2113 POSTER

Magnetic resonance-guided focused ultrasound for palliation of painful bone metastases

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Background: Magnetic Resonance guided Focused Ultrasound (MRgFUS) is a non-invasive treatment technique that recently has been shown to be effective for thermal ablation of a variety of benign and malignant tumors. We present here results of a clinical trial conducted in our facility prior to participation in a multi-center FDA regulated pivotal study. The main objective of the trial was to evaluate safety and effectiveness of MRgFUS treatment for palliation of pain caused by bone metastases.
Material & Methods: 5 patients with painful bone metastases were treated with MRgFUS at Petrov Research Institute of Oncology, St. Petersburg, Russia. Immediately after procedure patients were examined for any adverse events and after a brief recovery discharged in the care of a companion. Patients were followed up on 1 and 3 days, 1 and 2 weeks, 1, 2 and 3 months post treatment. During each visit treatment safety was evaluated by recording and assessment of device or procedure related adverse events. Effectiveness of palliation was evaluated using the standard pain scale (0-no pain/10-worst pain imaginable) and by monitoring changes in the intake of pain-relieving medications. Two types of pain scores were collected: the average and the worst pain in the last 24 hours. A reduction of 2 points or more on pain scale was considered a significant response to treatment. Targeted lesions were all osteolytic; 3 were pelvis metastases and another 2 were located in the humerus bone.
Results: No significant device or procedure related adverse events were recorded. 1 patient died during the follow-up period due to disease progression, thus 3 months follow-up data includes only results of 4 patients. All patients reported significant improvement in pain with no change in their medication intake. Mean worst pain score at baseline, 1 day, 3 days, 1 week, 2 weeks, 1, 2 and 3 months post-treatment was 6.2, 5.8, 4.6, 3.6, 2.2, 2 and 2 respectively and average pain score at baseline, 1 day, 3 days, 1 week, 2 weeks, 1, 2 and 3 months post-treatment was 4.6, 4.4, 3.4, 2.6, 2.2, 1.2, 1 and 1 respectively.
Conclusions: These results clearly show that MRgFUS can provide an effective, safe and noninvasive palliative therapy for patients suffering from painful bone metastases. The ability to achieve a rapid pain relief after only one treatment session combined with the high safety profile of the procedure implies that MRgFUS has a significant potential for both patients and physicians.

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Design of tumor targeting magnetic resonance imaging (MRI) agent based on gold/iron-oxide composite nanoparticle

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Background: Super paramagnetic iron oxide (SPIO) is used clinically as a magnetic resonance imaging (MRI) contrast agent for the diagnosis of liver cancer. SPIO in the blood is rapidly taken up by Kupffer cells and accumulates in normal liver tissue. This property, however, limits the applicability of SPIO for the diagnosis of other types of cancer. Here, we attempted to design a novel MRI contrast agent that can be used to visualize other types of tumors. We used a unique gold/iron-oxide composite magnetic nanoparticle that comprises a magnetic iron-oxide core with smaller gold nanoparticles immobilized on the surface. Gold nanoparticles bind strongly to thiol via a Au-S interaction without requiring a linker molecule. We coated the surface of the nanoparticle using thiol-modified polyethylene glycol (PEG) to extend its half life in the blood, thereby inhibiting its accumulation in the liver, and to target tumors by an enhanced permeability and retention effect (EPR effect).
Material and Method: We selected Feridex®, one of clinically used SPIO, as a core material of gold/iron-oxide composite magnetic nanoparticle. We synthesized Au-immobilized Feridex® (Au/Feridex) by irradiating gamma-ray on the mixture of $AuHCl_4$ and Feridex® solution. PEG-modified Au/Feridex (PEG-Au/Feridex) was synthesized only by mixing Au/Feridex and thiol-modified PEG at room temperature. The accumulation of PEG-Au/Feridex was assessed by MRI and radiochemical neutron activation analysis after intravenous injection in the B16/BL6 tumor bearing mice.
Results: Observations of Au/Feridex using transmission electron microscopy (TEM) suggested that Au nanoparticles were successfully immobilized on the surface of Feridex®. Intravenously administered PEG-Au/Feridex decreased the signal intensity in T2-weighted images and led to the clear identification of a B16/BL6 tumor at 1 hour post-injection. Radiochemical neutron activation analysis of the Au element in each tissue suggested that the accumulation of PEG-Au/Feridex in the tumor tissue was at least 10 times greater than that of unmodified Au/Feridex, with a decrease in liver accumulation. Similar results were observed in Meth-A and Colon-26 tumor-bearing mice, indicating that PEG-Au/Feridex is a candidate novel MRI contrast agent for various cancers.
Conclusion: PEG-Au/Feridex could detect tumors implanted in abdomen of mice using MRI, which suggested that PEG-modification of SPIO enhances the potency for tumor targeting.

