radiotherapy (IGRT), has highlighted deficiencies in target delineations based on CT. Several studies have shown large variability in target definitions based on CT, for multiple treatment sites. To address this issue, magnetic resonance imaging (MRI) has made its way into the clinical routine at modern radiotherapy departments over the last years. This, however, has presented several new problems that need to be solved.

The traditional method of including MR information in the radiotherapy process is as a complement to the CT. To accomplish this in an integrated and accurate fashion, the images must be placed in a common coordinate system through image registration. This process in itself introduces new uncertainties into the treatment chain, which must be quantified and minimized. Another method of using MR information is to base the entire treatment on MR and exclude the CT altogether. This alleviates uncertainties that stem from the image registration process, but introduces another set of problems. To perform accurate dose calculations, heterogeneity corrections based on CT data have been the clinical standard for many years. MR data does not provide information that can be used for such corrections; however, much research effort has been invested in creating valid photon attenuation maps from MR data over the last years. Whatever method employed, MR for radiotherapy purposes also imposes practical issues that need to be addressed. The patient needs to be positioned in the same way that will be employed during the radiotherapy itself. This includes a flat table top and immobilization devices such as cast masks and tilted boards, which may not be MR compatible. For example, many radiotherapy fixation devices can contain metal parts such as nuts and bolts, which cannot be used in the MR. Plastic replacements must be used instead. Also, the standard MR coils will often not accommodate the immobilized patient, which forces MR adopters to acquire special coils or coil holders for flexible coils to be able to scan the patient in the radiotherapy treatment position. MR images do not have the same geometric integrity as CT, which is an issue in the radiotherapy setting. The image distortions can come from the machine itself or from the patient that is in the machine. Machine specific distortions are caused by inhomogeneity in the main magnetic field or gradient non-linearity. Patient specific distortions are mostly caused by susceptibility effects. The machine specific distortions can be measured, modelled and corrected for to a certain extent, while patient specific distortions often needs to be handled by choosing imaging parameters wisely.

In the end, the images acquired from the MR scanner must be of sufficient quality to allow physicians to base the radiotherapy treatment on them. MR for radiotherapy has a different set of demands on the images than their diagnostic counterparts. For example slice thickness and gap, as well as other parameters. Also, the vast variety of MR contrasts may be an initial obstacle for radiotherapy oncologists. Many studies have shown differences in target definitions based on CT and MR images, and the effects of these changes in target volumes have not yet been studied in clinical trials.

Teaching Lecture: Patient specific quality assurance in proton therapy

SP-0007
Patient specific quality assurance in proton therapy
R. Amos1
1University College London Hospitals NHS Foundation Trust, Department of Radiotherapy Physics, London, United Kingdom

Interest in proton therapy continues to grow worldwide, yet access to proton therapy facilities remains relatively low compared to those offering conventional radiotherapy. As a consequence, proton therapy needs to be carefully planned, executed and evaluated in each facility. Most facilities operate 24 hours per day, 7 days per week to meet the demands of the clinical load and to complete machine maintenance, routine quality assurance, and patient specific quality assurance. With the advent of advanced delivery techniques such as pencil beam scanning, the complexity of patient specific quality assurance is increasing. However, there is a need to improve efficiency of these tests whilst maintaining accuracy. This presentation will summarize contemporary patient specific quality assurance practice for both passive scattering and pencil beam scanning proton therapy, and describe offline tests that potentially enable improved efficiency.

Teaching Lecture: Balancing toxicity and disease control in the evolution of radiotherapy technology

SP-0008
Balancing toxicity and disease control in the evolution of radiotherapy technology
B. O'Sullivan1, S. Huang2
1Princess Margaret Cancer Centre, Toronto, Canada
2Princess Margaret Cancer Centre/University of Toronto, Radiation Oncology, Toronto, Canada

