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Abstracts of Theses from the Scandinavian Countries

Abstracts of Scandinavian theses on oncologic subjects are published under this heading. The full theses are as a rule published by the universities or as supplements to different journals. They can usually be obtained after contact with the author.

Immunological aspects of papillary thyroid carcinoma

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Papillary thyroid carcinoma (PTC) is a puzzling disease. Although approximately 70% of patients with PTC have regional lymph node metastases at initial surgery, the long term survival is over 95%. A hallmark of the disease is an avid, T-cell dominated inflammatory reaction, which for over half a century has stimulated hypotheses of a tumor-specific immune response. We have investigated this possibility by examining indicators of humoral immunity, including immunoglobulin G (IgG) and complement by immunohistochemistry. Over 80% of PTC tumors were found to demonstrate significant deposits of both IgG and complement factors, indicating complete activation of the complement cascade. The main complement regulatory proteins CD55 and CD59, which normally inhibit complement deposition at the cell surface, were present in PTC tumor cells as well as normal thyrocytes. This suggests that complement regulation is circumvented by some other mechanism in PTC.

Having demonstated tumor-specific antibody deposits in PTC, we sought the antigens against which these antibodies were raised. Using immunoprecipitation and Western blot with serum from PTC patients as the antibody source, a 35 kDa protein was isolated from a PTC tumor, and peptide sequencing identified it as a fragment of cytokeratin 1. This 68 kDa intermediate filament protein is normally expressed only in the upper levels of the epidermis. Further investigations revealed the full length cytokeratin 1 protein in PTC tissues by immunohistochemistry, immunoprecipitation and Western blot using a monoclonal antibody specific for cytokeratin 1. Antibodies isolated directly from PTC tissue were also found to have bound cytokeratin 1 in situ.

As the etiology and behavior of PTC have been closely tied to the RET/PTC oncogene, which has also been demonstrated in autoimmune thyroiditis, we examined the presence of the RET protein in PTC by immunohistochemistry. 86% of the PTC tumors demonstrated cytoplasmic staining for RET, suggestive of RET/PTC activation, particularly in areas of intense inflammation. The results suggest that RET/PTC expression may be involved in the immunogenic response to PTC.

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Risk factors, prevention and treatment of early complications after allogeneic haematopoietic stem cell transplantation

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The aims of this thesis were to define risk factors for early complications after allogeneic haematopoietic stem cell transplantation (HSCT). such as bacteraemia during the aplastic phase, veno-occlusive disease in the liver (VOD) and acute graft-versus-host disease (GVHD). Furthermore, we wanted to evaluate new methods – e.g., intraosseous infusion, peripheral blood progenitor cell transplantation (PBPCT) and granulocyte-colony stimulating factor (G-CSF) post-transplant treatment for a shorter neutropenic period. And finally, we aimed to evaluate the effects and side-effects of recombinant tissue plasminogen activator (rt-PA) treatment and liver transplantation for VOD.

In 500 consecutive patients who underwent allogeneic HSCT in Huddinge Hospital between November 1975 and June 1995, receiving HSC from an unrelated donor was found to be the only significant risk factor ($p < 0.01$). In 251 patients grafted between January 1990 and June 1995, the following risk factors were associated with an increased risk of hepatic venoocclusive disease in multivariate logistic regression analysis: norethisterone treatment after transplantation ($p < 0.001$), bilirubin level > 26 μmol/l before transplantation (0.002), HLA-mismatched donor ($p = 0.003$), previous abdominal irradiation (0.02) and busulphan treatment (0.02). Heparin prophylaxis (100 IE/kg/24 hours), given from the start of the conditioning regimen until one month after BMT or discharge, did not influence the incidence or mortality rate of VOD. In 291 patients grafted with marrow from HLA-identical sibling donors between November 1975 and June 1993, the main risk factors for acute GVHD in logistic regression, multivariate analysis were: immunosuppression with monotherapy (CsA or MTX) ($p = 0.01$), pretransplant multiple-positive donor herpes virus serology ($p = 0.01$), early engraftment ($p = 0.02$) and CMV seropositivity in the recipient before BMT ($p = 0.04$).

