patient or peer pressure, but also, because reimbursement for services is more generous for Intensity Modulated Radiation and Particle Therapy, the same as for complex Surgical (robotic) techniques, new Biological Targeted and other complex drugs. In the future it will be critical to foster research studies of innovative diagnostic, staging or treatment modalities with well designed prospective trials on cost benefit, and Comparative Effectiveness, including evaluation of cost of care of patients with cancer throughout the lifetime of the patient and taking into account quality of life and productivity after treatment. Because of the concerns at political and administrative levels of governments with the cost of health care, Radiation Oncologists must remain vigilant and active in these circles, to defend our interest and those of our patients. As our distinguished colleague Anthony Zietman noted a few years ago, the seduction of technology should not detract from our primary objective, which is to be COMPLETE ONCOLOGISTS. In the future, that should continue to be a major emphasis in Radiation Oncology Training Programs and in the everyday practice of the Specialty.

209 INVITED

Personalized Medicine and Prostate Cancer Radiotherapy

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In intermediate risk prostate cancers (CaP) localized to the prostate, treatments such as active surveillance, radical prostatectomy (RadP), image-guided external beam radiotherapy (IGRT), or brachytherapy are used. Current prognostic factors such as T-category, serum PSA, and pathologic Gleason score explain only a proportion of the variation in clinical outcome. Better predictors of treatment outcome and patient prognosis are required to individualize CaP treatment and to provide optimal therapy with minimal side effects; this includes novel assays based on DNA Copy Number Variation and whole genome sequencing.
The Canadian Prostate Cancer Genome Network (CPC-GENE) is an outcomes-based initiative that will sequence specimens from 300 localized-prostate cancer patients who underwent surgery or radiotherapy. These samples are derived from pre-treatment biopsies, radical prostatectomies, and paired bloods and are directly linked to clinical outcome databases in which patients have more than 6.5 years median follow-up after treatment. Patients either responded (~70%) or did not respond to therapy (~30%). Using this approach, these DNA-based studies are directly linked to clinical outcomes and glean important new information regarding the genetic signature of localized versus occult metastatic diseaseto optimize treatment with radiotherapy in combination with molecular targeted therapies.
We are currently conducting pilot studies in which 40−50 specimens from fresh frozen pre-IGRT biopsies and radical prostatectomies, all with Gleason score 7, are being analyzed by array CGH/SNP array and whole-genome sequencing. The carefully selected samples will allow us to focus on characterizing the inter- and intra-tumoural heterogeneity of intermediate risk prostate cancer for a given Gleason score. As a first approach, our initial data using pre-IGRT biopsies in 120 modern-era radiotherapy patients with high-resolution, array CGH, demonstrates that copy number gains in *c-MYC* and losses in *NKX3.1* and *PTEN* are associated with increased genome instability (e.g. increased percent genome alteration). In a multivariate analysis, adjusting for the clinical prognostic factors PSA, Gleason score and T-category, we found that *NKX3.1* loss was prognostic for biochemical relapse (HR = 2.94, 95% CI: 1.19–7.26, p = 0.019) alone or when combined with *c-MYC* gain (HR = 4.32, 95% CI 1.36–13.71, p = 0.013). A similar negative prognosis (e.g. significant HRs greater than 2) was associated with allelic loss of PTEN or loss/mutation of p53. Interestingly, our data with TMPRSS2:ERG suggests that it may be a positive predictive factor in radiotherapy patients for response.
CNV and whole-genome sequencing of prostate cancers could help to generate predictors of treatment outcome and patient prognosis, enabling personalized medicine to become a reality.

