

and monoclonal antibodies anti-PCNA and anti-Ki-67 (MIB-1). The DNA flow cytometry to determine DI was also used.

**Results:** The greatest diameter (size) of the tumor measured by the pathologist was  $29 \pm 9$  mm. The mean survival of patients was  $47 \pm 37$  years (median 29 months, range 21–146). Diploid ( $DI = 1$ ) and aneuploid ( $DI > 1$ ) tumors were found in 4 and 11 cases, respectively. The median PCNA-LI was 13% (range 2–70%), and the median MIB-1 value was 11% (range 3–65%). The survivals of patients with diploid and aneuploid tumors were  $74 \pm 58$  months and  $34 \pm 18$  months ( $p = 0.21$ ), respectively. There was a linear relationship between PCNA-LI and MIB-1 ( $R = 0.93$ ,  $p < 0.01$ ), but no correlation between age and survival ( $R = 0.08$ ,  $p = 0.78$ ) was found. Moreover, there was no correlation between survival and DI ( $R = 0.17$ ,  $p = 0.55$ ), PCNA-LI ( $R = 0.07$ ,  $p = 0.72$ ), and MIB-1 ( $R = -0.05$ ,  $p = 0.86$ ).

**Conclusions:** PCNA-LI, MIB-1, and DI may be useful in confirming the diagnosis of malignancy, but they are of little value in predicting the clinical outcome of patients with PC.

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PUBLICATION

#### Expression of cystein proteases cathepsin B in inoperable squamous cell carcinoma of the head and neck

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**Background:** To determine the expression profile of CB and its prognostic value.

**Patients and Methods:** The expression of CB was determined on the tissue sections of primary tumors from 75 patients with inoperable SCCHN, treated with concomitant radiochemotherapy with Mitomycin C and Bleomycin. The data available for each patient were age, sex, performance status, tumor site, UICC TNM stage, histopathological grade, response to therapy and survival. The expression of CB was determined immunohistochemically using commercially available antibodies from KRKA D.D., Novo Mesto, Slovenia. The intensity of immunohistochemical reaction was scored as follows: G 0 = 0% tumor cells with positive nuclear reaction; G 1 = 1–10%; G 2 = 10–50%; G 3 = >50%.

**Results:** The expression of CB was scored as: G 1: 2 pts (3%); G 2: 8 pts (11%); G 3: 65 pts (86%). The grade of expression (grade 1+2 vs. Grade 3) correlated negatively with the primary tumor subsite (posterior wall vs. others,  $p = 0.001$ ), and positively with the response to therapy (partial response/ no change vs. complete response locoregionally,  $p = 0.05$ ), disease progression status (yes vs. no,  $p = 0.04$ ) and with the deaths for oropharyngeal carcinoma (yes vs. no,  $p = 0.01$ ). In all patients, staining intensity did not correlate with survival probability. However, significantly higher disease-free survival (DFS) and disease-specific survival (DSS) rates at 5 years were observed in the subgroup of patients with N+ regional disease ( $n = 59$ ) and with less intensive nuclear reaction to CB: DFS 70% vs. 36%,  $p = 0.07$ ; DSS 84% vs. 36%,  $p = 0.03$ . On multivariate analysis, performance status, radiotherapy dose, and UICC TNM stage of the disease, but not CB grade of staining, were identified as independent prognostic factors for DFS and DSS.

**Conclusions:** Predictive value of staining intensity of CB for response to therapy warranted further investigation, whereas its prognostic value seemed to be limited to N+ subgroup.

## Imaging

Oral presentations (Thu, 3 Nov, 8.30–10.30)

### Imaging

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ORAL

#### Monitoring of tumor oxygenation changes in head and neck carcinoma patients breathing a hyperoxic hypercapnic gas mixture (carbogen) with a non-invasive MR technique

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**Background:** Influenced by tumor blood flow, tumor tissue perfusion and oxygen supply, increased tumor tissue oxygen levels may improve the radiosensitivity of tumors. Therefore a non-invasive oxygenation-sensitive MR technique may be of prognostic value and useful to preselect patients

for individual treatments using hyperoxic gas mixtures like carbogen (5% CO<sub>2</sub> and 95% O<sub>2</sub>) or carbogen "light" (2% CO<sub>2</sub> and 98% O<sub>2</sub>).