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Breast MRI and preoperative factors associated with cancers of limited extent in wide-local excision specimens

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Background: To discriminate between invasive breast cancers with extensive subclinical disease around the MRI visible lesion and those without surrounding subclinical disease.
Materials and Methods: Sixty-two breast-cancer patients (64 breasts) eligible for breast-conserving therapy on the basis of conventional imaging and MRI were included. The wide-local excision (WLE) specimens were processed using complete embedding, reconstruction and correlation with MRI. Tumors were stratified by presence (extensive breast cancer) or absence (limited breast cancer) of subclinical disease beyond 10 mm from the edge of the MRI-visible lesion in the WLE specimen. Imaging features at mammography, ultrasonography, contrast-enhanced MRI as well as at core histology were evaluated for their ability to discriminate between the extensive and limited breast cancers. Interpretation of MRI was focused on morphological and kinetic properties of contrast uptake. Assessment of core histology included tumor grade and molecular subtype; basal-type (estrogen-receptor negative), luminal-type (estrogen-receptor positive), and Her2+ type.
Results: Of the 64 index tumors, 57 were visible at mammography, 59 at ultrasonography and 61 at MRI. Thirty-five (57%) tumors were limited breast cancers. Significantly associated with extensive breast cancer were presence of a Her2+ index tumor ($p = 0.04$, PPV = 69%, NPV = 65%), and moderate/extensive quantity of DCIS in the index tumor ($p < 0.001$, PPV = 78%, NPV = 64%). Absence of washout kinetics at MRI had high negative predictive value for extensive breast cancer ($p = 0.036$, NPV = 89%, PPV = 50%).
Conclusions: Risk of extensive occult disease around MRI-visible lesions decreases with absence of washout kinetics at MRI, but increases with Her2-positive tumor types and presence of DCIS in the index tumor. Tumors with the latter properties may be less suitable for more localized therapy such as partial breast irradiation or MRI-guided high-intensity focused ultrasound.

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Scintigraphic patterns of chemotherapy resistance: preliminary data of simultaneous scintigraphy with two tumor seeking agents: 67Ga and 99mTc-MIBI

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Background: Reverse correlation between 99mTc-MIBI uptake and MDR expression were shown by several studies. Scintigraphy with this tracer was proposed as the tool for prediction of possible chemotherapy resistance. Tumor uptake of 67-Ga by non small cell lung cancer (NSCLC) and

Hodgkin's lymphoma (HL) is strongly associated with tumor proliferative activity and viability. We speculated that different patterns of 99mTc-MIBI and 67-Ga uptake can reflect possible chemoresistance of NSCLC and HL.
Material & Methods: Simultaneous scintigraphy with 67-Ga and 99mTc-MIBI was performed in 90 patients with HL and NSCLC. Whole body visualization and computer emission tomography was performed during single examination. Acquisition started 48−74 hr after i/v injection of 130–175 MBq 67-Ga and immediately after i/v injection of 500–740 MBq of 99mTc-MIBI. All images for each agent were classified as positive and negative. Tumor uptake was graded as 0 (normal uptake), + (hyper fixation seen only on SPECT), ++ (moderately increased uptake), +++ (prominent hyper fixation).
Results: Dual isotope scintigraphy was positive in 41 of 90 evaluated patients. In this group we revealed 3 main patterns of 99mTc-MIBI and 67-Ga uptake. The first – characterized by active tumor uptake of both agents: this pattern determined in 12 (29%) of 41 patients with positive lesions.
The second – manifested by active accumulation of 99mTc-MIBI and negative (grade 0) or reduced 67-Ga uptake. In 5 cases (12%) 99mTc-MIBI uptake in the tumor was increased and scintigraphy with 67-Ga didn't reveal abnormality. In another 6 cases (15%) 99mTc-MIBI revealed more lesions and/or grade of 99mTc-MIBI uptake was higher than accumulation of 67-Ga. Most of patients (9/11) in the second group had NSCLC.
Third pattern characterized by intense pathologic uptake of 67 Ga with normal or only slightly increased (+) accumulation of 99mTc-MIBI. In this group 7 (17%) patients had tumors which were visualized only with 67-Ga. In 11 cases (27%) scintigraphy with 67-Ga revealed more lesions and/or uptake of 67-Ga was more intensive than accumulation of 99mTc-MIBI. We propose that the third pattern represent the group of patients with high risk of tumor chemoresistance and unfavorable prognosis. But this speculation needs further confirmation during follow-up
Conclusion: Active accumulation of 67-Ga with normal or slightly increased uptake of 99mTc-MIBI in the tumors revealed in 44% of evaluated patients with HD or NSCLC. This pattern can reflect increased probability of tumor chemoresistance.

