Essentially the same general radiobiological considerations apply to kilovoltage as to megavoltage x rays i.e. cell killing is adequately described by the linear-quadratic model, and for (most) tumour types, we expect a higher α/β than for normal tissues thus making fractionation theoretically advantageous. However, given the extremely rapid fall-off of dose with depth, and the fact that today only superficial tumours are treated with kilovoltage beams, the dose to any underlying normal tissues will inevitably be very low and may therefore pose a negligible complication risk. This enables large fractions to be used.

Megavoltage therapy was already well established when computer planning systems first came on the scene in the 1970s. Naturally all the current work was in developing algorithms for computing dose in patients from such beams and consequently no treatment planning systems model kilovoltage beams. The very large amount of (photon) scatter, which gives rise to a build-up of dose at small depths, would pose quite a challenge for algorithm developers, though secondary electron transport can be ignored as the low initial electron energies result in largely sub-millimetre ranges in tissue. We have created a simple 250 kV x-ray plan for a lung tumour using the GEANT Monte Carlo code in order to compare the DVHs to those derived from a megavoltage plan. For one particular NSCLC patient, treated with 6 MV x rays, this companion has yielded 0% TCP for the KV plan for the same 9.5% lung pneumonitis NTCP as for the MV plan. Increasing the NTCP to 15% for both plans (i.e. by winding up the MUs) has yielded TCPs of 94.6% for the MV plan against 1.9% for the KV plan. However, this was for a relatively large tumour.

It can be noted that kilovoltage therapy is undergoing a renaissance through 50 kV Papillon contact therapy for rectal tumours.

**SYMPOSIUM: IMPROVING ACCURACY IN IGRT TREATMENT DELIVERY**

**SP-0020**

Set up and repositioning by new technological oppor-tunities: 6 degree freedom couches

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**Purpose:** Accuracy in patients positioning with novel irradiation techniques, which allow tight conformation of dose distribution, is of great interest in image guided radiotherapy (IGRT) era.

**Material and methods:** Several studies have examined the relevance and the magnitude of rotational set up errors, using portal image registration, serial CT scans or recently employing kilovoltage cone beam CT (CBCT). They demonstrated that in prostate, head & neck and thoracic cancer, rotational errors are small in magnitude but statistically significant and that their magnitude is not correlated with the magnitude of the translational set up errors. Moreover several authors demonstrated that online correction of rotation can improve target coverage because rotational shift could have an impact on dose distribution, varying according to treatment site and to radiation techniques. Therefore an approach to improving accuracy of patient positioning is to develop devices that permit couch movement with 6 of freedom (6DOF). In our centre the Protura™ Robotic Patient Positioning System (CIVCO Medical Solution) was installed onto a Linear accelerator (Varian Medical System). We started a study to evaluate the relevaneance of rotational shift in IGRT and to validate the added value of 6DOF robotic couch to improve setup accuracy with the Cone Beam CT scanner (CBCT). The radiation therapist and technicians were instructed to use the system and, through daily use, determined the best application of the system.

**Results:** Guckenberger et al. found a rotational error < 2° in 3.7% of pelvic tumours, 26.4% of thoracic tumours and 12.4% of head and neck tumours; the corresponding mean rotational errors were 0.5°, 6°. Kaiser et al. observed in 96.6% of prostate and head and neck cancer a rotational correction < 4°, with no difference between week 1 and 4 of treatment; a smaller pitch variation but a larger yaw variation were recorded in head and neck. Concerning dosimetric results, Guckenberger et al. observed a decreased target coverage and an highly increased dose to the organat risk (OAR) when elongated target volume and sharp dose gradients were adjacent to OAR. Lang et al. observed a reduction of target coverage for pitch of 3° with no differences between dorsal or ventral direction. In our centre from October to December 2012, 5 prostate and 3 H&N patients were enrolled. The magnitude of roll variation was greater in both groups (mean ±(SD)) of -0.5±1.2° in prostate and a maximal value of 3.8° and a mean ±(SD) of 1.3±1.2° in H&N with a maximal value of 3.4°. The pitch variations were greater for patients treated to the pelvis (mean ±(SD)) of -0.4±1.1° vs. -0.1±0.8° with a maximal value of 2.8° vs 1.9°), while the mean ±(SD) interfractonal yaw was 0.1±0.7° in prostate and 0.0±0.6° in H&N patients. No correlation was observed between the magnitude of translational and rotational shift in either group. The online correction using CBCT studies added less than one minute to the treatment time when compared to IGRT without robotic 6DOF couch.

**Conclusions:** These data confirm the relevance of rotational shift and the feasibility of using a robotic 6 DOF correction table in routine radiotherapy. In our centre correlation between volumetric and geometrical shift data and evaluation of its dosimetric impact on adaptive dose is ongoing.

