Symposium (Tue, 25 Sep, 09:00−11:00)
Update on fractionation issues in radiotherapy – does the old dogma still hold?

61 INVITED

Alpha/beta ratios for human tissues and organs – an update

S.M. Bentzen. *USA*

Abstract not received.

62 INVITED

Time, dose and fractionation in squamous cell carcinoma – business as usual?

J. Overgaard. *Denmark*

Abstract not received.

63 INVITED

Hypofractionation in adenocarcinoma – are we getting clever, or have we forgotten the past?

P. Hoskin. *Mount Vernon Hospital, Marie Curie Research Wing, Northwood Middlesex, United Kingdom*

Hypofractionation is an attractive proposal for both the patient minimising their inconvenience from treatment and for the health professionals who reduce the use of expensive resources. It should however only be considered where it can be proven to have equivalent efficacy and toxicity to more prolonged treatment schedules using conventional or hyperfractionated treatment.
In palliative treatments there is good evidence to show that equivalent symptom control with minimal toxicity can be achieved using hypofractionation. Examples include single dose treatment for bone metastases and advanced non small cell lung cancer and short course treatments delivering three to five fractions for advanced bladder cancer, cerebral metastases, spinal cord compression and good performance non small cell lung cancer.
In radical treatments hypofractionation is not novel in UK radiotherapy practice and schedules delivering 50 -55 Gy over 3 to 4 weeks have been used for many years based often on a pragmatic use of resources rather than radiobiological constructs. The basis of our modern understanding of radioresponsiveness is the linear quadratic equation. Conventionally malignant tumours have been considered to have a relatively high alpha/beta ratio however it is now clear that this is not a universal rule.
Adenocarcinoma of the prostate has been evaluated by several groups all of whom consistently show a low alpha beta ratio in the range 1.5−3.5 for this tumour. The important implication of this when considering radiation schedules for radical treatment is that prostate cancer will have marked fraction size sensitivity with relatively greater biological effects being achieved as fraction size is increased.
The major drawback of a low alpha/beta ratio for a tumour is that if this is lower than the critical normal tissues, in the case of prostate the rectum, then fractionation cannot be used to spare late normal tissue damage. The alpha beta ratio for rectum is considered to be around 3.5 very similar to some estimates of the value for prostate cancer. In this setting fractionation will not result in rectal sparing and if hypofractionation is to be used to escalate the biologically effective tumour dose, the volume of rectum in the PTV becomes a critical factor in order to minimise late effects. Conformal and IMRT based external beam techniques will minimise rectal volumes however the mobile and variable nature of the rectum day to day during a prolonged fractionated course of treatment means this is only optimised if image guided techniques are used.
Large doses per fraction of 10 Gy or more can be delivered by high dose rate {HDR} temporary afterloading brachytherapy which may be used as a boost following external beam treatment to achieve total dose escalation; a recently reported UK randomised trial comparing 55 Gy in 20 daily fractions was compared with 37.5 Gy in 13 daily fractions followed by an HDR implant boost delivering a further 17 Gy in 2 fractions has shown an improvement in biochemical relapse free survival with this approach. HDR brachytherapy for prostate cancer is now under investigation as a monotherapy option delivering high effective biological doses in three or four fractions.
Hypofractionation may well have a role in other tumour sites; the results of the START trial in breast cancer comparing 40 Gy in 15fractions with 50 Gy in 25fractions and 41.6 Gy in 13 fractions with 39 Gy in 13 fractions with 50 Gy in 25 fractions suggests that this tumour may also be effectively and safely treated with larger doses per fraction than conventional schedules.
We must however reflect against the past and acknowledge concerns that large doses per fraction may result in greater normal tissue late damage. The critical issue lies in the volume of normal tissue included in the PTV and it is in this respect that modern radiotherapy techniques enable us to consider fractionation schedules which would otherwise be hazadous, by harnessing the tools of three dimensional imaging, conformal and intensity modulated planning and image guided delivery to ensure accurate and reproducable delivery of radiation dose. We have not forgotten the past, but may be clever enough to now reconsider hypofractionation as a safe, effective and efficient means of radical treatment.

64 INVITED

IMRT and fractionation: what to do with large volumes given small doses – vice versa

C. Nutting. *UK*

Abstract not received.

