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Konferencja Młodych Naukowców

Young Scientists' Forum

23 listopada 2017, Poznań

http://www.wco.pl/ysf2017/pl/

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Zaproszenie

Young Scientists' Forum Poznań 23. listopada 2017

Koleżanki i Koledzy,

Serdecznie zapraszamy wszystkich Młodych Naukowców, do udziału w kolejnej edycji Young Scientists' Forum, które odbędzie się 23.11.2017 r. w Poznaniu.

Jest to konferencja dedykowana młodym naukowcom przed 35 rokiem życia, specjalizującym się w radioterapii, fizyce medycznej oraz radiobiologii. Forum stwarza doskonałą okazję do wymiany doświadczeń zawodowych oraz zawierania nowych kontaktów na poziomie krajowym i międzynarodowym. Honorowy patronat naukowy nad wydarzeniem objął profesor Julian Malicki – Dyrektor Wielkopolskiego Centrum Onkologii. Zgłoszone abstrakty będzie oceniało międzynarodowe jury, reprezentowane przez światowych ekspertów z dziedziny radioterapii, radiobiologii oraz fizyki medycznej.

W tym roku udział w komitecie naukowym potwierdzili: **Prof. Wolfgang Doerr (Austria), Prof. Jesper Grau Eriksen (Dania), Prof. Filipe Garcia Moura (Portugalia), Prof. Philip Poortmans (Francja), Prof. Daniela Thorwarth (Niemcy).**

Prace zaakceptowane do prezentacji ustnej będą przedstawione w formie 10 minutowej prezentacji i 10 minutowej dyskusji. Obie części wystąpienia są jednakowo oceniane – zarówno pomysł, wyniki prezentowanego badania, jak i umiejętność przeprowadzenia naukowej dyskusji.

Dla autorów najwyżej ocenionych prac przewidziane są różnorodne nagrody wspierające karierę i rozwój naukowy:

Dla autorów najlepszych prac przewidziano następujące nagrody:

- 1 miejsce - udział w wybranym kursie europejskim ESTRO 2018 (opłata konferencyjna, zakwaterowanie, koszty podróży)
- 2 miejsce - udział w wybranej konferencji europejskiej o tematyce onkologicznej (opłata konferencyjna, zakwaterowanie, koszty podróży)
- 3 miejsce - roczna prenumerata Reports of Practical Oncology and Radiotherapy

Serdecznie zapraszamy do udziału!

W imieniu Komitetu Naukowego

Dr Joanna Kaźmierska

Invitation

Young Scientists' Forum Poznan November 23rd 2017

Together with Honorary Chair Prof. Julian Malicki, we would like to invite all young scientists to participate in the Young Scientists' Forum, which will take place in Poznan, Poland on November 23rd, 2017.

This conference is open to radiation oncologists, medical physicists and radiobiologists age 35 or younger. Residents in training, young specialists, and PhD students are all welcome.

The aim of this Forum is to promote the achievements of young scientists, to help in their professional development, and to create a strong platform to exchange professional experiences.

We encourage all young scientists involved in research to submit an abstract. Abstracts should be submitted in English. All abstracts will be evaluated by an international jury consisting of leading experts in radiotherapy, radiobiology, and medical physics. Oral presentations of accepted abstracts will consist of a ten-minute presentation of the research followed by a ten-minute discussion.

All presentations will be assessed by the international jury, which will consider both the content and presentation of the research as well as the presenter's ability to lead a scientific discussion. The best presentations will receive one of the many awards intended to support professional and scientific development.

Authors of the best presentations will be rewarded as follows:

- 1st Place - participation in a chosen European ESTRO 2018 Course (fee, travel, and accommodation)
- 2nd Place - particiaption in a chosen European oncology conference (fee, travel, and accommodation)
- 3rd Place - annual subscription of Reports of Practical Oncology and Radiotherapy Journal

We look forward to your participation in the Young Scientists' Forum.

See you in Poznan!