**Material and Methods:** A total of 14 patients with histologically proven head and neck carcinoma were investigated on a 1.5T clinical MR scanner. Over the course of the examination, different breathing gases were administered via a soft face mask system (3min air, 6min carbogen "light", 4min air, 3min oxygen). A multi-gradient-echo sequence was used for quantification of the apparent transverse relaxation time T2\* which is sensitive to oxygenation changes. A series of 32 acquisitions was conducted, each lasting 30s. Imaging parameters were:  $\alpha = 25^\circ$ ,  $N_{\text{echoes}} = 8$ ,  $\Delta TE = 12$  ms,  $TR = 110$  ms, matrix =  $256^2$ , FOV = 192 mm, slice thickness = 8 mm.

**Results:** Thirteen of fourteen patients (13m, 1f) with 16 lesions were studied successfully. MRI measurements were obtained from primary tumor (PT) alone in 7/13 patients, from PT and lymphatic node (LN) in 3/13 patients and from LN alone in 3/13 patients.

Marked interindividual tumor tissue oxygenation changes while breathing carbogen or O<sub>2</sub> were seen. Pixel by pixel analysis of the T2\* values showed a shift towards higher values corresponding to an oxygenation increase in most but not all patients. However, a considerable intratumoral heterogeneity was also observed.

**Conclusions:** Detection of oxygenation changes in head and neck tumor patients is feasible by the presented MRI technique. It may be used for monitoring individual tissue response to hyperoxia and help preselect patients for individual treatments using hyperoxic gas mixtures.

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ORAL

#### Improved delineation of lymph node basins at risk in pelvic malignancies using magnetic resonance lymphography with ferumoxtran-10 for radiotherapy treatment planning

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**Purpose:** To determine the utility of Magnetic Resonance Imaging (MRI) with an ultra-small superparamagnetic iron oxide that delineates phagocytotic activity within lymph nodes as a means of lymph node target definition to generate a nodal clinical target volume comprised of the nodal basins at risk of tumor spread.

**Methods:** All patients with histologically confirmed prostate, bladder, cervical or endometrial cancer were eligible for this prospective trial. Each patient underwent pre- and post-contrast MRI studies over two consecutive days. Axial images were obtained at 3 mm intervals through the pelvis. Ferumoxtran-10 (Combidex®: Advanced Magnetics, Inc, Cambridge, MA) was administered on the first day immediately after the initial MRI. The pelvic vasculature and lymph nodes were delineated from the origin of the inferior mesenteric artery to the ischial tuberosities using 3D modeling and image processing software (3D-DOCTOR®: Able Software Corp., Lexington, MA). Lymph node frequency and location relative to the adjacent vascular segments was analyzed using Matlab (MathWorks Inc., Natick, MA). Each lymph node was divided into  $0.5 \times 0.5 \times 3$  mm<sup>3</sup> nodal voxels. The minimal distance between the centre of each nodal voxel and the closest artery or vein (in three-dimensions) was calculated for each of the vascular segments.

**Results:** 50 patients were enrolled (32 prostate; 8 bladder; 5 cervical and 5 endometrial carcinomas). Preliminary analysis reveals the maximum distance of the lateral most aspect of the lymph nodes from the closest vessel (either artery or vein) to be between 2.5 and 32 mm (mean 7.5). Analysis by vascular segment revealed the distances between the nodal voxels (percent of total nodal volume) and the closest vessel edge (mm) to be: distal Para-Aortic Artery and Inferior Vena Cava: 50%-4.69; 90%-10.55; 95%-11.63; Common Iliac Artery and Vein: 50%-4.04; 90%-8.17; 95%-8.76; and Internal and External Iliac Artery and Vein: 50%-6.65; 90%-14.27; 95%-17.51. Radial expansion around the major pelvic vessels failed to adequately encompass all of the lymph nodes at risk.

**Conclusion:** The use of MRI lymphography with ferumoxtran-10 enables the visualization of pertinent lymph node locations in a three-dimensional projection. This imaging technique may improve IMRT treatment planning by identifying those lymph nodes at risk of harbouring occult metastatic disease.