Thirty-eight patients receiving marrow transplants from related donors were randomized to i.o. + i.v. ($n = 10$), i.o. ($n = 8$) or i.v. ($n = 20$) infusions of bone marrow. We found a significant reduction in the number of days on TPN ($p = 0.03$) and a tendency to a reduction in the number of days on antibiotics, using the i.o. technique ($p = 0.06$). However, intraosseous, compared to intravenous administration of bone marrow, did not accelerate haematological recovery.

Twenty-three recipients of peripheral blood progenitor cells (PBPC) were matched with 23 recipients of bone marrow (BM). Eleven in each group were recipients of unrelated HSC. A higher number of MNC ($p < 0.001$), CD34+ ($p = 0.05$), CD3+ ($p < 0.001$) and CD56+ ($p < 0.001$) cells in the graft, a reduced number of platelet transfusions ($p = 0.03$) and a significant hastening of neutrophil (ANC $> 0.5 \times 10^9$/l, 12 vs. 17 days after HSCT, $p < 0.001$) and platelet recoveries ($> 30 \times 10^9$/l, 15 vs 20 days, $p = 0.02$) were seen in the PBPC group, compared to the BM group.

Sixty-nine patients were randomized to G-CSF (5 μg/kg/day) treatment, starting on day 0 ($n = 23$), day +5 ($n = 23$) and day +10 ($n = 23$), respectively, after unrelated HSCT. G-CSF treatment starting on day +10 was found to be as effective in improving neutrophil recovery as starting on day +5 or on the day of transplantation (day 0). Starting treatment on day +10, rather than on day 0, reduced the costs of G-CSF by $1060. The 69 patients given G-CSF reached ANC $> 0.5 \times 10^9$/l a median of 5 days earlier than a retrospective control group of 30 recipients of unrelated HSC not given G-CSF ($p = 0.004$), and they were discharged a median of 8 days earlier from hospital ($p = 0.04$).

Treatment with rt-PA (n = 8), rt-PA + OLT (n = 2) and OLT (n = 1) for severe VOD was evaluated in 11 recipients of allogeneic bone marrow. Our findings suggest that 2rt-PA should not be given in high doses and not over a long period, because of the risk of severe haemorrhages. In patients with irreversible VOD, OLT may be considered in selected patients.

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p53 inactivation by point mutations and splice mutations in human and mouse tumors

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The p53 tumor suppressor gene is frequently mutated in human tumors. p53 induces cell cycle arrest and/or apoptosis in response to cellular stress, such as DNA damage, hypoxia and certain activated oncogenes like c-myc.

The status of p53 in Burkitt's lymphoma (BL) cell lines was investigated. The majority of BL lines expressed mutated p53 protein. Functional reconstitution with exogenous wild type (wt) p53 induced apoptosis in a BL line that carried a mutated p53 gene. These results substantiate the findings that c-myc induced apoptosis is p53 mediated, since all BLs carry activated c-myc by a c-myc/Ig translocation.

Established ascites tumor cells grow under highly crowded, virtually anoxic conditions. Hypoxia is a powerful inducer of p53-dependent apoptosis. Would conversion of relatively well-vascularized solid mouse tumors into freely growing ascitic cell variants favor cells with mutated or deleted p53? PCR and sequence analysis showed that all solid tumors tested carried exclusively wild type p53 while most of the ascites tumors carried mutant p53. The naturally occurring alternatively spliced p53 (p53as) mRNA was detected in all solid tumors, but was only present in few ascites tumors, in a mutated form. Our findings indicate that conversion of solid into ascites tumors favors the selection of cells with nonfunctional p53 or p53as.

