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Active surveillance activities in Europe for prostate cancer

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The incidence of early prostate cancer (PC) in Europe increases due to growing screening activities. Up to 30% of the cancers detected are of low risk, and indicated as harmless indolent tumours that are extremely unlikely to become symptomatic during life. In the European Randomised Study for Screening of Prostate Cancer, men that underwent surveillance for indolent tumours showed an almost 0% 10-year disease specific mortality, while 1 out of 4 men of those analysed died in the same period due to other causes than their PC. Expectant management is a generally accepted treatment option, as the outcome of localized PC may only partly be altered by radical surgery or radiotherapy. In the Scandinavian Prostate Cancer Group study 4, radical prostatectomy accomplished a decrease in PC specific mortality and metastasis compared to expectant management with delayed hormonal therapy of 18% to 13% and of 26% to 19%, respectively. This favourable effect was limited only to men aged <65 at diagnosis.
Active surveillance (AS) may provide a partial solution to the current overtreatment dilemma due to screening. In general, patients diagnosed with PC are selected for AS based on a number of well accepted inclusion criteria (like T1c/T2 PCa, PSA $\leqslant$ 10.0, PSA-density <0.2, Gleason score $\leqslant$3+3=6, and $\leqslant$2 positive prostate biopsy cores), and monitored till signs of tumour progression occur that initiate delayed invasive therapy with curative intent. While AS is offered in various non-validated schemes, a number of multicenter studies has been initiated in the EU that provide information and access for participation of patients with indolent tumours with the aim of validating and improving current AS protocols. Individual pre-treatment risk assessment for the presence of indolent cancers has been made feasible with validated nomograms.
The multicenter observational PRIAS study (www.prias-project.org) has recruited over 900 European and North American men from 2006 onwards. The follow-up protocol consists of PSA measurements, digital rectal examinations, and standard repeat biopsies. In the first 500 participants men baseline patient characteristics, PSA doubling time (PSA-DT) distributions, findings in repeat biopsies, clinical stage progression, treatment-free survival, compliance with the protocol, reasons for stopping AS, and outcomes after radical prostatectomy (RP) were studied. Also Quality of Life assessments at various time points were performed. After 2 years 27% of patients had shifted to invasive therapy. After Radical Prostatectomy, 13% showed T3 disease and 48% Gleason score >6; re-biopsies indicated these adverse findings in all cases.
In the UK, an AS study is coordinated from Royal Marsden Hospital for over 7 years, recruiting over 400 men. Analyses of biopsy related histologic markers, serum PSA isoforms, and diffusion weighted MRI all illustrate that extra value might be obtained from additional markers to predict the biological aggressiveness of these tumours.
Various analyses suggest that repeat biopsies seem essential in monitoring these patients. However, other monitoring parameters as well as inclusion criteria are under discussion. Compared to immediate therapy, the delayed treatment has not been associated with a higher risk of unfavourable outcomes. Analysis of surrogate clinical endpoints and evaluation of candidate biomarkers and imaging modalities may provide further guidance in AS.

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Watchful waiting in patients with prostate cancer – US

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Background: The majority of men (over 90%) diagnosed with low risk prostate cancer today in the United States undergo some form of intervention, despite high levels of evidence that older men with low risk, screen detected prostate cancers are unlikely to benefit from treatment. Active surveillance is an alternative approach to immediate intervention for the management of low risk prostate cancer in selected individuals thought to harbor low grade, low volume cancer.
Materials and Methods: Literature review of surveillance programs in the United States with published criteria for patient selection and triggers for intervention.
Results: Active surveillance or careful monitoring of individuals with the intention to cure should disease progression occur, has been described in multiple centers in North America that are gaining experience with this approach to management of low risk prostate cancer. Criteria for selection of men for surveillance, and appropriate triggers for intervention that will insure high rates of cure are being investigated.
Conclusions: Active surveillance as an option for management of low risk prostate cancer is underutilized in the United States, and barriers to acceptance of this approach should be addressed to reduce the over treatment of prostate cancer in an era of intense screening.

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(Bio) Imaging guided selection and application of personalized radiotherapy

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The radiotherapeutic management of prostate cancer relies heavily on optimizing its treatment based on the clinical parameters of disease that currently only include the prostate specific antigen (PSA) level at clinical presentation, histopathological Gleason score and the TNM staging system. In turn, the TNM system relies mainly on morphological staging using magnetic resonance (MR) imaging and bone scanning. Recent advances and developments in imaging methods and hardware such as MR particle imaging, dynamic contrast enhanced MR, diffusion weighted MR, MR spectroscopy, and positron emission tomography (PET) with CT using newer tracers such as choline are being investigated to assess its utility for improved staging of the disease extent, selecting patients with localized or local regional disease for radiotherapy, and optimizing tumour target volume delineation for personalized prostate radiotherapy. Herein lies the opportunity to define parameters of prostate cancer disease activity distinct from simple morphological size criteria such as regions of tumour density, proliferation, angiogenesis and hypoxia. This functional and biological information may substantially aid selection of patients for differing prostate treatment strategies. Therapy opportunities in prostate radiotherapy could include combined modality therapy with radiation using agents such as hormonal therapy, radiosensitizing agents, agents to limit angiogenesis and agents that affect growth factors associated with signal transduction and proliferation. In addition, there will be radiotherapeutic opportunities to improve local control by utilizing bio-imaging for selective targeting of regions of potential radioresistance such as hypoxia within the prostate gland. This may involve optimizing radiobiological rationale for dose escalation with hypofractionation. This may be achieved with intensity modulated radiotherapy (IMRT) with integrated simultaneous boosting of these biologically selected regions within the prostate gland or seminal vesicles. In addition, IMRT may permit tolerable irradiation of the pelvic nodal region where appropriate. The use of image guided methods will be needed to ensure accurate and reliable treatment delivery as well as targeting of any biologically relevant boost regions. Another important aspect of bio-imaging is the opportunity to assess disease response potentially during treatment to initiate alternate treatment options for poor responders. The rationale for integration of functional and biological targeting in prostate cancer needs careful study and its true utility and impact for clinical outcomes in prostate radiotherapy will need to be defined in clinical trials.

Scientific Symposium (Wed, 23 Sep, 09:00−11:00)
Is cytotoxic treatment outdated in advanced or early breast cancer

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Newer cytotoxics in breast cancer – are there any and are they still needed?

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The advent of targeted therapies has revolutionized the field of oncology and we now are in a much better position to understand and fight the scrounge called cancer. And as has been the habit of humankind, we now question the gold standard “old” chemotherapy with the glittering “new” targeted therapy.
Important part of early breast cancer patients treated only with surgery relapse. The introduction of chemotherapy and radiation therapy changed this dreadful scenario to give us cure rates of up to 70% in early stage breast cancer. The history is proof of this with the advent of CMF (Cyclophosphamide + Methotraxate + 5-FU) based treatment and then the introduction of anthracyclines followed by taxanes.
Anthracyclines and taxanes have now become an integral part of the chemotherapy regimes in the treatment of adjuvant and metastatic breast cancer. Both agents have been shown to provide better survival and clinical benefit to patients. But both, anthracyclines and taxanes, have some important side effects. Cardiotoxicity with anthracylines and neuropathy with taxanes are a reality. Newer agents are being required so as to mitigate the side effects and increase the therapeutic efficacy of these molecules. And newer agents which serve this purpose to increase the therapeutic