Conclusions: Video conference facilitates the centralization of decision making on treatment in an efficient way. Patients with complex tumours can count on assessment and decision making by experts at the highest possible quality level. The roll out of this good practice is planned for other tumours.

2165 POSTER

Targeting of Interferon Gamma to Stromal Fibroblasts Using a PDGF Receptor Recognizing Carrier Reduces Tumour Growth in Vivo

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Background: Stromal fibroblasts are the key cell types in tumour stroma, that support angiogenesis, tumour cell proliferation and metastasis. Therefore, inhibition of stromal fibroblasts activity might inhibit tumour growth. Interferon gamma (IFNγ) is a potent cytokine and has been used for the treatment of experimental fibrosis. However, poor pharmacokinetics and severe side effects prevented its clinical application. In this study, we hypothesized that specific delivery of IFNγ to stromal fibroblasts may be beneficial to inhibit the tumour growth. Since Platelet-derived Growth Factor beta receptor (PDGFβR) is abundantly expressed on stromal fibroblasts, we developed a PDGFβR-specific drug carrier (PPB-HSA) by modifying albumin with a PDGFβR-recognizing cyclic peptide to deliver IFNγ.
Materials and Methods: The IFNγ was conjugated to PPB-HSA carrier via a heterobifunctional PEG linker and characterized with Western blot analyses and nitric oxide release assay in RAW monocytes. In vitro, PPB-HSA-IFNγ was examined for its effectivity in 3T3 fibroblasts using wound healing assay, immunocytochemistry and qRT-PCR. To simulate fibroblasts-induced angiogenesis process, tube formation assay was developed in which conditioned medium from 3T3 fibroblasts (incubated with TGFβ and IFNγ or IFNγ constructs) was added to the endothelial cells (H5V) and tubes formed were counted. In vivo, the effects of the targeted PPB-HSA-IFNγ on tumour growth were determined in subcutaneous B16 melanoma tumour model in mice. Treatments with vehicle, IFNγ, PPB-HSA-IFNγ, PPB-HSA ($n = 5$ per group) at the equivalent doses (5 μg/dose/mouse) were administered intravenously.
Results: PPB-HSA-IFNγ construct was successfully synthesized and the conjugated IFNγ retained its biological activity. The construct showed PDGFβR-specific binding in 3T3 cells which was blocked with anti-PDGFR antibody. The IFNγ construct significantly inhibited the proliferation and migration of 3T3 cells as determined with wound healing assay. Treatment with the targeted IFNγ drastically reduced TGFβ-induced collagen-I, alpha smooth muscle actin and fibronectin expression in staining and gene expression. Furthermore, the PPB-HSA-IFNγ inhibited the 3T3 fibroblasts-induced angiogenesis as determined with the tube formation assay in H5V cells. In vivo, the targeted IFNγ construct attenuated the tumour growth by 60% ($p < 0.01$) compared to vehicle whereas untargeted IFNγ and PPB-HSA carrier did not induce any reduction in the tumour growth.
Conclusions: These data demonstrate that specific targeting of IFNγ to the stromal fibroblasts using PPB-HSA carrier is a potential therapeutic strategy to inhibit tumour growth.

Poster Presentations (Sat, 24 Sep, 14:00−16:30)
Surgical Techniques

2500 POSTER

Identification and Image-guided Resection of Occult Superficial Liver Metastases Using Indocyanine Green and Near-infrared Fluorescence Imaging

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Background: Near-infrared (NIR) fluorescence imaging using indocyanine green (ICG) is a promising technique for identifying and resecting colorectal liver metastases, however, optimal dosage and timing is not known.
Material and Methods: The Mini-FLARE™ imaging system was used for real-time identification of colorectal liver metastases in 22 patients undergoing liver resection. NIR fluorescence imaging was performed 24 or 48 h after administration of 10 or 20 mg ICG. Resected specimens were prepared for *ex vivo* macroscopic and microscopic evaluation of fluorescent patterns.
Results: A total of 40 superficially located (<6.2 mm beneath the liver capsule) colorectal liver metastases were identified and resected using NIR fluorescence imaging and ICG. In all patients, ICG fluorescence was seen as a rim around the tumour, located microscopically in the transition zone between tumour and normal liver tissue. Median tumour-to-liver ratio (TLR) was 7.4 (range 1.9–18.7) and no significant differences between time-points or doses were found. NIR fluorescence signal in normal liver had returned to baseline by 24 to 48 hours post-injection, eliminating the need to test longer time-points. Four metastases detected using NIR fluorescence were occult, and not visible using preoperative CT, palpation, or intraoperative ultrasound (IOUS). NIR fluorescence also distinguished benign liver lesions from metastases. Preoperative CT, IOUS, and/or palpation, however, found seven lesions, all deeper than 8 mm, which were not seen using NIR fluorescence.
Conclusion: This study suggests that NIR fluorescence imaging is complementary to conventional imaging for liver metastasectomies, and has the potential to improve surgical cure.

