2120 POSTER

Ultrasound dopplerography in the treatment monitoring of patients with sarcomas

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Background: The aim of the research was to improve the results of complex ray diagnostics and monitoring in the treatment stages of patients with malignant neoplasms of soft tissues and bones using ultrasound dopplerography (US-dopplerography).
Materials and Methods: US-dopplerography data in 38 patients with tumors of soft tissues and bone tumors with infiltrated soft tissues are studied in the course of treatment. The following criteria were investigated by dopplerography: arterio-venous blood-flow, venous blood-flow, maximal velocity (V_{max}) of blood, minimal velocity (V_{min}) of blood, index of resistance (IR), pulse index (PI).
Results: In 7of 38 patients US-dopplerography was performed repeatedly in dynamics. In 2 patients with fibrosarcoma character of neoplasm tissue blood-flow changed: in 1 patient after combined chemo- and ray-therapy neoplasm tissue blood-flow was not registered practically, in the 2nd patient indices of blood-flow decreased after chemotherapy. In 8 patients presented with fibrosarcoma blood-flow was not detected in the structure of neoplasm, and in 3 patients with the same diagnosis moderate peripheral blood-flow in the neoplasm was revealed. In one patient with osteosarcoma parameters of blood-flow in soft tissues infiltration were not changed even after 4 courses of chemotherapy. In the second patient parameters of blood-flow increased after 1st course of chemotherapy treatment, and after 3rd course blood-flow in the damaged area practically could not be detected. In 2 patients, presented with neuroblastoma and Khodjkin's lymphoma, parameters of blood-flow decreased until complete disappearance after 2 courses of chemotherapy. In one patient with rhabdomyosarcoma blood-flow indices did not actually change in the process of treatment.
Conclusion: Parameters of US-dopplerography in dynamic control can serve as an indicator in the treatment efficacy assessment in patients with soft tissue and bone tumors.

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Colorectal cancer liver metastases treated with target therapies: monitoring response with contrast-enhanced ultrasonography (CE-US)

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Background: Since anti-angiogenic treatment induces necrosis with no change in the volume of the tumor, new imaging technologies are particularly suitable for the early assessment of the response, for which the RECIST size criteria appear inappropriate. CE-US has recently been proposed for evaluating therapeutic response, demonstrating changes in tumor parenchymal perfusion and emergence of necrosis with no change in tumor volume. The aim of the study was to compare CE-US and CT (the gold standard) in assessing therapeutic response to antiangiogenic-based therapies for liver metastases from colorectal cancer.
Patients and Methods: Both CE-US and CT were used to prospectively evaluate 48 hepatic lesions in 21 patients (male 13, female 8; age range 44−78 years, mean 58.2 years) with colorectal adenocarcinoma receiving antiangiogenic therapy since January 2008 through February 2009. CE-US was performed the day before (day −1) starting target therapy (bevacizumab or cetuximab) and at days 28 and 90. The percentage of contrast uptake (Sonovue) before treatment and at follow-up was evaluated, thus rating all patients as responders or poor/non-responders. Re-evaluation total-body CT scan was performed at 90 days.
Results: Based on RECIST criteria, at the CT scan, 7/21 patients demonstrated stable disease (SD), 8/21 had partial response (PR) and 6/21 showed progressive disease (PD). When assessed by CE-US, 16 patients (33 lesions) were considered good responders and 5 patients (15 lesions) poor or non-responders. Of note, 4/7 patients with SD (57%) were categorized as good responder when evaluated by CE-US. A good response at CE-US preceded PR based in 5/8 patients by 2 months. Of the 6 patients characterized with PD, 4/6 (66.6%) demonstrated a corresponding lack of decrease in tumor contrast enhancement within the tumor.
Conclusion: In patients treated with anti-angiogenic drugs, CE-US identifies more good-responder patients compared with RECIST at an earlier time-point. When monitoring tumor response in patients treated with anti-angiogenic therapy, CE-US might need to be added to CT scan at different time of follow-up.