Furthermore, in three separate studies unusual point mutations in the p53 gene, which alter expression and function of the p53 protein are described. In a mouse sarcoma cell, a mutation in a splice donor site activates a cryptic donor site further downstream in the same intron and gives rise to an insertion of 5 extra amino acids to the p53 protein. Human skin fibroblasts derived from a patient with Bloom's syndrome (BS), lack p53 mRNA and protein. A highly sensitive RT-PCR and sequence analysis of p53 revealed that exon 6 was missing as a result of an unusual base substitution at a splice acceptor site of intron 5. These results thus suggest that the lack of p53 expression is due to aberrant splicing that destabilizes p53 mRNA. Analysis of a human tonsil tumor that expressed elevated levels of p53 showed a deletion of the entire intron 7 in one of the p53 alleles, leaving the coding sequence intact.

The p53 protein is a key tumor-suppressor, as evidenced by its frequent inactivation in human cancers and understanding the mechanism behind the functional inactivation of p53 is essential for developing new therapeutic strategies.

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Mitotic failure and genome stability in benign, premalignant and malignant human tissues

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Mitotic failure may occur throughout the human lifespan. Individual nuclear mistakes will escape detection within the mass of somatic cells. The probability of nondetection increases with progression in development. Cells not only in cancers, but already in precancers, are the result of repeated mitotic failure, preceded by genetic damage at different chromosomal sites. Tumors provide the topography in which genome stability is severely endangered. Therefore, this study was focused on mitotic failure occurring in tumorigenesis. An exact determination of genomic capacity of individual cell nuclei was learned with microsections of appropriate depths. A close positive relation was observed between interphase nuclei in 8 pm sections with their imprinted counterparts ($r = 0.99$; $n_1 = n_2 = 73$). Further 232 mitotic figures were measured in 15 μm sections of fetal liver and yielded 3.913 ± 0.01 c DNA content when calibrated to endogenous lymphocyte nuclei. Main results are listed in the following.

- Mitotic division contains 4.0 c DNA as a result of complete DNA replication. once per cell cycle. Mitoses occur predominantly in embryonic tissues, inflammations and hyperplasias.
- Chromosome division figures (CDFs) occur in human precancers and cancers. CDFs were defined by DNA contents deviating more or less than 0.5 c from 4.0 c values.
- The mass of CDFs were recorded above 4.5 c threshold and were described in lesions of uterine cervix, skin, oral mucosa, stomach, colon mucosa and breast.
- Psoriasis, pyogenic granuloma and bacterially induced colitis were found at maximum with 1.5% CDF frequency of total divisions.
- Low-grade dysplasia and well differentiated carcinoma showed 5%–10% CDFs. The range of high-grade dysplasia was 30%–60% CDFs. Poorly differentiated cancers comprised up to 70% CDFs of total divisions.
- A majority of telophase CDFs shows asymmetric morphology and unbalanced DNA contents in corresponding hemispheres.
- Unbalanced telophases characterize cell kinetics, beginning early in precancer.
- CDFs precede DNA aneuploidy of interphase nuclei not only in precancers, but also in malignancies with a diploid modal distribution of interphase nuclei.
- Frequent chromatin bridges suggest that unbalanced telophases and consecutive aneuploidy in interphase are caused by nondisjunction.
- Tumor progression from low-grade to highgrade dysplasias and to cancer is characterized by recurrent shifts from modal 2 c interphase nuclei to 4 c nuclei and a remarkable increase in the 5 c exceeding rate.
- Clonal selection is the gateway in tumorigenesis for aberrant karyotypes. Thus, few cancers are negative with CGH, but positive for CDFs with single cell microphotometry.
- Interphase DNA aneuploidy without CDFs characterizes noninvasive tumors. Nevertheless, they pose a potential for malignancy. Dysplastic nevi and atypical soft-tissue tumors are

examples of effective control suppressing CDFs, but are leaky with respect to interphase aneuploidy.