**SP-0021**

Development of guidelines for set up and verification requirements in head and neck radiotherapy

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This presentation discusses an ongoing project lead by members of the ESTRO RTT Committee on the Development of guidelines for set up and verification requirements in head and neck radiotherapy. This is the first set of ESTRO guideline to be developed by RTTs.

The presentation will give the background as to why ESTRO develops guidelines for its members, the rationale for the selection of this topic and the progress to date.

The methodology for the project includes an extended literature review, the development of online consultation and its translation and distribution to RTTs throughout Europe as well as case reports from selected clinical departments across Europe.

The results of the extended literature review will be presented, along with the preliminary results of the questionnaire and the focus of the case reports will be discussed.

**SP-0022**

Progress in adaptive procedures for bladder cancer irradiation A. Bel

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Irradiation of bladder cancer is challenging since the variable and deformable bladder and bowel filling makes the target highly mobile. Traditionally, large target margins (up to several cm) are applied with the high dose area comprising the full range of bladder filling. Innovations were enabled by the introduction of Cone Beam CT (CBCT) during the last decade. A challenge for image guided radiotherapy is that the tumor on the bladder wall is difficult to delineate on planning CT and not visible at all on CBCT. Several procedures are developed to demarcate the tumor, using cystoscopy. For instance, the contrast liquid lipiodol is successfully injected in the bladder wall to locate the tumor using a flexible scope. Lipiodol markers are well visible on CT for guiding target delineation. Moreover, markers are also visible on CBCT during the whole treatment course enabling daily target localization. The visibility of the target on CBCT in combination with a rather well visible bladder wall enabled application of adaptive radiotherapy (ART) procedures. Currently reported ART procedures are variations on the following scheme:

- Acquisition of planning CTs with varying bladder filling (typically a full and empty bladder).
- Creation of a number of ‘additional bladders’, with proportioned (or also extrapolated) volumes.
- Design of plans-of-the-day (PDs) for each bladder volume.
- Treatment with daily CBCT acquisition.
- Patient repositioning, based on bony anatomy or tumor markers.
- Based on the amount of bladder filling the correct PD is selected and delivered.

This approach has shown to enable a significant reduction of the target margins and sparing of organs-at-risk like the small bowel and healthy part of the bladder.

One of the challenges for clinical introduction of ART is the PD selection. This selection is based on the bladder volume. It is possible to automate the bladder delineation on CBCT. An approach with a ‘restricted bladder shape’ has been investigated, fitting the shape on the grey value gradient of the CBCT image. As final check, the automatically obtained bladder shape can be corrected manually. This approach turned out to be effective in selecting the correct PD and corresponds in 81% with the manually chosen PD.

To report the actually given dose to each daily deformed target and bladder shape, the daily dose must be accumulated. It requires an anatomically correct deformable registration, defining the correct...
A number of feature-based approaches are used like the Finite Element Method (FEM). The FEM describes the forces in the bladder and deforms the organs according to the dose distribution using the stress equations. Such models are in principle capable of achieving a good anatomical correspondence. However, for their best performance they require a detailed knowledge of the tissue properties which is not yet available. A more heuristic approach can be followed by application of the Symmetric Thin Plate Spline Robust Point Matching algorithm. Points are placed on the surfaces of the volumes that have to be matched. Subsequently, the distances of these points are minimized. Recently, the algorithm is modified with a weight parameter to allow flexibility control of the tumor and bladder wall. They are considered as separate structures, with a more flexible bladder. Rather coherent registrations are achieved, with fewer marker errors for the modified algorithm (Figure).

It can be concluded that important progress has been made to effectively improve bladder cancer irradiation. An important role is played by the cystoscopic guided tumor demarcation to visualize the tumor during treatment. Sparing of normal tissue is achieved by the adaptive procedures. Improvements have to be achieved for better practical support of clinical ART procedures and deformable image registration for accurate dose accumulation.

**Figure** Visual representation of non-rigid registration results for one example case, illustrating the effect of several methods.

Transformational approaches are applied to the lipiodol spots. Planning bladder (grey) is registered to the bladder in repeat-CT (pink) and the resulting transformation is applied to sampled surface points of lipiodol spots. w refers to relative bladder weight for the non-rigid match. a) Original position of the lipiodol spots after bone match. b) S-TPS-RPM registration of bladder alone; c) w-S-TPS-RPM registration with w=0.8.


