AA-induced gene transcription. In an animal model the production of TNF-α by PCa cells was responsible of the maintenance of a chronic inflammatory status in metastatic bone marrow, evidentiated by the presence of mature T-cells. Moreover the over-expression of TNF-α by AA-primed PCa cells resulted particularly effective in modifying cell behaviour of cultured bone stromal cells (BMSCs) and osteoclasts. In fact we observed an increment in the number of osteoblasts and in the production of RANKL by BMSCs, and a concomitant activation of osteoclasts. These cross-talks may contribute to the osteolytic appearance of bone lesions observed in vivo in PCa metastasis models.
Conclusions: These findings provide a possible molecular mechanism by which dietary n-6 fatty acids accumulating in bone marrow may influence the formation of PCa-derived metastatic lesions and indicate new molecular targets for therapy of metastatic PCa.

4016 POSTER

MR-guided prostate brachytherapy in a low-field open MR system: canine and in vitro dosimetry study

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Background: MRI provides excellent visualization of the prostate, its substructure and surrounding tissues, making it the modality of choice for guiding and monitoring interventions like brachytherapy and biopsy. Our objective was to demonstrate the feasibility of transperineal MR-guided prostate interventions in an open-MR unit focusing on needle-placement accuracy and rectal dosimetry.
Materials and Methods: The procedures were performed on 6 canines in an open-configuration 0.35T MR scanner. For interventions an MR compatible custom-made device was used consisting of 3 major parts: template-obturator rod, immobilization arm and patient tray. The canines were placed feet first in the right lateral decubitus position. Template reconstruction, trajectory planning, target and OAR delineation were based on T2 FSE images. For image guidance and target confirmation, fast gradient spoiled echo (FSPGR) sequence was used. MR compatible coaxial needles were inserted through the perineum to the base of the prostate. After satisfactory position was confirmed, brachytherapy catheters were placed through the coaxial needles, which were then removed. For the imitation of our 5-channel rectal dosimeter an MR compatible model was designed, inserted into the obturator and tested in gel phantom.
Results: MRI allowed clear definition of the prostate, periprostatic tissues, needles and catheters. Mean and standard deviation was 2.1 mm$\pm$1.2 mm, with a median of 1.9 mm. 97% of the errors were less than 4.0 mm; maximum error measured was 4.5 mm. The average time needed for each step was: setup and positioning – 20 min, initial imaging – 15 min, template registration and trajectory planning – 15 min, insertion of 10 needles – 45 min The five separated detector within the obturator was clearly visualized on the MR images. In gel phantom study the planned and measured doses at the different levels of the detectors was favorably and adequately matched.
Conclusions: A system for transperineal MR-guided prostate intervention has been developed and applied successfully on canines. This method seems to be a promising approach for performing feasible, accurate, reliable and high-quality image guidance within a reasonable time span. MR modeling of rectal dosimeter seems to be promising device to provide a more accurate prediction about the rectal doses. Our results facilitate us to introduce MR guided high-dose-rate (HDR) brachytherapy into the daily clinical practice in the near future.

4017 POSTER

Mutation of epidermal growth factor receptor in hormone sensitive and refractory prostate cancers

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Background: Hormone refractory prostate cancer (HRPC) is a significant cause of morbidity and mortality. Androgen receptor mutations and amplifications may explain relapse in some patients, but in approximately 70% of cases, alternative mechanisms must be invoked and type I receptor tyrosine kinases may play a role in mediating HRPC. In this study, EGFR and ERBB2 gene amplification and alteration were analyzed in HRPC.
Materials and Methods: EGFR were analyzed by fluorescence in situ hybridization in prostate cancer. We sequenced exons 18−24 of the EGFR and exons 19, 20 of the ERBB2 from genomic DNA isolated from matched tumor pairs (one taken in hormone sensitive and one in hormone refractory) from 10 prostate cancer patients. Amplification and mutation was compared with clinicopathologic features.
Results: EGFR amplifications were observed in 6 (30%) out of 20 specimens. A total of 9 EGFR mutation were detected in 3 (30%) of the 10 prostate cancer patients. EGFR mutation were not associated with ductal type but acinar type in adenocarcinoma prostate cancer. The EGFR mutations were in exon 18 (2 cases), exon 19 (5 cases), and in exon 23 (2 cases). Of them, 6 mutations showed aminoacid change and these aminoacid changes occurred in both hormone sensitive and hormone refractory specimens. No significant correlation was found in shifting of mutation between hormone sensitive and refractory status. Meanwhile, ERBB2 mutations were absent in prostate cancers.
Conclusions: EGFR may represent one of independent routes to metastatic and advanced prostatec cancer. EGFR deletion mutation and gene amplification may be occurred in far advanced prostate cancer, but which do not appear to play a significant role in the hormonal refractory pathway but is associated with prognosis.

4018 POSTER

Post-treatment prostate biopsies in the era of three-dimensional conformal radiotherapy. What can they teach us?

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Background: The vast majority of studies indicating a dose–response relationship are based on biochemical control as the primary end point. However, post-radiotherapy prostate biopsies are useful in evaluating innovations such as dose escalation protocols, or combined modality treatments. The present study was undertaken to correlate post-treatment biopsy results with PSA and clinical outcome in prostate cancer patients treated with three-dimensional conformal radiotherapy (3DCRT) in a dose escalation trial.
Materials and Methods: This study included 129 patients with localized prostate cancer treated with 3DCRT to a median isocenter dose of 73.1 Gy that consented and underwent a trans-rectal ultrasound (TRUS) guided prostate biopsy 24−36 months after radiotherapy. Thirty seven per cent (48/129) of biopsies were performed in patients under PSA failure conditions and the remaining 63% (81/129) in patients with PSA control. Risk-adapted short-term and long-term androgen deprivation (STAD and LTAD) was associated in 22 and 82 of patients respectively. The median follow-up was 66 months (range 26–147).
Results: Seventeen percent (22/129) of patients had post-treatment positive biopsies (PB), 35% (17/48) with prior PSA relapse and 6% (5/81) with prior PSA control. Patients receiving higher radiation dose experienced a lower incidence of PB after treatment ($p = 0.051$). The 6-year biochemical disease-free survival (bDFS) was 81%, 63% and 86% for the whole series, PB and negative biopsies (NB) patients respectively ($p = 0.044$). In multivariate analysis, only biopsy status at 24–36 months ($p = 0.043$) was independent predictor of clinical failure-free survival (cFFS).
Conclusion: The results of the present study show a strong correlation between a post-treatment PB and the 5-year probability of cFFS and suggest a relationship between radiation dose and histological response.

Results of multivariate analysis of potential factors affecting bDFS

Variable	Beta	Hazard ratio	P value	95% CI
PSA nadir $\leqslant 1$	−1.285	0.284	0.044	0.083−0.967
Post-treatment positive biopsy	0.771	2.163	0.014	1.166−4.011
Radiation dose (continuous)	0.185	1.203	<0.001	1.097−1.320