performed to test the role of neoadjuvant chemotherapy. Some of these trials showed contradictory results (esp. Kelsen-RTOG(3) versus Allum/Clark-MRC(4)), but the overall 5-year survival advantage with neoadjuvant chemotherapy is probably <5%.(5) In most RCTs comparing neoadjuvant chemoradiotherapy followed by surgery versus surgery alone no significant benefit for the combined modality arm could be demonstrated. However, most of these (older) trials did not meet today's standard of care and were generally underpowered. In the meta-analysis a survival benefit was suggested with the use of preoperative chemoradiotherapy.(6)
Recently, we published the results of a multicenter Dutch RCT, comparing chemoradiotherapy (5 courses of weekly paclitaxel/ carboplatin and concurrent radiotherapy, 23x 1.8 Gy) followed by surgery versus surgery alone.(7) In general, toxicity was mild. In-hospital mortality was comparable (4% in both groups) and no difference in postoperative morbidity was observed. The R0-radical resection rate was higher in the multimodality arm (92% vs. 69%). Median overall survival was superior in the multimodality arm (49% vs 24%), while 5-year overall survival was 47% in the multimodality arm versus 34% in the surgery alone arm (p=0.003). Therefore, we now consider neoadjuvant chemoradiotherapy plus radical surgical resection as standard treatment for patients with potentially curable (cT1b-N1M0, cT2-4aNxM0) esophageal cancer.

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SP-0621

Chemoradiation therapy for locally advanced esophageal cancer - Japanese perspective

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In this short lecture, recent progress in radiation therapy (RT) for locally advanced esophageal cancer in Japan will be presented. At present, concurrent chemotherapy (CT) of 5-FU/cisplatin combined with RT is a standard chemo-radiotherapy (CRT) regimen for locally advanced esophageal cancer. Although full dose 5-FU/cisplatin is combined with RT in the USA, several Japanese investigators showed promising clinical results using low dose protracted infusion CT combined with full dose RT of 60-66 Gy for locally advanced esophageal squamous cell carcinomas. Low dose protracted infusion of 5-FU or 5-FU plus cisplatin were proposed to reduce the acute toxicities due to concurrent CRT. In addition, to obtain maximum radio-sensitization by CT, daily administration of low dose protracted CT combined with RT may be better than full dose short-term CT plus RT. To test the above hypothesis, a randomized phase II study was conducted to compare the relative toxicity and efficacy of combining full dose short-term CT (arm A) or low dose protracted CT (arm B) with RT for esophageal cancer (KROSG0101/JROSG021) (1). As a final analysis, low dose protracted infusion CT with RT is not superior to full dose short-term infusion CT with RT for esophageal cancer. For both groups, late toxicities of grade 3 or more were noted 17-18% of the patients. Most of the toxicities were cardiac or pleural toxicities, and patients with severe late toxicities often had coexistent hypothyroidism.
To determine the clinical results of CRTfor esophageal cancer in Japan, a questionnaire-based survey for esophageal cancer treated by definitive RT between 1999 and 2003 was conducted (2). Clinical results of definitive RT for patients were collected from 9 major institutions. Only patients with good performance status (PS0-2) who received a total dose of 50 Gy or more were included. Patients were classified into three groups; A) stage I-B) resectable stages II-III-C) unresectable stages III-IVA. For group A, all patients treated by RT alone or chemo-radiotherapy (CRT) were included. For groups B and C, only those treated by CRT were included. The median total RT dose ranged from 60 Gy to 66 Gy. The median and range of the 5-year overall survival rates were 56% (48-83%) for group A,29% (12-52%) for group B, and 19% (0-31%) for group C, respectively. A significant disparity in survival rates wa snoted among the institutions for stage II-IVA tumors treated by CRT. Interestingly, a significant correlation between the number of patients treated per year and the 5-year overall survival rate was noted for groups B and C (both p<0.05). A similar volume-outcome relation was demonstrated between the number of esophagectomy operations performed per year and the operative mortality (3). Thus, treatment of esophageal cancer should be done in limited number of large cancer center hospitals.
To reduce the late toxicities, improvement in spatial dose distribution for esophageal cancer was obtained by conformal RT including intensity modulated RT (IMRT). IMRT is an ideal boost technique for locally advanced cervical and upper thoracic esophageal cancers to exclude the spinal cord. We are planning a phase II trial for cervical esophageal cancer using IMRT.