Mitotic failures result from multiple overrun of cell cycle checkpoints. CDFs are the pathological manifestation of mitotic failure. This study quantitatively confirmed asymmetric telophases detected by Hansemann (1890) in cancer. Mitotic failure was also monitored with prophase and metaphase CDFs; this was done not only in cancer, but also in precancer.

The penetrance of mitotic failure decides on malignancy.

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From a candidate region to gene characterization: analysis of three new genes with respect to meningioma tumorigenesis

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Meningioma is a common and usually benign tumor arising from the meninges covering the central nervous system (CNS). The yearly incidence of symptomatic meningiomas is 1.2 cases per 100000 individuals but autopsy findings reveal an occurrence ten times higher. In adults, intracranial meningiomas represent 15–20% of all primary brain neoplasms, while spinal meningiomas account for 25% of all spinal tumors. The vast majority (90%) of meningiomas are sporadic but rare familial aggregations can be found. These families indicate that a genetic predisposition for meningiomas exists. However, genetic linkage analysis is restricted as these families often contain only two affected members. Meningiomas are also found in 50% of the patients suffering from neurofibromatosis type 2 (NF2), which is an autosomal dominant disease with the hallmark of bilateral vestibular schwannomas. The *NF2* gene is well characterized and is frequently inactivated in NF2-associated and sporadic meningiomas. However, approximately 50% of sporadic meningiomas do not display *NF2* gene mutations or aberrant gene expression. It is therefore clear that additional genes responsible for the tumorigenesis of meningioma need to be identified.

Monosomy 22 is a primary event involved in meningioma development which is detected in up to 70% of the tumors. We examined a series of 170 sporadic meningiomas with 45 chromosome 22-specific markers in an attempt to identify a candidate chromosomal region. Interstitial deletions were found in six tumors (3.5%), revealing that at least four regions from this autosome may harbor meningioma tumor suppressor genes (TSGs). Physical maps, based on YAC and cosmic contigs, were constructed in three of these candidate regions, encompassing a total of approximately 4 Mbp.

One candidate region was further studied to identify active genes. Two new genes were isolated using axon-trapping: a functionally anonymous gene, named *pK*1.3, and a new member of the adaptin family, the β′-adaptin gene (GDB symbol, *ADTB1*). *ADTB1* was totally inactivated in one tumor and therefore represented a putative meningioma TSG. Our meningioma series was searched for additional genomic rearrangements, point mutations and/or aberrant mRNA expression. The *ADTB1* gene was found to be totally inactivated in 12% of 71 sporadic meningiomas, either via homozygous deletion (one case) or via total loss of gene expression (eight cases). We therefore named it **b**eta-**a**daptin-**m**eningioma-chromosome **22** (*BAM22*). The genomic structure of the *ADTB1*/*BAM*22 gene is composed of 23 exons, one being alternatively spliced, and has a genomic size of 60 kb. We also cloned the mouse ortholog of the *BAM22* gene, *adtb1*, and protein sequence comparison of the murine and human genes revealed 96.5% identity.

Adaptins are important subunits of heterotetrameric complexes, termed adaptors or assembly proteins (APs), which are components of clathrin-coated vesicles (CCVs). CCVs are responsible for endocytosis and intracellular transport of membrane-spanning receptors from the plasma membrane or the *trans*-Golgi network (TGN). The AP-1 type of adaptor is composed of a β′- and a γ-adaptin, a small and a medium subunit, AP19 and AP47, respectively. The total lack of β-adaptin in meningioma cells is likely to disrupt intracellular transport involving AP-1, i.e. transfer of lysosomal hydrolases from the TGN to lysosomes via mannose-6-phosphate receptors. It can therefore be assumed that a dysfunction of other components of the AP-1 adaptor will also inactivate this transport pathway. We therefore determined whether the genes encoding for the γ-adaptin, AP19 and AP47 subunits would also be located on chromosome 22. The human γ-adaptin gene (*ADTG*) was characterized and mapped to chromosome 16q23, a region deleted in prostate and hepatocellular carcinomas as well as in Wilms' tumor. The *AP19* and *AP47* genes were localized to human chromosomes 7 and 19, respectively.