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Measurements of malignancy signs by atomic force microscopy

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Background: In present work Atomie Force Microscopy (AFM) has been used for searching signs of malignancy in cytological specimens prepared identically to those used in traditional cytological studies, while most of earlier investigations have studied specimens prepared by complex techniques like attaching ligands to AFM tips, design of hybrid cell/polyelectrolyte systems, taking measures in fluids and so on which are unusual for ordinary hospitals.
Material and Methods: Diagnostic procedures: Fine-Needle Aspiration Cytology/Biopsy (FNAC/FNAB) and Imprint Cytology Smears. All specimens were investigated by AFM (NTEGRA Prima, NT-MDT Co., Russia). AFM images were treated with different Image analyses functions like filtering, flatten correction, equalization, statistics.
Results: Signs of Malignancy and premalignant lesions:
1. The visible measurable nucleoli in all cancer specimens.
2. Intranuclear Cytoplasmic Inclusions (INCI) in thyroid papillary carcinoma. We managed to measure those inclusions – the depth is about 600 nm.
3. The Presence of koilocytes. Presence of koilocytes is one of known signs of virus lesion. Koilocytes have halo nuclei on cytologic examination. Morphologic appearance of halo is perinuclear groove about 200 nm depth.
4. Evaluation of the immunocytochemical reaction's intensity. AFM-images of Her2/neu overexpressed specimens demonstrate a packing of the membrane of tumor cells. The estimation of the intensity of immunocytochemical reaction is possible according to the height of the painted membrane.
5. Alteration of nuclear:cytoplasmic ratio and shapes of nuclei.

Tissue	Cytoplasm height (nm)	Nucl. height (nm)	Ratio Nucl. height/ Cytoplasm height	Presence of nucleoli
Breast cancer	1000	1150–1200	1.15−1.2	Visible nucleoli 250–300 nm in cancer cells, irregular shape of nucleus
Fibroadenoma of the breast	200	500	2.5	
Papillary thyroid carcinoma	700	1300	1.8	Visible nucleoli 150–200 nm in cancer cells, irregular shape of nucleus, nuclear enlargement. Presence of INCI) – the depth is about 600 nm.
Intact thyroid gland	400	700	1.7	
Normal epithelium	200	1050	5.5	
Cervical cancer	1000	2000	2	Visible nucleoli 500–600 nm
Virus lesion (Koylocytes)	200	600–800 Perinucl. groove 200 nm		

Conclusions: AFM is capable of distinguishing tumor cells in vitro on actual cytological samples.
The preparation of samples is quite simple and may exercised in ordinary hospitals, which should accelerate the adaptation of nanotechnology tools (AFM) into everyday medical practice.

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Expression of solute carrier genes related to molecular imaging in breast cancer

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Molecular imaging of cancer relies on specific cellular mechanisms, operating differently in various tumor types. Positron emission tomography (PET) is a powerful method to detect focal tracer uptake in breast cancer

patients; however, the level of glucose uptake in breast ca is highly variable and limits the diagnostic usefulness of PET. Brown et al demonstrated that glucose uptake in breast cancer is primarily depending on Glut-1 (SLC2A1) expression. Paralelly, it has been demonstrated that a subgroup of breast cancers may be imaged by iodine or technetium-based scintigraphy, due to the expression of sodium-iodide symporter gene (SLC5A5), gene normally expressed in thyroid. The new positron tracer, 124-iodine, might increase the importance of these laboratory findings in breast cancer management. The aim of this study was to analyze the expression of SLC2A1, SLC5A5, other thyroid-specific iodine transporters (SLC5A8, SLC26A4) in the context of markers of breast cancer subtypes (ESR1, ERBB2, GATA3, VIM) and thyroid-specific genes (TPO, TSHR, TG).
Material and Methods: Breast cancer samples were collected from 157 patients, operated in MSC Memorial Cancer Center, Gliwice, Poland, in 38 patients with corresponding normal breast tissue. All samples were collected upon approval by local Ethics Committee. RNA was isolated by Chomczynski-Sacchi method, quality was assessed by Agilent 2100 Bioanalyzer. Real-time quantitative PCR (Q-PCR) analysis was performed on Applied Biosystems SDS 7700 machine with Universal Probe Library fluorescent probes (Roche). We analyzed 6 reference genes: ACTB, ATP6V1E1, B2M, EIF5, HADHA, UBE2D2, data were normalized by geNorm software.
Results: We compared gene expression of all markers according to estrogen receptor and HER2 status, we did not find any statistically significant differences. We noted a significant decrease of glucose transporter in patients operated after neoadjuvant chemotherapy ($p < 0.05$); the reduction of iodide transporter expression was much less pronounced. Similarly, SLC2A1 gene correlated with tumor grade; no such relationship was noted for SLC5A5. The groups of patients with high expression of glucose or iodide transporter (over 75th percentile) did not show any major overlap; thus it seems that these genes are up-regulated in distinct tumor subtypes.
Conclusions: Expression of glucose transporter SLC2A1 and iodine transporter SLC5A5 in breast cancer are independent, thus, the combined use of both markers in positron-emission tomography shall be considered and further studied.