Radiotherapy (RT) is an effective option for treatment of many cancers. It offers organ and functional preservation and enhances surgical outcomes when administered preoperatively or postoperatively for some diseases, such as nasopharyngeal cancer, it is often the only curative option. Disease control is generally paramount importance to most patients during the urgent point of decision-making following diagnosis. However toxicity will almost certainly emerge as being just as relevant in the aftermath of treatment and in the subsequent follow-up period. In essence, when a patient dies of toxicity or treatment-related complications, it is just as tragic as dying of disease. The long-term result of RTOG 1111 and 9501 suggest that treatment-related deaths are blunting originally observed differences in cancer-related outcome. The recent RTOG 0617 trial was designed to test whether a higher RT dose (74 Gy vs 60 Gy) +/- cetuximab could confer a survival benefit but showed an unexpected therapeutic “disadvantage” with higher RT dose attributable to significant acute and late toxicities. These findings highlight the importance of balancing toxicity and disease control to optimize therapeutic gain. Several strategies have been employed to mitigate toxicities, such as respecting the biology of radiation injury by altered dose fractionation (typically using smaller than conventional fractions), or optimising radiotherapy technical delivery to reduce dose to vulnerable anatomy. Implementing novel RT technologies need to be closely monitored to prove clinical benefit. Historical lessons have shown that putative benefits may not always transfer to real clinical advantages since many unforeseen factors may modify potential anticipated gains. Without modern RT technologies, such as IGRT, adaptive, and IMPT provide opportunities to reduce RT late toxicity by providing more conformal dose distribution to spatially avoid normal tissue, the steps to achieve this are complex. One needs to appreciate many diverse factors. These include radiobiology of normal tissue (dose/constraints), optimal imaging quality and registration, systematic quality control involving “target” delineation to delivery, and knowledge of a variety of inherent pitfalls in the process(e.g. poor delineation, dose dumping, erratic planning, tumor or normal tissue deformation, and set up uncertainties that may emerge throughout the treatment course). For example, beam path toxicities have been reported due to “dose dumping” from parotid-sparing IMRT in head and neck cancer. Increased local failure has been observed when delivering tight margin carotid-sparing partial organ irradiation for T2 glottic cancer using vertebrae rather than laryngeal soft tissue as the image guidance surrogate. Adaptive radiotherapy appears to be feasible in some situations but the therapeutic advantages are yet to be proven and may be tedious and inefficient under the current technical configurations of many departments. Also, with intensity-modulated proton therapy (IMPT) is an attractive emerging approach that is probably able to spare normal tissue, indications and clinical benefit are also largely unproven at this time. The path to implementing these approaches will require rigorous
attention to the radiotherapy planning and delivery elements, and careful systematic and prospective documentation of tumor and normal tissue outcomes. Even if randomised trials are deemed unsuit for the setting, protocol based approaches in registered phase I/II trials are appropriate to enhance standards and should probably include audit and quality assurance processes, as well as realistic stopping rules to address unexpected or aberrant outcomes.

Symposium: Selection of patients for proton therapy

SP-0009 Patient selection for proton therapy: a clinicians view
A. Mahajan

1MD Anderson Cancer Center, Proton Therapy Center, Houston, USA

Proton therapy is a radiation modality that has become increasingly available world wide over the past decade. It is an attractive radiotherapy intervention because of the charged particles dose deposition profile of characterized by the Bragg peak. By using proton therapy strategically, there is the potential to deliver effective radiation dose to the target while reducing radiation to the surrounding non-target structures. The goals of any radiotherapy approach is to improve tumor control and/or reduce side effects and proton therapy offers an opportunity to achieve either one or both of these goals. Despite the promise of proton therapy, one must consider the risks and benefits, and as with any other radiation approach, to maximize the benefit to the patient. In general concepts that are useful in selecting and predicting a the benefit of proton therapy in individual patients include the following:

1) Proton therapy has the same risk of injury within the target area and high dose as other radiation therapies. For infiltrative tumors that require irradiation of a margin of normal tissue (example rhabdomyosarcoma) or those that have normal cells embedded within the tumor (example low grade glioma), the tissues receiving the high dose of radiotherapy will have similar risks of injury as non-proton approaches; therefore, one would not expect a lower risk of injury in the high dose area.

2) Since proton therapy is typically associated with a lower risk of late effects Patient who has a very low chance of surviving a long time due to the natural history of the disease, may not benefit from proton therapy, experience widely metastatic cancer.

3) Patients, for example children, who can derive benefit from normal tissue radiation dose reduction are usually good candidates.