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The expression and function of protein kinase C isoforms in differentiating neuroblastoma cells

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The human neuroblastoma cell line SH-SY5Y can be induced to differentiate into a neuronal sympathetic phenotype after treatment with 16 nM 12-*O*-tetradecanoyl phorbol 13-acetate (TPA) in serum, or by a combination of the growth factors basic fibroblast growth factor and insulin-like growth factor-I (bFGF/IGF-I). SH-SY5Y cells stably transfected with *TrkA*, the nerve growth factor (NGF) receptor, differentiate in response to NGF. The function of protein kinase C (PKC) isoforms in these processes was investigated. SH-SY5Y cells were shown to express PKC-α, PKC-ε and PKC-ζ protein. All three isoforms remained present during TPA- and bFGF/IGF-I-induced differentiation, while a higher TPA concentration (1.6 μM), that does not promote differentiation, down-regulated PKC-α completely. The use of the PKC inhibitor GF 109203X demonstrated that TPA-induced differentiation is completely, while growth factor induced differentiation is partially, PKC-dependent. Cells with down-regulated PKC-α differentiated in response to growth factors, implicating a role for PKC-ε in this process. Growth cones isolated from differentiated SH-SY5Y cells were enriched in PKC-α and PKC-ε. Addition of GF 109203X provoked retraction of growth cone filopodia. Together with the finding that cells with down-regulated PKC-α form functional growth cones, this result suggests a role for PKC-ε in growth cone function. A yeast two-hybrid assay was performed using the regulatory domain of PKC-ε as a bait, in order to isolate PKC-ε binding proteins. A clone encoding the ribosomal protein fte-1/S3a was isolated and was shown to interact with the regulatory domains of PKC-α and PKC-ε in vitro. *Fte-1* expression decreased in differentiating SH-SY5Y cells, and

overexpression of *fte-1* prevented induced differentiation, suggesting a function for fte-1 as a negative regulator of PKC. The docking protein $p130^{cas}$ was shown to be PKC-dependently tyrosine phosphorylated in differentiating SH-SY5Y cells. The early phase of $p130^{cas}$ phosphorylation (5–30 min) was independent of $pp560^{c\text{-}src}$ or other herbimycin A sensitive kinases, while the late phase could be blocked by herbimycin A. $p130^{cas}$ protein and tyrosine phosphorylated $p130^{cas}$ were enriched in growth cones, indicating a function for the protein in this structure.

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Modeling heart and lung complication data in radiation therapy of the breast

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Breast cancer is the most common type of cancer in Sweden and in western countries. In breast cancer treatment radiotherapy is the most effective adjunct to primary surgery to prevent loco-regional recurrences. Recently a survival benefit was found in randomized studies by adding loco-regional radiotherapy to adjuvant chemotherapy. Relevant complications after radiotherapy for breast cancer is ischemic heart disease, which can be fatal, and lung complications in form of radiation pneumonitis.

The present work is focused on the quantification of these side effects and the implications for radiotherapy in breast cancer. Complication- and dose distribution data were modeled to quantitatively describe the probability of complications after a given treatment. The relative seriality model was used for the parametrization.