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SP-0622

Chemoradiation therapy for locally advanced esophageal cancer - European perspective

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Radiotherapy in combination with concurrent cisplatin based chemotherapy of patients with locally advanced esophageal cancer results in 5 year overall survival between 10-30%. In meta-analysis of randomized trials comparing surgical treatment with or without neoadjuvant chemoradiation to chemoradiation, overall survival was identical (Hazard ratio 0.98) for both treatment strategies (1). Chemoradiation was associated with a significantly higher locoregional recurrence rate (HR:1.54) and a borderline significant lower distant metastases rate (HR 0.72; 95%CL 0.52 – 1.01). Treatment related mortality was higher with surgical treatment (8.9% vs. 1.3%). The vast majority of patients in these trials had squamous cell cancer. The lack of a survival benefit for surgery in spite of improved locoregional tumor control is mainly a consequence of the relatively high treatment related mortality. In randomized trials comparing surgery to neodjuvant chemoradiation followed by surgery (2), an increased treatment related mortality was reported for patients with squamous cell carcinomas, but not for patients with adenocarcinomas. Whether this observation is simply the consequence of the less complicated surgery of typically distally located adenocarcinomas or is also due to lifestyle associated differences in weight and cardiopulmonary function, is not well understood. The clinical consequence is that patients with locally advanced adenocarcinomas should be treated with neoadjuvant treatment followed by surgery, whereas patients with squamous cell cancer patients have two options, neoadjuvant chemoradiation followed by surgery or primary chemoradiation. Since treatment related mortality is higher in patients with impaired cardiopulmonary function or poor performance status, primary chemoradiation is the preferred treatment, if these conditions are present. Tumor location above the carina seems also to be associated with a higher risk of perioperative mortality favouring chemoradiation for the majority of these patients. Treatment decision based on early response to neoadjuvant chemoradiation has also been propagated. Patients with responding tumors have a much better clinical outcome regardless of whether treatment is completed with surgery of further chemoradiation (3), and chemoradiation as the less toxic treatment is propagated in case of response. Independent of these considerations, new treatment strategies are needed to improve clinical outcome. Chemoradiation with total doses between 50 to 65 Gy in combination with cisplatin based chemotherapy is standard at the time. The addition of taxanes and cetuximab is currently under investigation. Improved radiation technology like IMRT and IGRT are also under investigation and are expected to lower treatment related toxicity.

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SYMPOSIUM: NEW ICRU REPORTS AND HOW THEY ARE CHANGING PRACTICE…

SP-0623
Basic principles of ICRU concepts applied to IMRT
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ICRU 50 and ICRU 62 documents established recommendations and procedures for the practice of Two-Dimensional Radiation Therapy (2D-RT) and to a lesser extent, Three-Dimensional Conformal Radiation Therapy (3D-CRT). Some of these recommendations were however only concepts, which, although extremely valid, were impractical to implement in modern radiotherapy. In addition, new concepts to account for the practice of Intensity-Modulated Radiation Therapy (IMRT) were required. In this framework, ICRU 83 provides updates to the earlier documents to take into account changes in practice with IMRT and evolving improved practice in 3D-CRT.
IMRT and 3D-CRT required the use of accurate guidelines for the selection and delineation of the various target volumes on a volumetric basis. In addition, various imaging modalities (including molecular imaging) may be used for planning not only before the start of treatment, but also during treatment to adapt the dose distribution.The concepts of gross tumor volume (GTV) and clinical target volume (CTV) have been crucial conceptually, but recommendations for outlining were needed for a practical implementation on a daily basis. Refinement for OAR delineation (e.g."tube" organs, "parallel-like or serial-like) were also provided.
The IMRT planning process uses an optimizer, which expresses the radiation oncologist's treatment goals. The committee has designated the set of optimizer parameters the "planning aims" to differentiate from the usual meaning of "prescription". Multiple recent publications have pointed out that the choice for planning target volume (PTV) margin should be based on clinical QA measurements and should place more emphasis on systematic uncertainties as they have more impact on the accuracy of dose delivered to the patient as compared to random uncertainties. Unlike 3D-CRT, IMRT does not deliver dose to all of the target volume a tone time. IMRT delivered to moving organs may allow hot and cold spots to develop in the CTV even though a generous PTV margin has been drawn. IMRT has gained prominence because it allows a lower dose to neighboring sensitive normal tissues even though it may result in less dose homogeneity to the tumor. Therefore, the use of a single reference point for prescription and reporting recommended in earlier protocols can lead to unnecessary dose uncertainty and so the committee recommended dose-volume reporting, for example, the dose which covers some high fraction of the target volume as preferable. Last, the implementation of IMRT requires adequate quality control of the equipment as well as of any individual plan to ensure proper dose delivery in accordance with the presciption.

