

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 cytoprotective 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.

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

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SP-0005

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

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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 cysto-prostatectomy 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 dose was 60-65 Gy delivered in one to three 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 perioperative 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 local excision. The doses ranged from 50 to 70 Gy, depending on chemotherapy response, and surgical margins. With a median follow-up of 4.4 years (1.7-33), 10 patients relapsed: 4 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.

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

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##### Challenges in MR guided radiotherapy

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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