Data of excess long-term cardiac mortality for breast cancer patients treated with different radiotherapy techniques were derived from the randomized trials of Stockholm (1971–76) and Oslo (1964–72). Dose distribution data were reconstructed for a number of model patients with a three-dimensional treatment planning system. A dose–response relationship describing the data was determined. This model was used to predict the probability of excess cardiac mortality in a group of one hundred stage I breast cancer patients planned for radiotherapy using a conventional technique. It was shown that a subgroup of the patients had a significant risk of excess long term cardiac mortality. This was shown to be due to the irradiation of a significant volume of the heart, which could be decreased either by an extended blocking of the beams or by applying a treatment method based on intensity modulation. Radiation pneumonitis data were obtained from a cohort of patients treated between 1993 and 1994 at Radiumhemmet. For this cohort individual three-dimensional dose distributions were available. Model parameters together with the uncertainties were determined by using the maximum likelihood method. The uncertainty in the dose–response curve due to the uncertainties in the parameter was also considered. The determined parameters were then used to calculate the probability of pneumonitis in five different groups of breast cancer patients which had been treated with radiotherapy. The clinical incidence of pneumonitis was not significantly different from the predicted values in three of the five groups.

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Prognostic factors in squamous cell carcinoma of the head and neck with emphasis on 11q13 rearrangements and cyclin D1 overexpression

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At present, clinical outcome or response to therapy cannot be fully predicted in individual cases of squamous cell carcinoma of the head and neck (SCCHN).

The overall aim of the present studies was to investigate potential prognostic factors, more closely related to the malignant progression of a tumor than the established markers, such as the TNM-classification system. Tumor samples were investigated using cytogenetic analysis, immunohistochemistry (IHC), flow cytometry (FCM), slot blot hybridization, differential PCR and RT-PCR, and fluorescence in situ hybridization (FISH). The findings were compared with clinical data.

Rearrangements of chromosome 11, band q13 (11q13), overexpression of the oncoprotein cyclin D1, complex karyotypes, and high histopathological malignancy scoring were all correlated to poor prognosis in SCCHN. They all yielded independent prognostic information in multivariate analysis. Cyclin D1 overexpression was correlated to partial or complete response to neoadjuvant chemotherapy. Chromosomal translocations of 11q13, together with genomic amplification, are involved in cyclin D1 oncogene (*CCND1*) deregulation, leading to cyclin D1 overexpression. Complex karyotypes are observed in DNA-diploid tumors, as assessed by FCM, partly explaining the low prognostic information yielded by this method in certain SCCHN.

The present findings indicate 11q13 rearrangements and cyclin D1 overexpression, as assessed by cytogenetic analysis and IHC, respectively, to be new, independent prognostic factors in SCCHN. Furthermore, the latter parameter might predict response to induction chemotherapy. Cyclin D1 overexpression by IHC could easily be introduced to clinical work, in the hope that therapy will be brought a step closer to individualized treatment schedules.

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Mangafodipir trisodium (MnDPDP)-enhanced magnetic resonance imaging of the liver and pancreas

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Contrast-enhanced magnetic resonance imaging (MRI) of the liver and pancreas is frequently performed to improve the sensitivity and specificity of lesion detection in these organs. The concept of using tissue-specific contrast media is to selectively enhance the normal parenchyma, but not lesions, so that the contrast between tumorous and normal tissue is increased, and lesion detectability improved. Mangafodipir trisodium (MnD-

PDP) has been developed as a hepatocellular-specific contrast agent, but uptake has also been found in pancreatic tissue. In this study the safety and diagnostic efficacy of MnDPDP were investigated in both healthy volunteers and patients with liver and pancreatic tumors.

In healthy volunteers (n = 8), dose-dependent enhancement in T1-weighted images was observed in the normal liver and pancreatic parenchyma after infusion of MnDPDP at doses of 5 and 10 μmol/kg. The maximal enhancement in the two dose groups was 77 and 110% in the liver, and 57 and 84% in the pancreas, respectively. The enhancement-over-time profiles demonstrated that the effective imaging window was about 2 h for the liver, and over 4 h for the pancreas. There was no measurable enhancement in brain structures protected by intact blood–brain barrier, and no changes of clinical importance were found in vital signs or in blood and urinary chemistry variables.