SP-0624
Upcoming ICRU report on bioeffect modelling
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Abstract not received

SP-0625
ICRU GEC ESTRO report on image guide adaptive brachytherapy in cancer of the cervix (IGABT)
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The new joint ICRU/GEC ESTRO report (88, 2013) reflects and further structures the on-going developments in the field of IGABT and was preceded by 4 GEC ESTRO recommendations on adaptive target concepts, dose volume parameters, biological modelling, applicator reconstruction and imaging. They have become widely accepted in the international community and have become the basis of this report.
The current report focuses on the volumetric image guided adaptive approach. It also includes traditional 2D planning which is linked to the 3D world by recommending point A.
The GTV and CTV concepts follow the ICRU tradition with a special focus on the change of CTV during treatment. The High Risk CTV is introduced which represents residual GTV and surrounding are assumed to carry a high risk for residual cancer cells after 40-45 Gy EBRT plus chemotherapy and always the whole cervix. An additional Intermediate Risk CTV is suggested representing the area of tumour spread at diagnosis and a margin around the CTVHR. Uncertainties for GTV/CTV selection and contouring are recognized as due to internal motion and applicator reconstruction and discussed in the frame of intracavitary brachytherapy. The addition of margins (as in EBRT) is discouraged (dose escalation). PTV has to be designed when planning the application which has to be adapted as appropriate.
For adjacent OARs rectum, bladder and sigmoid 2cm^3 and 0.1 cm^3 are defined as reference. For the vagina anatomical reference points are recommended due to contouring and dosimetric uncertainties. Uncertainties due to internal motion are recognized for OARs and corrected through repetitive imaging.
Dose (rate) per fraction is recommended to be reported as physical dose and calculated and reported as iso-effective dose in EQD2 following the LQ model. Its pragmatic use is encouraged for treatment planning withan α/β value of 10 Gy for tumour and 3 Gy for OAR although its limitations are recognized.
For the target the main dose volume parameter is D90, complemented by D98 as near-minimum dose and D50 indicating the high dose volume. Dose variation is around 200%.
Point A is encouraged to be continued for dose reporting, clearly defined based on the applicator geometry. It will allow reproducible dose assessment for the 2D approach, but also consistency and comparability for the 3D approach. The TRAK remains an essential reporting parameter.
For normal tissues D2cm^3 and D0.1cm^3 are the main parameters for the 3D approach. Additional parameters for the mid and low dose region arediscussed, mainly reflecting EBRT. Applicator related points are recommended for the upper vagina (at 0/5 mm (ABS)) and anatomy related points for the mid and low vagina. For the 2D approach the dose points for rectum and bladder remain as defined in ICRU 38.
The report also contains recommendations and information on treatment planning, applicator reconstruction, 3D dose summation, source strength specification and dose calculation.
"Planning aim" (ICRU 83) is also introduced for brachytherapy treatment planning and represents a certain "treatment schedule" for a specific clinical scenario including a set of dose and volume parameters fora specific applicator. During the treatment planning optimization, adaptations are performed according to dose volume constraints for the target and OARs. "Prescription" is based on the final set of parameters which presents the treatment plan finally used for irradiation.
The upcoming report is based on concepts and terms developed within the frame of the on-going technical and clinical developments. The terms support the transition from 2D to 3D/4D gynaecologic brachytherapy and have become integrated into the educational programmes of leading international Societies. They are being clinically validated in a spreading number of centres in Europe and worldwide. Research validation is on-going within various multi-centre trials (e.g. EMBRACE) which will help to define the"true" clinical value, reliability and reproducibility. These evaluations may require further adaptations.