2501 POSTER

Three-Dimensional Imaging Navigation Using an IPad During a Lung Segmentectomy

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Background: Lung screening using computed tomography (CT) has recently become widespread and many small lung lesions have been detected using this method. The requirement for anatomical lung segmentectomies has also therefore increased. We herein present the benefits of using three-dimensional (3D) imaging navigation during a lung segmentectomy via the intraoperative use of an iPad.
Materials and Methods: Images were obtained using a 16-channel multi-detector CT (MDCT). Contrast agent was injected at a rate of 5 ml/s (total dose, 1.2 ml/kg) and this was followed by a 40 ml injection of normal saline injection to wash the contrast agent from the pulmonary artery (PA). Contrast-enhanced scanning was then performed twice, at 7 seconds after the start of the injection for enhancement of the PA and at 18 seconds after the injection for enhancement of the pulmonary vein (PV). 3D images were constructed from 1.0 mm data slices using a workstation. Images of the PA, PV, airway (from the trachea to the subsegmental bronchus) and of the tumours to be resected were constructed separately and subsequently merged. These 3D images were then transferred to an iPad and analyzed during the operation using DICOM image viewer software. In the operating room, the iPad was placed inside a sterile bag and manipulated directly by the surgeons in the operative field.
Results: We performed six segmentectomies (right S1, right S2, right basal segment, left S1+2, left upper division, and left basal segment) between October 1, 2010 and March 31, 2011 using this procedure. Preoperatively, we identified the branches of pulmonary artery, pulmonary vein, and bronchus in the affected or adjacent segment using the 3D images, and simulated which branches should be divided or preserved for necessary and sufficient resection. During the operation, the surgeons were able to review and manipulate the 3D images interactively, and to easily identify actual anatomical structures.
Conclusion: A 3D-CT navigation using an iPad enhances the ability to perform a safe and secure segmentectomy.

2502 POSTER

Microwave Ablation of Ex Vivo Human Liver and Colorectal Liver Metastases With a Novel 14.5 GHz Generator

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Background: Ablation of colorectal liver metastases relies on the focal delivery of energy to a lesion causing tumour destruction. Targeted ablations minimise the removal of healthy parenchyma, and are useful in patients with borderline parenchymal volume and function, or anatomically difficult lesions which may not be amenable to formal resection. Previous attention has focused on radiofrequency ablation (RFA). Interest is now turning to microwave ablation which offers several theoretical advantages. Microwave radiation causes polarised water molecules to oscillate, generating heat by an active mechanism. This active heating mechanism means microwave energy is not reduced by transmission through charred and desiccated tissue, allowing more controlled and predictable tissue

ablation than RFA. Histopathological examination of microwave ablated tissue has identified an area of ultrastructurally normal but non-viable tissue within the ablation zone. It has been suggested that this tissue may have undergone a novel type of microwave cell death caused by protein cross-linking. This study aimed to characterize the relationship between ablation time, applied power and size of ablation produced by a novel high-frequency 14.5 GHz microwave applicator in ex vivo human hepatic parenchyma and colorectal liver metastases, and investigate the mechanism of microwave cell death.
Material and Methods: Multiple ablations were performed in 8 ex vivo human hepatic resections and colorectal liver metastases at a variety of time (10–180 seconds) and power (10−50 watt) settings. Histological, enzyme histochemical and transmission electron microscopic analysis was performed, as well as preliminary proteomic analysis using 2-D SDS-PAGE.
Results: Increasing time and power settings led to a predictable and reproducible increase in size of ablation. At 50 watts and 180 seconds application, a maximum ablation diameter of 38.8 mm (±1.3) was produced. Ablations were produced rapidly, and at all time and power settings ablations remained spherical (longest:shortest diameter <1.2). Routine histological analysis using H&E confirmed well preserved cellular ultrastructure after ablation. Transmission electron microscopy demonstrated marked subcellular damage. Enzyme histochemical showed complete absence of viability in ablated tissue. 2-D gel electrophoresis showed no difference in protein expression between ablated and non-ablated tissue, irrespective of reducing or non-reducing conditions, suggesting consistent cross-linking is unlikely.
Conclusions: Large spherical ablation zones can be rapidly and reproducibly achieved in ex vivo human hepatic parenchyma and colorectal liver metastases using a 14.5 Ghz microwave generator. Despite well preserved cellular ultrastructure, ablated tissue is non-viable. Consistent cross-linking of proteins does not occur following ablation.

