia in primary head and neck cancer.

Debate: Particle therapy: Randomised trials are obligatory

SP-0336
For the motion: particle therapy: randomised trials are obligatory
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Randomized controlled trials (RCTs) are the gold standard for comparative effectiveness research of medical interventions. Treatment guidelines rank evidence of using a hierarchy with evidence from RCTs at the highest level, Level I. Many authorities require Level I evidence from RCTs for registration and reimbursement of a new drug. When Level I evidence is not available, the treatment is often viewed as being “unproven”. Ideally, every new diagnostic or interventional procedure should be tested in RCTs before becoming standard care to avoid ineffective or harmful treatments. The reason is that even treatments supported by a clear biological rationale and strong pre-clinical data may not produce a therapeutic gain; examples include the detrimental effect of erythropoietin when used together with radiotherapy for head and neck cancer or class 1c antiarrhythmic agents in myocardial infarction patients. The unexpected result of these studies provides a strong argument in favour of randomization. Engineers and physicists often tackle the problem of obtaining “evidence” by making models to calculate the quantitative relationship between parameters and a particular outcome. The acceptance of the latter kind of empirical model spring from its ability to predict the outcome of experiments with accuracy, reliability and prospective reproducibility that is sufficient to be useful. The analogy with human biology is far from perfect because of the complexity of the processes involved. In physics controlling a rather limited set of known experimental conditions will suffice to standardize outcome measurements. The utility of models predicting clinically relevant outcomes could theoretically indeed be established by prospective comparisons between expected and observed outcomes. However, this is no simple task and has not been accomplished convincingly in the past. Nearly all proton therapy studies are retrospective, with heterogeneous patient groups recruited over long time periods, treated with varying techniques and with often very incomplete follow-up data. The radiobiology of the complex DNA damage in the Bragg peak is large unexplored and is not taken into account in current proton TPS. Some TCP and NTCP models are without doubt of merit for photon therapy, but they should not be extrapolated blindly to proton therapy as long as the latter models too have undergone extensive validation. The model-based approach is clearly a field where much more research is needed before this can be accepted as an alternative for RCTs. Except for some quite extreme cases, e.g. in some CNS and childhood tumours, randomised trials are still necessary, scientifically, legally and for obtaining reimbursement.

SP-0337
Against the motion
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Joint Symposium with Proffered Papers: ESTRO-PROS: Paediatrics: Late effects

SP-0338
Neuro-cognitive sequelae after brain irradiation
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Purpose / Objective: Cognitive impairment is frequently present in childhood brain tumour survivors and greatly impacts psychosocial development and quality of survival. Major contributing factors are related to tumour, the presence of hydrocephalus, surgery, chemotherapy and radiotherapy. The neurocognitive functions primarily involved are including memory, attention, visual perceptual ability and verbal function.

Materials and Methods: The majority of data are essentially based on past treatments with varying treatment volumes (craniospinal irradiation followed by a boost, whole brain irradiation, local irradiation with varying dose prescriptions) for medulloblastoma, low grade glioma, ependymoma, germ cell tumours and leukemia. The literature is replete of data based on retrospective evaluations spanning many years during which general disease management was improved. Additionally, radiotherapeutic approaches considerably changed with the introduction of 3D conformal technologies including IMRT and recently proton therapy that essentially permit a more precise coverage of tumour while sparing normal brain tissue.

Results: Post radiation changes include a wide spectrum of abnormalities from subclinical changes detectable only by MRI to focal neurological deficits and intellectual impairment. It appears that all changes are likely to result from complex alterations within several functional compartments with the following contributing factors: damage to vessel structures, deletion of oligodendrocyte progenitor cells and mature oligodendrocytes (white matter), deletion of neural stem cell population in the hippocampus. Additionally, the tumours significantly differ between the inherent disabling potential with respect to tumour location and the therapeutic approach. The major risk factors are young age at treatment and a dose relationship in whole brain irradiation. Recent data indicate that particular radiosensitive regions of the brain are more susceptible to the adverse effects of radiation such as frontal lobes, temporal lobe and hippocampus including anatomical subcompartments in which neurogenesis occurs (subventricular zone). However, the relationship between radiation dose to these areas and a decline in neurocognitive function remains a controversial issue. Recent data indicate that radiation dose to neuronal progenitor cell niches and temporal lobes causes a decline in cognitive function. Modern radiotherapy technologies are able to selectively reduce the dose to organs at risk. Correspondingly, reducing the dose to the hippocampus in adults appears to preserve memory with conformal avoidance of the hippocampal neural stem cell compartment during whole-brain radiotherapy (recently