Compared with unenhanced images (including T2-weighted images), significantly more lesions were detected on MnDPDP-enhanced T1 images in 82 patients with liver tumors (mostly metastases). Features such as rim enhancement and the enhancement in hepatocellular carcinomas can provide information for differential diagnosis.

In a study on patients with pancreatic tumors, mainly adenocarcinomas (n = 21) and islet cell tumors (n = 19), two additional lesions were found in the MnDPDP-enhanced images. The contrast enhancement in the pancreatic parenchyma can vary greatly, depending on the site of the enhancing part of the organ in relation to a large tumor. The tumors of both origins were also enhanced post-contrast, but to a lesser degree than the normal pancreatic tissue.

MnDPDP enhancement was investigated in 30 liver metastases from endocrine tumors in 13 patients. These lesions showed a signal increase of about 49% post-contrast, which lasted longer than that in the normal liver tissue. The findings may help to distinguish these tumors from other metastatic tumors.

T1-weighted sequences of four types, including a spin-echo and three variants of fast gradient-echo sequences, and various parameter combinations, were investigated in healthy volunteers (n = 6), with the aim of finding the optimal sequence for MnDPDP-enhanced MRI of the liver and pancreas. The fat-and-water out-of-phase, fast field (gradient)-echo sequence was the best for imaging of both the liver and pancreas.

The studies have shown that MnDPDP is safe when given as an infusion, and is effective as a liver- and pancreas-specific contrast medium, with improved lesion detection in MRI of these organs. It is also useful for the characterization of liver tumors.

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Soluble intercellular and vascular cell adhesion molecules-1 in lymphoid neoplasms—A clinical and prognostic study of Hodgkin's disease, non-Hodgkin's lymphomas and chronic B-lymphocytic leukaemia

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The interaction of soluble adhesion molecules with adhesion ligands expressed by immunological cells interfere with the cell-cell adhesion essential for the signal transductions that initiate immunological responses. Preliminary data suggest that soluble adhesion molecules also promote angiogenesis. Thus dysregulated production of soluble adhesion molecules may emerge as participants of disturbed immuno-surveillance, lymphocyte trafficking and dissemination of cancer cells. Vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) are inducible and/or upregulated by cytokines in different cells types such as endothelial cells, follicular dendritic cells, and stromal cells. Lymphoid neoplasms, representing malignant counterparts of immunological cells, are characterised by heterogeneous histopathologies and clinical manifestations.

Serum levels of soluble ICAM-1 (sICAM-1) and soluble VCAM-1 (sVCAM-1) were elevated in Hodgkin's disease (HD) and chronic B-lymphocytic leukaemia (B-CLL), while only sICAM-1 was elevated in non-Hodgkin's lymphomas (NHL). Serum levels of sICAM-1 and sVCAM-1 correlated with tumour burden and other known prognostic markers. sICAM-1 was an independent prognostic variable in HD and B-CLL. sVCAM-1 was an independent prognostic variable in HD. The discriminative power of serum levels of sVCAM-1 in smouldering and non-smouldering B-CLL could prove clinically valuable.

Both ICAM-1 and VCAM-1 were overexpressed by vascular endothelium and stroma in biopsies of HD, B-CLL and NHL. No correlation between tissue expression of the adhesion molecules and the serum levels of sICAM-1 and sVCAM-1 appeared. VCAM-1 was expressed by two of seven HD cell lines, and sVCAM-1 was detectable in supernatants from these two cell lines. ICAM-1 was expressed by all HD cell lines and detectable in supernatants. In the majority of B-CLL and NHL cultures ICAM-1 expression was upregulated by tumour cells, resulting in detectable sICAM-1 in supernatants.

In conclusion, serum levels of both sICAM-1 and sVCAM-1 had prognostic powers equalling or surpassing known prognostic markers in lymphoid neoplasms. The functional consequences of dysregulated serum levels of sICAM-1 and sVCAM-1 in lymphoid neoplasms is at present largely unknown.

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