Dr Joanna Kazmierska
Chair Scientific Committee

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Scientific program

08.30	**The Opening of the Young Scientists' Forum - dr Joanna Kaźmierska**
08.40-10.20	**Session 1, Chair: dr Joanna Kaźmierska, Presentation of 5 abstracts selected for oral presentation** 1. The role of stereotactic body radiotherapy and radiosurgery in the management of soft tissue and bone sarcomas. Mateusz Spałek, Aneta Borkowska, Dorota Kiprian, Robert Madejek, Piotr Rutkowski (CO Warszawa) 2. Impact of pelvis irradiation on toxicity of further oxaliplatin-based chemotherapy in rectal cancer. Mateusz Spałek, Wojciech Michalski, Krzysztof Bujko, Lucjan Wyrwicz (CO Warszawa) 3. The influence of chemotherapy on stereotactic radiotherapy of liver metastases in colorectal cancer patients. Magdalena Stankiewicz, Tomasz Dworzecki, Kamil Krysiak, Leszek Miszczyk (CO Gliwice) 4. Advanced radiation therapy techniques in pediatric brain tumor therapy: preservation of neurocognitive function. Katharina Weusthof, Semi Harrabi, Sebastian Regnery, Stefan Rieken, Peggy Lüttich, Olaf Witt, Denise Bernhardt, Klaus Maier-Hein, Martin Hettich, Jürgen Debus, Sebastian Adeberg (Heidelberg Unversity Hospital) 5. Preoperative radiotherapy and local excision of rectal cancer: Long-term results of a prospective multicentre study. Katarzyna Wiśniowska (CO Warszawa)
10.20-10.50	**Coffee break**
10.50-12.30	**Session 2, Chair: dr Wiktoria Suchorska, Presentation of 5 abstracts selected for oral presentation** 1. Prostate cancer bone metastases evaluation: 18F-fluorocholine PET/CT, 18F-fluorodeoxyglucose PET/CT and 99mTc–methyl diphosphonate bone scintigraphy. Agata Karolina Pietrzak, Rafał Czepczyński, Ewa Wierzchosławska, Michał Smoleń, Witold Cholewiński (WCO Poznań) 2. The role of let-7d and miR-18a in the biology of the head and neck cancers: TCGA data analysis. Tomasz Kolenda, Kacper Guglas , Marcel Ryś , Anna Teresiak, Renata Bliźniak, Katarzyna Lamperska (WCO Poznań) 3. DHMEQ – an inhibitor of NF-KB pathway as a new drug improving response to platinum-based treatment in ovarian cancer. Michał Lach, Wiktoria Suchorska, Marcin Michalak (WCO Poznań) 4. Surgical wound fluids from patients treated with intraoperative radiotherapy induce radiobiological response in breast cancer cells Igor Piotrowski, Katarzyna Kulcenty, Dawid Murawa, Wiktoria Suchorska (WCO Poznań) 5. hTERT promoter methylation status as a molecular marker of cancer progression in head and neck cancer patients. Agnieszka Sobecka, Wojciech Barczak, Wiktoria Blaszczak, Pawel Golusiński, Blażej Rubis, Michał M. Masternak, Wiktoria M. Suchorska, Wojciech Golusiński (WCO Poznań)
12.30-13.20	**Lunch**

13.20-15.00	**Session 3, Chair: Prof. Julian Malicki, Presentation of 5 abstracts selected for oral presentation** 1. Ferrofluid as a sonosensitizer for ultrasonic hyperthermia. Katarzyna Kaczmarek (UAM Poznań) 2. Evaluation of the Smart Deviceless4D 4DCT system. Tomasz Kostecki (NUMED Katowice) 3. Comparison of imaging procedures and irradiation of patients in three oncology centres using ionizing radiation based on clinical audit. Aleksandra Misiura (UAM Poznań) 4. Proton radiography for inline treatment planning and positioning verification of small animals. Johannes Muller (OncoRay Dresden) 5. Enhanced treatment planning and response evaluation at Ultra-High-Magnetic Fields: potentials and limitations. Sebastian Regnery, Nicolas Behl, Daniel Paech, Benjamin Knowles, Jan Eric Meissner, Heinz-Peter Schlemmer, Mark E. Ladd, Armin Nagel, Stefan Rieken, Jürgen Debus, Sebastian Adeberg (Heidelberg University Hospital)
15.00-15.15	**Coffee break**
15.15-15.45	**Poster discussion, Chair: Bartosz Urbański** 1. Radiation Therapist workflow after 2 months extended scope of practice. Justyna Michalewska 2. Forced differentiation proces in vitro leads to stress-induced activation of DNA damage response. Ewelina Stelcer, Katarzyna Kulcenty, Marcin Ruciński, Karol Jopek, Magdalena Richter, Tomasz Trzeciak, Wiktoria Suchorska (WCO Poznań)
15.45-16.45	**Satellite session - Sponsors'presentations**
16.45-17.15	**Award Ceremony and closing remarks**