Society Session (Sun, 25 Sep, 16:45−18:15)
European Association of Urology (EAU)

210 INVITED

The Role of Screening in Prostate Cancer

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The European Randomized Study of Screening for Prostate Cancer (ERSPC) is a randomized cotrolled trial of men aged 50−74 years (core age grouup 55−69) recruited in 8 European countries. To the core age group, to which all centers contributed, 162,243 men were randomized. 20,437 tested positive, 20,437 tested positive with PSA values ges;3.0 ng/ml and 85.8% of these were biopsied resulting in a PPV of 24.1%. In the screen arm 5,990 cancers were found (8.2%) and 214 died of prostate cancer, in the control arm these figures amounted to 4,307 (4.8%) and 326 cancer deaths.
At the time the described information was obtained with a median 9 year follow-up. Relative risk reductions of 21%, 27% and 31% were found in intention to screen analyses (ITS) and analyses adjusting for non compliance alone or in conjunction with adjustment for contamination in the control group. The data of the ITS analysis translated into numbers needed to screen (NNS) and to treat (NNT) to save one cancer death of 1,410 and 48 (Schröder et al NEJM 2009).
The Swedish partner of the ERSPC study, the Göteborg Randomized Screening Trial was initiated in 1994 as an independent study but joined the ERSPC in 1996. It applied a population based randomization which allowed the inclusion of the whole population of participants at the same time. As a result, non participation occurred only in men randomized to screening, and a 14 year follow-op period was reached with a complete data set to the end of 2008. The analysis was carried out in line with predesigned power calculation, the resulting data were published in 2010 (Hugosson et al Lancet Oncology). With the longer follow-up achieved in this part of the ERSPC study the relative risk reductions in the ITS analysis and after adjustment for non compliance amounted to 44% and 56% with NNS and NNT of 293 and 12.
The main down side which at this time and with the applied screening remains is seen is an amount of over diagnosis which is estimated to be in the range of 42−66% (Draaisma et al 2003 and 2009). Mechanisms are available to reduce over diagnosis and will be described. The best solution to the problem, the development of amor selective marker whic identifies potentially indolent disease is a future perspective.
Regular evaluations of the ERSPC data will be carried out, the data set will be updated every six months. At this time only about 25% of the participants have died. The end point of the study is to be determined based on future development of the data.

211 INVITED

Radical Prostatectomy − the Gold Standard in the Treatment of Localised and Locally Advanced Prostate Cancer

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In Europe, prostate cancer is the most common non-skin malignancy in males. The application of PSA as a tool for early detection has led to a stage shift with localized and thus potentially curable stages representing the majority of newly detected cases. Among patients referred for radical prostatectomy, recently, an inverse stage shift has been observed because of an increased use of active surveillance in low-risk cases. Up to now, however, only radical prostatectomy has been demonstrated to improve survival in clinically diagnosed prostate cancer in the setting of a randomized trial, compared with watchful waiting. Radical prostatectomy is the standard treatment of localized prostate cancer in men with an adequate life expectancy. It enables overall disease-specific 10-year survival rates of more than 90%, when considering histopathologically organ-confined cases, disease-specific 10-year survival rates reach narrowly 100%.
The treatment of clinically locally advanced prostate cancer (cT3−4) is subject to some controversies. Patients with lymph node metastases as well as patients with overstaged localized and thus curable disease may fall into this category. Radical prostatectomy, external beam radiotherapy and early or deferred hormonal therapy are possible treatment options for clinically locally advanced prostate cancer. Multimodal treatment (a combination of these options) is frequently used, but there is only few evidence available defining patients who could benefit from such aggressive treatment. After radical prostatectomy, the Gleason score-adjusted disease-specific survival does not differ meaningfully between the tumour stages pT2 (localized) and pT3−4 (locally advanced). Radical prostatectomy for locally advanced disease has the advantages of the remaining option of adjuvant radiotherapy. Furthermore, in patients with localized tumours in the prostatectomy specimen (about 25% of clinically locally advanced cases), adjuvant hormonal therapy (that would be given after external beam radiotherapy) is spared. Adjuvant radiotherapy may improve biochemical and local control in locally advanced prostate cancer. A survival benefit has, however, only been shown in one study yet, whereas others found no difference. External beam radiotherapy alone provides unfavourable survival rates in locally advanced prostate cancer. Adjuvant hormonal treatment for three years improves outcome in this setting. When no curative treatment is chosen, early hormonal treatment seems to provide modest benefit compared with deferred therapy. In the future, patients with locally advanced prostate cancer should be enrolled in controlled clinical trials to find out which treatment is best.