The expense of radiation-induced late toxicity. Progressive cell depletion and inflammation are the leading mechanisms of acute toxicity which is observed during or shortly after treatment. The pathogenetic pathways of late toxicity, developing 90 days or later after the onset of radiotherapy, are more complex and involve processes such as vascular sclerosis and fibrosis. Since many patients have become long-term survivors, awareness and recognition of radiation-related toxicity has gained in importance and increased efforts are made for its prevention and management.

Technical innovations contribute to a reduction in radiotherapy-associated toxicity. The steep dose gradients of highly-conformal radiotherapy techniques allow for an accurate dose delivery with optimal sparing of the normal tissues. Several studies have demonstrated the dosimetric benefit of intensity-modulated radiotherapy (IMRT) and volumetric modulated arc radiotherapy (VMAT) compared to conventional radiotherapy techniques. It has been shown that the dosimetric benefit of IMRT translated into a clinically significant reduction in lower gastrointestinal toxicity compared with three-field conventional radiotherapy. In the near future MRI-linacs and proton therapy are likely to broaden the therapeutic window further. Prone positioning on a bellyboard reduces small bowel toxicity by pushing away the small bowel loops from the high dose region. Image-guided radiotherapy allows for an accurate definition, localization and monitoring of tumor position, size and shape before and during treatment and may help to reduce set-up margins.

Small randomized controlled trials have shown that the administration of several agents might have a beneficial effect for the prevention of acute (e.g. intrarectal amifostine, oral sulfasalazine and balsalazide) and/or late-onset radiation-induced toxicity (intrarectal beclomethasone and oral probiotics). Once severe toxicity develops, total replacement of the diet with elemental formula may be appropriate. Probiotics influence the bacterial microflora and seem promising in reducing the incidence and severity of radiation-induced diarrhea. Currently there is insufficient evidence for cytotoxic and anti-inflammatory drugs in the management of radiation-induced toxicity. Future challenges lie in the prediction of treatment-related toxicity, which might be a promising step towards an individualized risk-adapted treatment.

**Teaching Lecture: Role of brachytherapy in the management of paediatric tumours**

**SP-0005**

**Role of brachytherapy in the management of paediatric tumours**

C. Haie-Meder\(^1\), H. Martelli\(^1\), C. Chargari\(^1\), I. Dumas\(^2\), V. Minard-Colin\(^3\)

\(^1\)Institut Gustave Roussy, Brachytherapy Service - Radiation Oncology Department, Villejuif, France

\(^2\)CHU Bicêtre-Paris XI, Department of Pediatric Surgery, Le Kremlin-Bicêtre, France

\(^3\)Gustave Roussy, Brachytherapy Service - Radiation Oncology Department, Villejuif, France