Streszczenia / Abstracts

Session 1 (clinical) ***chair: Joanna Kaźmierska***

1.1 The role of stereotactic body radiotherapy and radiosurgery in the management of soft tissue and bone sarcomas

Mateusz Spałek[1], Aneta Borkowska[2], Dorota Kiprian[3], Robert Madejek, Piotr Rutkowski[5]

[1]Department of Radiotherapy I, Maria Sklodowska-Curie Institute - Oncology Center, Warsaw, Poland,[2]Department of Radiotherapy I, Maria Sklodowska-Curie Institute - Oncology Center, Warsaw, Poland,[3]Department of Head and Neck Cancer, Maria Sklodowska-Curie Institute - Oncology Center, Warsaw, Poland,[4]Students' Scientific Society of Radiotherapy, Medical University of Warsaw,[5]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Institute - Oncology Center, Warsaw, Poland

Background: Contemporary highly conformal radiotherapy techniques, such as stereotactic body radiotherapy (SBRT) or stereotactic radiosurgery (SRS) allow to obtain high local control rate (LC) in many primary and metastatic cancers, however their role in the management of sarcomas has not been yet established. The aim of the study was to determine the usefulness and efficacy of SBRT/SRS in the management of sarcomas.

Methods: The study group was a cohort of patients with soft tissue and bone sarcomas treated in our cancer centre that received SBRT/SRS. The following parameters regarding radiotherapy was analysed: indication for SBRT/SRS, site, number of lesions, number of recurrences before SBRT/SRS, previous irradiation in-field, total dose (TD), dose per fraction (DF), method of dose prescription, treatment technique, volumes of GTVs and PTVs, early and late toxicities, best obtained SBRT/SRS result, in-field and field border progression. Additional parameters included, tumour grade, date of primary diagnosis, primary tumour site, systemic therapy received before and after SBRT/SRS, and date of overall disease progression, if occurred. The Kaplan-Meier estimator was used to calculate progression-free survival (PFS).

Results: Totally n=31 patients who underwent 1-3 SBRT/SRSs on 1-5 target lesions were included. The indications for irradiation were: oligometastatic disease (59.5%), oligoprogression (21.6%), primary definitive treatment (5.4%), recurrence definitive treatment (10.8%), and adjuvant setting (2.7%). The irratiated sites were: lungs (43.2%), head&neck (21.6%), bones (16.2%), central nervous system (8.1%), liver (5.4%), lymph nodes (2.7%), and soft tissues (2.7%). DF varied from 4 to 18 Gy, and TD from 8 to 60 Gy. GTVs and PTVs were between 0.5-110.94 cm3 (mean GTV 17.16 cm3) and 3.29-138.1 cm3 (mean PTV 38.64 cm3), respectively. SBRT/SRS allowed to obtain complete response in 18.9%, partial response in 10.8%, stable disease in 62.1% and progressive disease in 8.1%. No acute or late toxicity grade 3 or above was observed. In-field progression (at any time) was identified in 18.9% of patients. Median PFS was 9.4 months (95% CI: 2.7-16.0).

Conclusions: SBRT/SRS allows to obtain high LC with excellent treatment tolerance in patients with sarcomas. This treatment modality may be considered as an alternative to surgery in selected clinical situations, especially in oligometastatic and oligoprogressive disease.

1.2. Impact of pelvis irradiation on toxicity of further oxaliplatin-based chemotherapy in rectal cancer

Mateusz Spałek[1], Wojciech Michalski[2], Krzysztof Bujko[3], Lucjan Wyrwicz [4],

[1]Department of Radiotherapy I, MSCMCC-IO, Warsaw, Poland,[2]Laboratory of Bioinformatics and Biostatistics, MSCMCC-IO, Warsaw, Poland,[3]Department of Radiotherapy I, MSCMCC-IO, Warsaw, Poland,[4]Department of Oncology and Radiotherapy, MSCMCC-IO, Warsaw, Poland Laboratory of

Bioinformatics and Biostatistics, MSCMCC-IO, Warsaw, Poland

Background: Radiotherapy is used in the neoadjuvant setting in majority of rectal cancer patients, while its effect on overall survival is limited mostly to patients with threatened resection margin. Preoperative pelvic irradiation might damage bone marrow. In consequence, relative dose intensity (RDI) and efficacy of further adjuvant or palliative CT might be reduced. The aim of the study was to assess whether radiation damage to the pelvic bone marrow influences the tolerance of further oxaliplatin-based CT.

