2113 POSTER

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

V.G. Turkevich[1], V.V. Savelyeva[1], I.V. Dunaevsky[1], P.I. Krzhivitsky[1], O. Dogadkin[2], M. Bernstein[2], S.V. Kanaev[3]. *[1]N. N. Petrov Research Institute of Oncology, Nuclear medicine and Radiation Oncology, Saint Petersburg, Russian Federation; [2]InSightec LTD, Clinical research, Hifa, Israel; [3]N.N. Petrov Research Institute of Oncology, Nuclear medicine and Radiation Oncology, Saint Petersburg, Russian Federation*

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.

2114 POSTER

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

H. Kojima[1], Y. Mukai[1], K. Kamei[1], M. Morita[2], T. Inubushi[2], T. Yamamoto[3], Y. Yoshioka[4], N. Okada[1], S. Seino[3], S. Nakagawa[4]. *[1]Osaka University, Graduate school of Pharmaceutical Science, Osaka, Japan; [2]Siga Medical University, Biomedical MR Science Center, Osaka, Japan; [3]Osaka University, Graduate school of Engineering, Osaka, Japan; [4]Osaka University, Graduate school of Pharmaceutical Science/The Center of Advanced Medical Engineering and Informatics, Osaka, Japan*

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.

2115 POSTER

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

K.G.A. Gilhuijs[1], A.C. Schmitz[2], K. Pengel[1], C.E. Loo[1], J.L. Peterse[3], M. Gertenbach[4], M.A. Van den Bosch[5], H. Bartelink[6], E. Rutgers[7]. *[1]The Netherlands Cancer Insitute/Antoni van Leeuwenhoek Hospital, Radiology, Amsterdam, The Netherlands; [2]The University Medical Center Utrecht/The Netherlands Cancer Insitute, Radiology, Utrecht, The Netherlands; [3]The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Pathology, Amsterdam, The Netherlands; [4]Peterborough District Hospital, Pathology, Peterborough, United Kingdom; [5]The University Medical Centre Utrecht, Radiology, Utrecht, The Netherlands; [6]The Netherlands Cancer Insitute/Antoni van Leeuwenhoek Hospital, Radiotherapy, Amsterdam, The Netherlands; [7]The Netherlands Cancer Insitute/Antoni van Leeuwenhoek Hospital, Surgery, Amsterdam, The Netherlands*

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.

2116 POSTER

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

S. Novikov[1], M. Girshovich[1], S. Kanaev[1]. *[1]N.N. Petrov Scientific Research Institute of Oncology, Radiation Oncology & Nuclear Medicine, St-Petersburg, Russian Federation*

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