4) Patients who require high doses of radiation to achieve tumor control, but would otherwise be limited due to normal tissue tolerance, for example patients with skull base chordoma or primary or secondary liver.

5) Tumor geometry and surrounding anatomy must be evaluated to estimate the potential benefit of proton therapy. For example, a 2 year old patient requiring flank radiation for Wilms tumor may have benefit with proton therapy, whereas an 18 year old with a paravertebral Ewing's sarcoma may have significant advantage with proton therapy.

6) Patient set up, tissue uncertainties, external devices or implanted need to be evaluated to minimize the risk of uncertainties and disruption in the proton dosimetry.

7) Proton therapy may be a good option for re-irradiation in selected patients. In summary, proton therapy can be an excellent option to provide better local control and/or reduced toxicities in selected patients.

SP-0010 Selection of patients for proton therapy: a physicists view
M. Hoogeemans 1, T. Arts 1, S. Van de Water 1, S. Van der Voort 1, Z. Perko 2, D. Lathouwers 2, S. Breedveld 1, B. Heijmen 1

1University Medical Center Groningen, Department of Radiation Oncology, Groningen, The Netherlands
2Delft University of Technology, Radiation Science and Technology, Delft, The Netherlands

Intensity Modulated Proton therapy (IMPT) is a highly promising approach for radiotherapy treatment of cancer patients due to its increased potential to reduce side effects and improve quality of life compared to contemporary radiation therapy techniques, such as IMRT. However, IMPT is associated with high costs and hence limited availability. Ideally, patient selection for IMPT should be based on the highest expected complication reduction compared to IMRT. For a given patient, it is possible to predict the risk of side effects for proton and photon therapy by applying Normal Tissue Complication Probabilities (NTCP) models to optimized dose distributions. Only patients with clinically relevant reductions in NTCP exceeding minimum pre-defined thresholds will then qualify for proton therapy. While this approach should guarantee effective use of proton therapy, there are several concerns that will be discussed in this presentation:

1. The generation of a radiotherapy treatment plan is a complex procedure and its quality is highly dependent on the planner skills. To enable unbiased comparisons between IMRT and IMPT for each patient, automation of the treatment planning process is imperative.

2. IMPT is highly susceptible to inaccuracies in patient setup, anatomic changes, and to uncertainties in the calculation of the proton range. IMRT, uncertainties in dose delivery are accounted for in the CTV-to-PTV margin. In IMPT, however, the PTV concept is not applicable. Alternatively, robust treatment planning can be used to take into account patient setup and range uncertainties. However, it is currently unknown which robustness settings need to be used to achieve an acceptable HTCP. For historical reasons. The applied image-guidance technology will have an impact on the magnitude of NTCP reduction and hence on the selection of patients qualifying for proton therapy.

SP-0011 Future selection practice for proton therapy: selection of patients based on treatment planning comparison and NTCP-modelling
H. Langendijk

1University Medical Center Groningen, Department of Radiation Oncology, Groningen, The Netherlands

The last decade, many new radiotherapy delivery techniques have been clinically introduced without being subjected to randomized controlled trials. Many of these new techniques have been introduced in order to reduce the dose to the healthy tissues and subsequently to prevent radiation-induced side effects. Due to its superior beam properties, radiotherapy with protons compared to photons enables similar dose administration to the target volume with substantially lower dose to the normal tissue. In the Netherlands, we applied a 4-step model-based approach to select patients for proton therapy and to validate the benefit of protons compared to photons with regard to reducing the risk on radiation-induced side effects.

Step 1 consists of the development and validation of multivariable Normal Tissue Complication Probability (NTCP) models. NTCP models describe the relationship between radiation dose distribution parameters and the probability of a given side effect (NTCP-value). One of the output parameters of this step are the most relevant Dose Volume Histogram (DVH) parameters that can be used to optimize radiation treatment. Step 2 includes in silico planning comparative studies. In this phase protons are compared with photons with regard to their ability to reduce the most relevant DVH-parameters resulting from step 1 (Delta).

Step 3: Integration step 1 and 2. By integrating the results of the individual in silico planning comparison into the validated NTCP-models, the differences in dose can be translated into a difference in NTCP-value in each individual patient.

Step 4: Analysis of clinical feasibility and outcomes.