Methods: We have performed the cohort analysis of patients with adenocarcinoma of rectum or colon receiving FOLFOX-4 chemotherapy in adjuvant or palliative setting between 2011-2016. Oxaliplatin relative-dose intensity (RDI) within 8 weeks from the beginning of CT was calculated for each patient. The major factors, which can reduce oxaliplatin RDI, were analyzed independently (hemathological toxicity, neurological toxicity, occurrence of hypersensitivity reactions to oxaliplatin). The data regarding the first disruption of oxaliplatin dose within all planned courses of FOLFOX-4 was also collected.

Results: 220 patients met eligibility criteria. 41 of them received neoadjuvant radio(chemo)therapy (study group), the remaining 179 patients were assigned to control group (n = 179). RDI did not differ significantly between irradiated and non-irradiated patients (p = 0.794). There were no statistically significant differences in observed oxaliplatin-related toxicities. The median time between the start of chemotherapy and the first disruption of oxaliplatin administration was also not statistically different between the two groups (p = 0.156).

Conclusions: An impact of preoperative radio(chemo)therapy on RDI or tolerance of FOLFOX was not found in rectal cancer.

1.3. The influence of chemotherapy on stereotactic radiotherapy of liver metastases in colorectal cancer patients

Magdalena Stankiewicz[1], Tomasz Dworzecki[2], Kamil Krysiak[3], Leszek Miszczyk[4]

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Background: The aim of the study was to determine the most effective way of combining chemotherapy with stereotactic radiosurgery of liver oligometastases in colorectal cancer patients.

Methods: The analysis included 80 colorectal cancer patients with liver oligometastases treated with stereotactic radiotherapy. Patients mean age was 65 years (+/- 10 yrs) with a median of 64 yrs. Average follow-up was 2,1 years (+/- 1,4 yrs) with a median of 2,0 yrs. In 78% of patients liver was the only site of metastatic disease. In the remaining patients stagnation or regression of all other lesions was observed. 73% of patients had single liver metastasis and the rest of the analyzed group had 2-4 metastatic lesions in the liver. Radiation dose was 30-50 Gy in 2-3 fractions. Patients were treated according to three treatment schemes: in 53% of patients stereotactic radiotherapy (SBRT) was the only treatment, in 33% SBRT was applied shortly after completion of chemotherapy and in the remaining 24% of patients SBRT was applied only when local progression during follow-up after prior chemotherapy was observed. For statistical analysis Kaplan-Meier estimator with log rank test and multivariate Cox regression model were used.

Results: Two-year local control in the analyzed group was 33%. In multivariate Cox regression analysis radiation dose and treatment scheme had statistically significant impact on local control. Time interval

between chemotherapy and SBRT had no influence on treatment results. Two-year local control in patients who received BED <66 Gy, 78 Gy and 80-112 Gy was 14%, 30% and 50% respectively (p<0,01). Two-year local control in patients treated with SBRT alone was 40%, in patients who received SBRT on residual tumor (after chemotherapy) was also 40% and in patients treated with SBRT due to local progression during follow-up after prior chemotherapy was 8% (p=0,02).

Conclusions: The effectiveness of stereotactic radiotherapy in local control of liver metastases depends on radiation dose and its application in early phase of therapy.

1.4. Advanced Radiation Therapy Techniques in Pediatric Brain Tumor Therapy: Preservation of Neurocognitive Function

Katharina Weusthof[1], Semi Harrabi[2], Sebastian Regnery[3], Stefan Rieken[4], Peggy Lüttich[5], Olaf Witt[6], Denise Bernhardt[7], Klaus Maier-Hein[8], Martin Hettich[9], Jürgen Debus[10], Sebastian Adeberg[11]

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Background: Tumors of the central nervous system are a common issue in pediatric oncology, representing the second largest group of malignancies in childhood. Improved multimodal therapy approaches led to increased survival rates over the last decades. Therefore neuronal functionality, quality of life and preservation of neurocognitive outcome shift into focus. Radiation to the brain, especially in children, is often associated with long-term neurocognitive deficits. Recent studies show that increased conformality of RT, which can be achieved e.g. with proton irradiation, leads to fewer long-term deficits in neurocognitive function. The goal of our study is to evaluate the neurocognitive outcome of pediatric brain tumor patients after proton and photon radiation therapy. Our research efforts focus on the different impacts of these two methods as well as determining other potentially contributing factors.