Special session (Tue, 25 Sep, 09:00−11:00)
The European Society of Surgical Oncology (ESSO)

65 ESSO Award

Personalized surgical treatment for colorectal liver metastases

I. Taylor. *University College London Medical School, Department of Surgery, London, United Kingdom*

The last 20 years has seen a remarkable expansion in the number of treatments available for patients with colorectal liver metastases. The key to improving outcome however, lies with careful selection of patients and treatments and for this reliance on quality imaging is essential.
To personalise the optimum treatment, all patients with colorectal liver metastases should be discussed within a multidisciplinary team structure. Often, such a group meets with the colorectal cancer multidisciplinary team. Pre-operative investigation involves high quality contrast CT. More recently FDG-PET and PET CT have been introduced and results in a higher sensitivity and specificity.
In the absence of metastases elsewhere, solitary liver metastases should be resected. Numerous prospective studies have confirmed the benefit of this approach. Actuarial 5 year survivals of up to 40% with a median survival of 54 months has been reported. There is an increasing tendency to consider all patients for resection provided an R0 resection can be achieved irrespective of number or location. However, a resection margin of greater than 1 cm is important.
In situ ablation has become increasingly popular. Indications for radiofrequency ablation include patients with significant morbidity precluding major surgery, and patients who refuse surgery or have tumours in anatomically difficult situations.
Finally, chemotherapy is frequently utilised both for patients with advanced disease involving hepatic and extrahepatic sites and as adjuvant therapy, following liver resection or ablation treatment. In an attempt to increase the resectability rate, neoadjuvant chemotherapy as a down staging modality prior to liver resection is becoming accepted.
In personalising treatment, care must be exercised to avoid potentially unpleasant and dangerous treatment in patients with advanced disease and limited survival. Improving quality of life with appropriate palliative therapy is most important.

66 INVITED

Personalized surgical treatment for localised prostate cancer

H. van Poppel. *University Hospital Leuven, Department of Urology, Leuven, Belgium*

Background: Radical prostatectomy is the treatment of choice for localized prostate cancer. Through the years, the surgical technique has been more and more developed.
Material and Methods: Since the initial experience of radical prostatectomy, where mostly palpable and locally advanced prostate cancers were the vast majority, the technique of radical prostatectomy has changed substantially. Nowadays, mostly T1c prostate cancers constitute the majority of radical prostatectomy cases while however locally advanced tumours are still around at unchanged incidence.
Results: In the 1980s–1990s most radical prostatectomies were done with an excision of the neurovascular bundles, a resection of the bladder neck and a racket reconstruction and anastomosis, with an indwelling catheter for two weeks or more, more or less important blood loss and acceptable results for urinary continence but poor results for erectile function. Nowadays, bilateral or unilateral nerve sparing techniques with preservation of the entire length of the urethral sphincter and preservation

of the bladder neck, have made radical prostatectomy for T1c and small T2a lesions to rather be defined as a "total" prostatectomy with a very marginal resection of the gland. The surgical technique performed by the author is not an intrafascial nerve sparing procedure but rather an enucleation (extrafascially) of the prostate gland out of the neurovascular bundles.
For the locally advanced cases wide excision of the neurovascular bundles is mandatory and also this technique is extensively described.
Conclusions: Total prostatectomy with preservation of continence and potency and radical prostatectomy for locally advanced prostate cancer belong to the modern surgical approach in the battle against localised and locally advanced prostate cancer.