Symptom science

Poster discussion presentations
(Wed, 23 Sep, 11:15−12:15)
Symptom science

3000 POSTER DISCUSSION

HFS 14: a specific quality of life scale for patients with hand-foot syndrome

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Background: Hand-foot syndrome or Hand-Foot skin reaction is a common adverse effect of certain chemotherapy agents, such as capecitabine or pegylated doxorubicin, where it is estimated to occur in 50% of cases. It is also frequently reported with some new targeted anticancer therapies, such as sorafenib or sunitinib, although its clinical presentation is slightly different [1]. There is currently no validated consensus on how to treat this condition, besides dose reductions [2]. It can have a major functional impact [3], sometimes preventing all professional activity and may even require discontinuation of the chemotherapy. However, there is no specific, validated clinical instrument to measure its intensity and its impact on patients, apart from NCI-CTC grading which is relatively insensitive and is not specific. The aim of this study is to develop and validate a hand-foot syndrome-specific quality of life scale in order to be able to measure the impact of the condition on patients and secondly to be able to assess the value of certain specific treatments in this indication.
Method: The questionnaire was developed after conducting a series of structured interviews with patients with forms of hand-foot syndrome of varying severity, which yielded a detailed and rigorous collection of verbatim transcripts. The Pilot-Testing are realised.
Results: Thirty-one items were identified, and 14 items were selected as being relevant and non-overlapping after initial evaluation. The first question in the HFS14 addresses which member is affected (hand, foot or both). The second question addresses the pain with three possible responses (very, moderately or not painful). The 14 items can be organised in 2 modules: the first module more specifically assesses the handicap generated by involvement of the “feet” and the second assesses the handicap generated by involvement of the “hands”. Six (6) items are considered common to both modules, 4 are hand-specific and 4 are foot-specific. The validation confirmed the internal consistency and very high reproducibility of the questionnaire.
Conclusion: The hand-foot syndrome-specific HFS14 scale is easy to use and meets the requirements of a quality of life scale. This scale now needs to be tested in longitudinal studies (for example in clinical trials) to confirm its ability to measure a change in status.

References

[1] Yang et al. Br J Dermatol 2008; 158: 592−6.
[2] Van Moos R et al. Eur J Cancer 2008; 44: 781−90.
[3] Lacouture ME et al. Ann Oncol 2008; 19:1955−61.

3001 POSTER DISCUSSION

Factor analysis of the Health-Related Quality of Life indicators of the QLQ-C30 in 6798 cancer patients

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Background: When treating cancer patients, preservation of quality of life is an important goal. There is an emerging consensus that quality of life should be one of the endpoints in clinical trials. The specific aim of this study was to explore the underlying factor structure of the 15 Health-Related Quality of Life (HRQoL) indicators and to generate hypotheses about the inter-relationships of the indicators.
Material and Methods: Pooled data from 6798 patients on 29 European Organisation for Research and Treatment of Cancer (EORTC) randomized clinical trials were used for this analysis. Principal Factor Analysis was performed to extract factors from the 15 HRQoL indicators. An oblique rotational technique (Harris-Kaiser) was used. Cronbach’s alpha coefficient (α) was calculated to measure internal consistency. Validity of results was evaluated by using clinical parameters World Health Organisation (WHO) performance status (0−1 vs 2−3) and metastases status (no vs yes) to divide the patients into subgroups that were expected to differ in HRQoL. Subgroups were compared using the t-test, with response variables being the obtained factors.
Results: Two main factors emerged from the analysis. The first factor had high loadings from 8 of the 15 indicators: physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning, global health status, fatigue and pain. This factor appears to describe a ‘general functioning’ status. The second factor had high loadings from 2 of the 15 indicators: nausea and vomiting and appetite loss. This factor appears to describe a ‘gastrointestinal functioning’ status. Internal consistency was $\alpha = 0.87$ for the ‘general functioning’ factor and $\alpha = 0.68$ for the ‘gastrointestinal functioning’ factor. Both factors were able to detect differences in subgroups defined according to WHO performance status ($p = 0.0008$ for the ‘general functioning’ factor, $p < 0.0001$ for the ‘gastrointestinal functioning’ factor) and to metastases status ($p < 0.0001$ for the ‘general functioning’ factor, $p < 0.0001$ for the ‘gastrointestinal functioning’ factor).
Conclusions: Factor scores are useful to monitor quality of life in patients. Patient assessed HRQoL indicators have demonstrated prognostic power; summary indexes of HRQoL indicators should be employed as stratification variables alongside conventional variables. This approach may also allow simplification of data and analysis in clinical trials.