### SYMPOSIUM: NORMAL TISSUE TOLERANCE: THE LESSONS OF POPULATION-BASED APPROACHES

**SP-0023**

Large cohort studies on late effects of childhood cancer

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By using the unique resources for conducting epidemiological research that we have in the Nordic countries, facilitated by the existence of nationwide population and health registries that can be accessed with unique individual identification numbers, several population-based studies have been conducted within the Nordic countries to evaluate the impact of cancer therapy at a young age on the health of the patients and their offspring.

These different population-based, nationwide studies will be presented as examples of clinical epidemiological studies on late effects of childhood cancer with outcome data derived from health registries and a ‘gold standard’ approach being used for exposure assessment including organ radiation dosimetry: (1) A case-cohort study based on the population-based cohort of Danish childhood cancer patients and all their children with the purpose to quantify the extent to which cancer therapy contributes to genetic disease in the children of survivors including chromosomal abnormalities, congenital malformations, stillbirths, and neonatal deaths as possible indicators of genetic damage in the next generation. Preconception radiation doses to the genetic, uterine and pituitary areas and administered chemotherapy have been quantified from medical records and related to adverse outcomes using a generalized estimating equation model and the results will be presented. (2) A greater international collaboration to study trans-generational effects of cancer treatment in children and adolescents - the Genetic Effects of Childhood Cancer Treatment (GECT) study - currently under way in Denmark, Finland and the USA with a similar design but with an increased sample size by adding the offspring of cancer survivors diagnosed in early adulthood in both Denmark and Finland (www.gect.org). This study is expected to provide more definitive answers to questions about the integrity of the germine in human populations that have been exposed to mutagenic cancer therapy. (3) A large ongoing Adult Life after Childhood Cancer (ALiCCS; www.aliccs.org) study of late effects in childhood cancer patients. The Nordic cohort consists of nearly 33,000 children and adolescents with cancer diagnosed below age 20 in Denmark, Finland, Iceland, Norway, and Sweden. Morbidity-specific incidence and cause-specific mortality in these patients will be compared with that of a combined Nordic cohort of more than 212,000 population-based comparisons. In a cohort surveillance approach, the relative and absolute risks for different chronic diseases in adult survivors will be assessed based on discharge diagnoses in national patient registries. In the initial phase of this research priority is given to late effects in terms of cardiovascular and pulmonary disorders, endocrine disorders and reproductive failures, and renal and gastrointestinal disorders. Based on the findings in this screening phase, specific, well-defined outcomes will be investigated in case-cohort studies among 5-year survivors in order to investigate associations, including dose-response, between specific treatment regimens and selected outcomes. Detailed information on chemotherapy including drugs and doses and radiotherapy will be abstracted from medical records and for some of the studies organ radiation doses from direct and scattered irradiation will be estimated. The strengths of these studies include the unbiased ascertainment of cancer cases through a search in nationwide cancer registries, complete identification of the children (or other designations used) and unbiased identification of population comparisons, and long-term, virtually complete follow-up of all study populations.

**SP-0024**

Questions in radiotherapy and answers from late effects population studies: Proposed approaches to bridge the gap

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Adverse effects of cancer treatment (normal tissue damage, new malignancies) represent well-studied phenomena across all radiation disciplines. Novel steps are needed to fully exploit current technical opportunities to avoid normal tissue radiation exposure. Pediatric oncology represents a good model to illustrate the proposed approaches. On average pediatric cancer patients have a better prognosis than adults, they are not exposed to radiotherapy and chemotherapy vulnerable periods of growth and development, treatment field delineation can be challenging due to close proximity of surrounding organs in small children, and these patients are at potential risk for a variety of health problems at different points in their life span. Valid dose effect studies require accurate characterization of radiation dose characteristics combined with complete and accurate follow-up for health effects, including unique definitions for such health outcomes. In the past, collaborative groups of pediatric oncologists, epidemiologists, and radiation oncologists have initiated large observational follow-up studies of cancer survivors, to quantify dose effect relationships for chemotherapy and radiotherapy. The professionals who treat childhood cancer patients typically follow trial protocols, thus allowing for large, often international, trial based late effects follow up studies. These studies seemly represent rather separate, parallel efforts, often using different terminology but seeking answers to closely related or identical questions. From a methodologic perspective, trial based follow up efforts are based on excellent dose assessment methods but face challenges in achieving uniform and complete health outcome follow-up beyond 10 or even 5 yrs post treatment. Conversely, observational retrospective follow-up studies typically have reasonable or good health outcome data ranging spanning 30+ yrs of follow-up for the oldest pediatric cancer survivors, however, it has remained challenging to accurately describe doses at organs at risk according to the standards common (and expected) in clinical radiation oncology. In essence, we need to combine the dose estimation standard from clinical trials with the follow-up methods applied in observational studies. Several parallel approaches should