unpleasant surprises may yet eventuate. There is no doubt that substantial improvements in supportive care have enhanced our ability to deal with early treatment toxicity and has raised our expectations as to what our patients will tolerate. This talk also draws attention to shortcomings in the way we assess and measure some of the delayed consequences of both old and new therapies.

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IMRT, SECOND CANCERS, AND THE SPECIAL CASE OF CHILDREN.
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Objective: To assess the impact of IMRT on the risk of second malignancies following radiation therapy. **Material and methods:** IMRT allows dose to be concentrated in the tumor volume while sparing normal tissues. This is a step forward, especially for children, to spare normal tissues and avoid subsequent growth detriment. The downside of IMRT, delivered with current Linacs, is the potential to increase radiation induced second cancers. There are two reasons for this. First, IMRT requires the accelerator to be energized for longer (more monitor units by a factor of 2 to 3) compared with delivering the same dose from an unmodulated field. Consequently, the total body dose due to leakage radiation will be increased. The leakage from a modern Linac through the treatment head, amounts to about 0.1% of the iso-center dose. Leakage through the multi leaf collimator is higher, around 1.5% of the delivered dose. Second, IMRT involves the use of more fields, with a bigger volume of normal tissue exposed to lower doses. The impact of this depends on the shape of the dose response relationship for carcinogenesis. **Results:** It has been estimated that, in elderly patients, IMRT in place of conventional 3D-CRT, may double the incidence of second cancers from about 1.5 to 3%. This may be acceptable in elderly patients if it is balanced by a significant improvement in tumor control and a concomitant reduction in acute toxicity. However, in children the situation is different. Children are much more sensitive to radiation-induced cancer by a factor of 10 or more, depending on their age. Doubling this larger number may not be acceptable. It must be assumed that the widespread application of IMRT in pediatric cases will result in a significant increase in second cancers in long term survivors. **Conclusions:** Present day machines were not designed with IMRT in mind and the high leakage doses from current Linacs are not inevitable. Strategies are available to reduce leakage; this will involve a substantial cost but may be worth-while for pediatric cases. The other possible strategy is to use protons for pediatric cases. However, there is an inherent problem with the present generation of proton therapy installations in the United States, in which a scattering foil is used to produce large enough fields. This process inevitably produces neutrons that deliver a larger total body equivalent dose than the leakage radiation from conventional Linacs. A scanning beam avoids the production of neutrons and consequently reduces the leakage dose. Scanning beams are available on a few facilities in Europe, but to date not on US facilities. The use of a scanning beam will allow the full potential advantage of protons to be realized.

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TUMOR TARGETING AND TISSUE PROTECTION BY IMRT OF HEAD AND NECK (HN) CANCER: CURRENT CHALLENGES
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Current challenges in targeting the tumor in HN IMRT include the need for better definition of the gross tumor volume (GTV) and the clinical target volume (CTV), and efforts to determine whether dose escalation can be planned for parts of the GTV predicted to be non-responding to therapy. Better imaging of the GTV using innovative techniques and better understanding of the relative accuracy of clinically available imaging modalities, notably CT/MRI vs. FDG-PET, are expected to be gained from on-going radiology research. In contrast, only careful documentation of the clinical experience in the pattern of local/regional tumor recurrences following IMRT can lead to better understanding of the extent of the CTV for each clinical scenario. Relevant experience in these issues will be presented. Sensitive tissues like mucosa, blood vessels and nerves are embedded within the GTV in the HN. This limits the ability to escalate the fraction and total doses to the GTV, and in particular it increases the toxicity of dose escalation concurrent with chemotherapy. If we could identify resistant sub-volumes within the GTV, dose escalation to these smaller volumes may be safer. The identification of resistant sub-volumes may be achieved with innovative imaging modalities (discussed elsewhere in this conference), or it may be based on imaging the shrinkage of the GTV at certain time points during RT, facilitated recently by cone-beam CT. Whether or not it is clinically sound to re-contour the GTV and re-plan during the course of RT, will be discussed, taking into account the differences in tumor burden between the radiologically detectable and non-detectable parts of the original GTV. Reducing xerostomia by sparing partly the parotid salivary glands has been a major achievement of IMRT. Dose-response relationships in the glands have been investigated with notable differences among some of the publications. The reasons for these disagreements may be related to recent experimental data about the importance of the spatial distributions of the doses within the glands. How much do sparing of the parotid gland saliva improve patient-reported xerostomia and quality of life, and what are the limitations in achieving further improvements, will be discussed. Late dysphagia is one of the main factor limiting the intensity of chemo-RT regimens for locoregionally advanced HN cancer. In order to study the utility of IMRT in reducing dysphagia and related aspiration, it is necessary to identify the anatomical structures whose damage causes these abnormalities, to test whether their sparing by IMRT is possible without compromising tumor irradiation, and to assess whether a clinically relevant benefit is gained. Studies addressing these issues will be described.

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TCP AND NTCP IMPORTANT: TOOLS OR TOYS?
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As long ago as 1937 (Holthusen), it was recognized that radiotherapy is a delicate balance between cure and complications. Consequently, there is a perennial need to prospectively estimate the effectiveness of alternative dose distributions for the individual patient. Due to widely varying patient geometries and disease characteristics, the issue *cannot be settled on the basis of clinical trials and requires patient-specific mathematical Important.* Initial efforts to predict tumor control probability (TCP) and normal tissue complication probability (NTCP) were based on simplified theoretical ideas, but that has given way to more data-driven and empirical approaches. Recently, large datasets have been accrued based on 3-D treatment planning to provide an improved basis for NTCP Important. TCP and NTCP model-building represent fundamentally different problems which seem superficially similar. Normal tissues often have similar geometrical and physiological status with a given patient population (exception: lung for lung cancer patients). As is well-known, tumors vary greatly in Important phenotypical and micro-environmental parameters, including the ability of tumor cells to withstand hypoxia; nutrient delivery efficiency; probability of microscopic extension; tumor regression, etc. This heterogeneity is an obstacle to developing truly accurate TCP models. In contrast, significant data has been published and used to better define dose-volume-fractionation treatment tolerance in various normal tissues. NTCP models can be considered tools, rather than 'toys', when: (1) the model building process carefully avoids over-fitting the data (*fairness*), (2) the model is shown to correlate well with the underlying dataset (*effectiveness*), and (3) any new case to which the model is being applied is similar to (some) data in the basis/training dataset (*similarity*). Unfortunately, it is currently not easy to discern when these conditions have been met. Moreover, the desire to modify the dose distribution under consideration to reduce the NTCP value,