As the cure rates for childhood cancers continue to improve with better local control and outcome, the incidence and management of long-term consequences are a constant challenge. Conservative treatments include a combination of chemotherapy, radiotherapy and surgery that may lead to 5 year-survival rates > 90%. The use of brachytherapy, whenever feasible, is an attractive alternative when ionizing radiation is needed for the treatment of paediatric cancers, especially rhabdomyosarcomas (RMS). In genital RMS, brachytherapy represents an alternative to radical surgery: hysterectomy or colpectomy in girls and cystoprostatectomy in boys. When brachytherapy is properly applied, the probability of late complications remains low with a high cure-rate. At Gustave Roussy Hospital, since decades, brachytherapy -when possible- has been proposed as an alternative to external irradiation or radical surgery. So far, more than 150 children have been treated with brachytherapy, in the context of multidisciplinary approach, including chemotherapy +/- conservative surgery. The most frequent tumour sites were vagina/uterine cervix, bladder/prostate and nasolabial fold, the most common histopathological type being RMS. In a series of 39 girls treated between 1971 and 2005, interstitial brachytherapy was used for vulval tumors, and endocavitary brachytherapy was used in vaginal tumours with individually tailored moulded vaginal applicators. Among them, 20 patients were treated before 1990, where the initial tumoral extension was included in the brachytherapy volume, while after 1990, only residual disease after initial chemotherapy was treated. The usual prescribed effective dose was 65 Gy relative dose to the brachytherapy applications, taking into account the doses to organs at risk. With a median follow of 8.4 years, local recurrence was reported in 2 patients (5.1%) in the first year following the treatment, regional relapse in 1 patient (2.6%) and distant recurrences in 7 patients (17.9%). Among the 20 patients treated before 1990, 15 presented long-term sequelae, (vaginal or urethral sclerosis or stenosis) with three requiring surgical treatment. By contrast, among the 19 patients treated after 1990, four patients had vaginal or urethral stenosis, none of them requiring surgery. A recent long-term toxicity analysis confirmed the increase of the total number of G3-4 late effects in patients treated before 1990. From 1991 to 2007, 26 boys with bladder/prostate RMS were treated with brachytherapy as a peroperative procedure. All of them underwent a conservative surgical procedure, with bladder-neck and urethra preservation. Brachytherapy was systematically performed after tumor resection, consisting of two loops encompassing the prostate and the bladder-neck area. A total dose of 60 Gy was delivered with low dose rate. With a median follow-up of 4 years (10-months-14.5 years), only one patient locally relapsed out of the brachytherapy treated area. Among 11 boys older than 6 years, 9 (82%) were normally continent, two had diurnal dribbling treated by bladder education. Recently, sexual and urinary functions, assessed with a quality of life (QoL) questionnaire, were studied in a cohort of 22 long-term survivors. The results showed that the great majority of long terms surviving males (76%) considered themselves as having normal QoL. Between 1971 and 2005, 16 children with RMS of the nasolabial fold were treated with brachytherapy. Ten presented embryonal RMS and six alveolar RMS. In 12 cases, brachytherapy was combined with chemotherapy +/− conservative surgery. The most local, 6 regional, and 2 metastatic failures were reported. In this particular context, brachytherapy provided an acceptable local control rate, but with a poor regional control. The ballistic interest of BT has been clearly demonstrated in paediatric RMS, with a very high dose gradient, sparing normal tissue and very high tumor dose. In our experience low dose-rate brachytherapy was used and recently had to move to pulsed dose-rate brachytherapy. Such conservative approach, minimizing late sequelae without detrimental effect on local control, should be offered whenever possible. This treatment is a clear demonstration of the multidisciplinary team approach, including surgeons, pediatricians and radiation oncologists.

**Teaching Lecture: Challenges in MR guided radiotherapy**

**SP-0006**

**Challenges in MR guided radiotherapy**

J. Jonsson\(^1\)

\(^1\)Umeå University - Norrlands Universitetssjukhus, Department of Radiation Sciences, Umeå, Sweden

Radiotherapy has relied on computed tomography (CT) for both target definition and treatment planning during the last decades. However, the increasing accuracy in radiation delivery, through highly conformal techniques such as intensity modulated radiotherapy (IMRT) and image guided
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 treatment can 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 or 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 need 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. Amos

University 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 patients often require extended travel periods, to obtain the best cancer care. Intensity-modulated proton therapy (IMPT) offers an attractive alternative for many patients, but 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'Sullivan, S. Huang

Princess Margaret Cancer Centre, Toronto, Canada
Princess 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, and for some diseases, such as nasopharyngeal cancer, it is often the only curative option. Disease control is generally of 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 9111 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. Wherever novel RT technologies, such as IGRT, IMRT, 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 gliotic cancer using vertebrae rather than laryngeal soft tissue as the imaging surrogate. Adaptive radiotherapy appears to be feasible in some situations but the therapeutic advantages are yet to be proven and may be limited and inefficient under the current technical configurations of many departments. Also, the intensity-modulated proton therapy (IMPT) is an 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