67 INVITED

Personalized surgical treatment for early breast cancer

E. Rutgers. *The Netherlands Cancer Institute, Department of Surgery, Amsterdam, The Netherlands*

Definition of early breast cancer: For this purpose EBC is defined as T1/2 (<3 cm) N0/1. The issue of neo-adjuvant chemotherapy in larger breast cancers is not part of this presentation.
What are the factors to take into account to enable a fully personalised loc0-regional treatment in a woman with breast cancer?
Optimal imaging:
– mammography (digital), magnification views, ultrasound, MRI (if this can be afforded it is very helpful to select patients for breast conservation and to exclude multifocality etc.)
– Image guided histological and cytological diagnosis of the index lesions.
– Imaging of the axilla: ultrasound (mandatory, if suspicious FNA Cytology of nodes)
– PET-scan (not considered to be standard).
Patient related factors:
– Age, the younger the patient, the higher the risk for local relapse and second primaries
– Family history: hereditary breast cancer likely?
– Patient preference after optimal information
The surgical options:
– Wide local incision with the intention of a 1 cm free margin including reconstruction of the breast where dead space should be kept to a minimum. Any oncoplastic technique should always be applied.
– Skin sparing mastectomy (with or without nipple sparing) and immediate reconstruction
– Sentinel node biopsy (if preoperative assessment is negative)
– Axillary lymph node dissection (if pre lymph node assessment or SN is positive (> isolated tumor cells)
– Mastectomy with or without ALND
– Thermo ablation of the tumour is to be considered experimental.
Histological work-up. The following steps are indispensable:
– Marking the specimen for orientation
– Full margin assessment
– Paraffin and fresh frozen tumour samples to enable RNA/DNA analysis including storage.
The report should include minimally:
– Type of breast cancer (IDC, ILC, medullary, etc)
– Margins: minimal margins, close, involved, focally involved and more than focally involved,
– Differentiation grade, vascular invasion
– ER, PR and HER-2 testing is mandatory; P53, KI 67 helpful but not standard
Radiation therapy:
– Whole breast including yes or no boost (partial breast irradiation is in general considered to be experimental)
– Internal mammary chain / supra clavicular (as elective treatment not generally applied)
– Axilla (as alternative for ALND)
– Axilla and peri clavicular area in node positive disease (indications are shifting!)
Systemic therapy:
– Adjuvant hormonal therapy (if endocrine responsive) and/or chemotherapy is able to reduce local relapse rates by 30−50%.
All these different steps should be taken and discussed with the patient, leading to optimal local regional control breast cancer with optimal cosmetic outcome. Loco-regional relapse rates should be kept within 1% per year and cosmetic results should be good to excellent in over 80% of the women.

68 INVITED

Personalized surgical treatment for sarcoma

P. Hohenberger. *Klinikum Mannheim der Universität Heidelberg, Head Section of Surgical Oncology and Thoracic Surgery, Mannheim, Germany*

During this presentation, I would like to discuss my personal beliefs and decision making process that includes the following steps:
1. Is it really sarcoma?
2. Is it a molecularly characterized sarcoma with distinct treatment options (DFSP, GIST, myxoid/round cell liposarcoma, angiosarcoma)
3. Is it low grade or high-grade?
4. If it is low grade, is it primary respectable?
5. Is a plastic or reconstructive procedure required?
6. If it is high-grade, which options for combined neoadjuvant/adjuvant treatment fits best to location of the tumor, Karnofsky status of the patient, availability of technique?
7. In case postoperative irradiation of the tumor will be required with high probability, any effort should be performed to schedule it preoperatively, this is particularly of interest in retroperitoneal sarcoma.
8. High-grade sarcoma of the limb with deep location or extracompartimental extension require preoperative treatment, preferably by isolated limb perfusion with TNFa and melphalan, alternatively by a combined radiochemotherapy.
9. Any locally recurrent tumor following adequate resection must be considered for combined modality therapy!
10. Resection following preoperative radio-/chemotherapy or ILP should use the preoperative imaging findings to decide on resection margins.
11. Long-term functional outcome needs to be assessed by validated tools.
12. Most important: explain the schedule of treatment and the time required until final recovery from rehabilitation to the patient and his/her family. This may take half a year or even longer. Adapt your schedule to the ability of the patient to cope with the sarcoma.

Special session (Tue, 25 Sep, 09:00−11:00)
The European Branch of the International Society of Paediatric Oncology (SIOP Europe)

69 SIOP-Europe Award

Teenage and Young Adult Cancer (TYA) "The Forgotten Tribe"

T. Eden[1], J. Birch[1], L. Fern[2], J. Whelan[2], M. Rogers[3], S. Smith[3].
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All of the advances in the survival of children with cancer has highlighted the relative lack of focus and understanding of TYA cancer. We are making a concerted effort to focus on: the absolute/relative incidence of tumours in those aged 13−24 years; aetiology; assessing if referral and diagnosis is timely and appropriate; who should treat and care for TYA?; why is trial entry so low?; does biology affect outcome?; why is survival worse than in childhood?; and is there an optimal environment for care. Preliminary data demonstrates that TYA cancer constitutes 1% of all malignancy (nearly twice as much as in childhood, 2000 versus 1200/year in UK), but 13% of all deaths. 10% of the tumours are the tail of those seen in childhood, 30% of the tumours peak in this age, but 60% are early onset adult tumours. The pattern provides clues to aetiology. Delay in diagnosis has been identified but professional delay is greater than patient for all tumours studied. Ways to reduce delay are being explored. Survival has improved 1970–2000 but less than in childhood. The contribution of biology and treatment will be explored. Trial entry falls off exponentially with increasing age. Paediatric and adult oncologists/nurses must work together to provide timely, optimal care for this needy group.

70 INVITED

Recent childhood cancer survival in Europe

G. Gatta.

Abstract not received.