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The efficacy of Tc-99m MIBI for sentinel node mapping in breast carcinoma: comparison with Tc-99m antimony sulfide colloid

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Background: Sentinel lymph node (SLN) biopsy has become the standard for axillary lymph node staging in breast cancer. To date, several randomized trials (1−5) have confirmed that SLN biopsy is feasible, accurate and safe staging technique with minimal morbidity. We studied the value of peri-areolar intra-dermal injection of Tc-99m sestamibi (MIBI) for sentinel node mapping in breast carcinoma.
Material and Method: 50 patients with early-stage breast cancer were included in our study. 17.5 MBq Tc-99m-MIBI was injected intra-dermaly to 25 patients and the remainders were injected with the same dose of Tc-99m-Antimony sulfide colloid. Anterior and lateral static images were taken at 2 minutes. If sentinel lymph node was not detected, delayed imaging up to 180 minutes was done. The patients were operated on, 2−4 hours post-injection. Sentinel lymph node biopsy was performed by the aid of gamma probe and blue dye during surgery.
Results: In the Tc-99m-MIBI group 23 patients had lymph nodes on scintigraphy images. Sentinel node was detected at surgery in all 23. In the Tc-99m-antimony sulfide colloid group 24 patients had lymph nodes on scintigraphy images. Sentinel node was identified at surgery in 24 patients.
Conclusion: We conclude that 99mTc-MIBI is a suitable radiopharmaceutical for sentinel node detection.

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Accuracy of TransRectal UltraSonography (TRUS) in the preoperative staging of rectal lesions suitable for Transanal Endoscopic Microsurgery (TEM)

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Background: Transanal Endoscopic Microsurgery (TEM) is performed in patients with premalignant or, in selected cases, stage T1 rectal lesions. Transrectal ultrasonography (TRUS) seems to be an important diagnostic tool in the preoperative staging of rectal lesions, assessing whether the lesions are suitable for TEM. The aim of this study was to analyse the accuracy of TRUS in distinguishing between rectal lesions requiring local (TEM) or more radical excision (TME = total mesorectal excision).
Materials and Methods: From January 2006 until June 2008 thirty-six consecutive patients with rectal lesions were included. All patients underwent TRUS, using an endorectal probe to asses the T-stage in rectal lesions. Following TRUS and/or additional imaging, patients underwent surgery. Preoperative TRUS staging was correlated to postoperative pathology.
Results: In 30 patients TRUS was conclusive. Postoperative pathological findings confirmed the preoperative TRUS findings in 29 patients; in 1 patient, a T3 staged tumour was an overstaged benign lesion also biopsied as a Tubulovillous Adenoma (TVA). No understaging occurred. The accuracy level in the conclusive TRUS group was 97% (29/30).
In 6 patients TRUS was not conclusive; in 5 of these patients MRI was performed showing no tumour invasion in all 5 patients, confirmed by pathological findings.
Proper TRUS interpretation was possible in 83% (30/36). Overall accuracy of TRUS was 80% (29/36). However, accuracy in the conclusive group was 97%.
Conclusion: TRUS is an accurate diagnostic tool in distinguishing rectal lesions suitable for TEM from the lesions invading the muscularis propria needing more radical surgery. If TRUS is inconclusive or high stage rectal lesions ($\geqslant$T2) are shown on TRUS, additional imaging (MRI) should be performed.

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Delay in implementation of international guidelines forcomputed tomographies with iodinated contrast media

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Background: This study was conducted to determine the degree to which the clinical practice concerning computed tomographies (CTs) with iodinated contrast media in patients with lung cancer was in accordance with European Society of Urogenital Radiology (ESUR)'s international guidelines.
Methods: Lung cancer is treatable with platinum-based cytostatic drugs, which can be nephrotoxic. According to the ESUR's guidelines this adds to the risk of developing contrast- induced nephropathy.
Before CT with iodinated contrast media ESUR's international guidelines recommend evaluation of the patient's risk factors. The guidelines also recommend measurement of S-creatinine 7 days or less before CT scanning risk patients.
This stydy is a retrospective study of lung cancer patients at Hillerød Hospital, Denmark. Inclusion criteria: Patients in current treatment with platinum-based cytostatic drugs up to and including September 20th, 2006, who had undergone an elective CT with iodinated contrast media. A total of 51 patients where included. P-creatinine and other potential risk factors for development of contrast- induced nephropathy were collected.
The following data was registered; age, gender, cancer diagnosis, renal disease, diabetes mellitus, hypertension, congestive heart disease, P-creatinine, type, volume and time for cytostatic treatment. Time for the first CT performed after the initiative treatment with platinum-based cytostatic drugs, and whether they had need for nephrologic assistance.
The study has not registered whether the patients where dehydrated or were given other nephrotoxic drugs beside NSAID and platinium based cytostatics. It was not registered when a NSAID drug was taken before CT.
Results: In 31.4% of the patients included, P-creatinine was measured no earlier than seven days prior to their CT. All the patients had S-creatinine measured with in 6 months prior to CT.43.1% of the patients included had received a platinum-based cytostatic drug after the latest measurement of their P-creatinine prior to their CT scan. 45.1% of the patients been received a platinum-based cytostatic 14 days or less before CT scan. 66.7% had additional risk factors. None needed nephrologic assistance.
Conclusions: Significant deviations were found between the clinical practice and the international guidelines covering prevention of contrast-induced nephropathy. This study has led to changes in the guidelines and clinical practice regarding contrast- induced nephropathy at Hillerød Hosipital. Now all elective patients have P-creatinine measured no more than seven days prior to CT with iodinated contrast media.
This study is an example of the delay in implementation of science based preventive methods into clinical practices.