2503 POSTER

Immediate Breast Reconstruction of Segmentectomy Defects Using Extended Lattisimus Dorsi Flap via Single Axillary Incision

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Background: Aim of this study is to describe the technique of extended autologous latissimus dorsi flap to reconstruct segmentectomy defects via single axillary incision; and to assess the outcomes of this procedure.
Methods: Between December 2008 and December 2009, 20 patients with early breast carcinoma, underwent extended latissimus dorsi flap for reconstruction of segmentectomy defects (reaching about 20−3-% of breast volume). Measured outcomes included: surgical complications, cosmetic outcome, and functional disability.
Results: Acceptable results were noticed with this technique as regard: postoperative complications (4 patients) with no further surgical intervention, sensory loss (nipple-areola complex; 2 patients, quadrant; 8 patients), restricted activities in 2 patients. Considering aesthetic evaluation, very much acceptable results were noticed as regard panel assessment and patient satisfaction.
Conclusion: This technique is associated with few adverse surgical and physical sequalae, without compromising cosmetic outcome, representing good alternative to mastectomy (if similar), avoiding additional scars and use of prosthesis.

2504 POSTER

Oncoplastic S-shaped or Reverse S-shaped Rotation Flap Reconstruction After Quadrantectomy as a New Option for Lower Half Located Breast Cancer − a Technical Report

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Background: When performing breast conserving operations, inferior cosmetic outcome has been reported in lower half breast tumours. We report here about the use of S-shaped or reverse S-shaped rotation flap reconstruction to improve cosmetic outcome in patients with lower half-located breast cancer.
Patients and Methods: Twenty three patients with invasive breast cancer located in the lower half of the breasts, which were more than two centimeter apart from the nipple, were included. After completing quadrantectomy, single S-shaped or reverse S-shaped incision was made from axilla to breast including two triangular skin islands on axilla and breast. Once the fibroglandular tissues and the additional fatty tissue of the flank were appropriately mobilized, the breast defect was closed at the mid-point of the parenchymal thickness in order to keep the natural position of the inframammary fold.
Results: Median tumour size was 2.3 cm, ranging from 0.7 to 3.5 cm. With a median follow up of 18.5 months, ranging from 3 to 27.5 months, cosmetic outcome were good (91.3%) to fair (8.7%) after the radiation therapy and there was no local or systemic recurrence.
Conclusion: Clearly, this type of rotation flap reconstruction is an oncologically safe and a cosmetically sound procedure. Hopefully this rotation flap reconstruction will become more widely available and perhaps a standard procedure for lower half located breast tumours, especially in the small to medium sized breasts.

2505 POSTER

Towards More Efficacy in HIPEC − Optimization of Fluid Mechanics

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Background: 'HIPEC' (Hyperthermic IntraPeritoneal Chemotherapy) is a loco-regional treatment and was first described by Spratt in 1980 [1]. He described the procedure in the closed method and it took him 1.5 hours to reach intraperitoneal 42ºC before he started the chemoperfusion. But little is known about fluid mechanics and its influence on the procedure until today. As a new HIPEC-center in Germany we have developed special interest in fluid mechanics during the procedure.
We started using placement of catheters for HIPEC as described by many authors (e.g. Roviello [2], Dahlke [3]) with inflow in the right upper quadrant and deep pelvis and outflow in the high pelvis and left subphrenic space or paracolic gutters. In contrast to the widely used technique we placed our temperature probes far away from the catheters. The results were disappointing! So we modified our HIPEC protocol step by step.
Material and Method: HIPEC was performed using the equipment of RanD (Performer LRT − 1 procedure and Performer HT all other procedures) together with the perfusion sets consisting of a set of catheters for in- and outflow with 2 catheters for inflow and 3 catheters for outflow. 2 temperature probes are integrated and 3 probes can be used separately from the catheters.
We modified the equipment by introducing a third catheter for inflow. In a second step we introduced polyurethane sponges and wrapped 2 outflow catheters to increase the surface and to open up recessus and spaces around the liver and in the left upper quadrant. We could demonstrate in a very small patient population (11 procedures; 3 without modification and 8 with our modification) the efficacy of this approach by measuring the temperature far away from the catheters.
Results: The homogenicity of distribution of the heated chemoperfusate highly improved as demonstrated by the temperature values.
An additional beneficial effect on the turnover of the chemoperfusate was noticed resulting in increased flow rates up to 1500 ml/min with only minor variations. With this high turnover it seems possible to overcome the intra-abdominal cooling effects of the well-perfused organs like the liver or great vessels. It is also possible to shorten the 'warming-up' period from 1.5.hours (Spratt?) to only 10−15 min.
Conclusions: With our modified placement of the in- and outflow catheters combined with using perfused spacers of polyurethane-sponges we could significantly increase the flow rate/turnover of the chemoperfusate, abbreviate the warming-up phase of the procedure and demonstrate a more homogenous distribution of heat and chemoperfusate.
Outlook: Further investigations are necessary to study the intra-abdominal processes and fluid mechanics during HIPEC procedures in order to increase efficacy to control peritoneal surface malignancies. The next step will be to evaluate the design and the placement of the catheters and to develop fluid dynamic models of the HIPEC-procedure to overcome preferential flow and cooling effects of large organs and vessels.

References

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