Methods: Twenty-three pediatric patients with brain tumors were treated with proton therapy from 2010 to 2015. 50 % of the patients (n=11) were diagnosed with low grade (WHO °I/ °II) and 46 % (n=10) with high grade tumors (WHO °III/°IV). Approximately 60% were localized supratentorial and 40% infratentorial.

Fifteen patients (65 %) additionally received chemotherapy; twenty patients (87%) underwent brain surgery. Throughout their therapy, the patient's neurocognitive function was assessed up to four times (before RT - 0.5 – 1.5 – 4 years after RT). A broad range of different tests, accounting for memory, word fluency, motor skills, analytical skills and processing speed, as well as three different questionnaires were conducted.

Results: Descriptive analysis of the first data show promising results. Whereas most of the tests show steady performance, some domains seem to be affected. The visuomotor integration, working memory and fluid reasoning are seemingly not affected, while the verbal memory function as well as short-term and long-term memory seems to show mild deterioration.

Conclusions: The significance of this finding needs to be clarified and validated also in coherence with confounding and correlating factors. This is subject to our further comprehensive investigation, also encompassing the comparison with photon therapy and an untreated reference group.

1.5. Preoperative radiotherapy and local excision of rectal cancer: Long-term results of a prospective multicentre study

Katarzyna Wiśniowska
on behalf of the Polish Colorectal Study Group

Background: Performing local excision after preoperative radiotherapy is of doubtful value for poor pathological responders. In order to guide optimal management after radiotherapy, appropriate clinical tumour response criteria to predict poor pathological responders are thus required.

Methods: 89 patients with cT1-3aN0 <3–4 cm rectal adenocarcinoma received 5 × 5 Gy plus a 4 Gy boost (71.9%) or 55.8 Gy in 31 fractions with a 5-FU bolus and leucovorin (28.1%). Local excision was performed 6–8 weeks later. Patients with good pathological responses (ypT0–1) were observed. Completion total mesorectal excision (TME) was recommended for poor responders (ypT1 with surgical margin+ and ypT2-3).

Results: Good pathological responses to radiation were observed in 63 (71%) patients. The remaining 26 (29%) had poor responses; 8 underwent completion TME and 18 either refused TME or were deemed unfit. Clinical complete responses were seen in 24% (group 1) and residual tumours in the remaining patients; tumour size being ≤1 cm in 30% (group 2) , >1 cm - ≤2 cm in 24% (group 3), and >2 cm in 19% (group 4). Good pathological responses were observed in 86%, 83%, 58% and 47% of patients from respective groups 1, 2, 3, and 4; p=0.02. Median follow-up was 8.9 years (IQR 7.4-11.3 years). Recurrence rate after local excision was 13% for good pathological responders and as high as 56% for poor responders. In total, the success rate of local recurrence salvage was only 44% (R0 resection and no subsequent local re-recurrence or distant metastases). Three out of five patients who were suitable at baseline for anterior resection and who underwent completion or salvage TME, were subjected to abdomino-perineal resection (APR).

Conclusions: In patients with poor pathological responses the local recurrence rate was high. The success rate of local recurrence salvage was poor. Whenever TME was performed, either because of a need for completion or because of local recurrence, it was associated with a high APR rate. The extent of clinical tumour regression after radiotherapy might be considered as a guide for further management.

Session 2 (radiobiology) ***chair: Wiktoria M. Suchorska***

2.1 Prostate cancer bone metastases evaluation: 18F-fluorocholine PET/CT, 18F-fluorodeoxyglucose PET/CT and 99mTc–methyl diphosphonate bone scintigraphy

Agata Karolina Pietrzak[1], Rafał Czepczyński[2], Ewa Wierzchosławska[3], Michał Smoleń[4], Witold Cholewiński[5]
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Background: To compare the usefulness of the 99mTc-MDP-BS, 18F-FDG-PET/CT and 18F-FCH-PET/CT in detecting bone metastases in prostate cancer patients.

Methods: The total of 56 patients with confirmed prostate cancer underwent 99mTc-MDP BS and 18F-FDG PET/CT or 18F-FCH PET/CT within four to six weeks. We evaluated 27 patients with 99mTc-MDP-BS and 18F-FDG PET/CT (mean age: 67.96±9.04 years) and 29 patients examined with 99mTc-MDP BS and 18F-FCH PET/CT (mean age: 73.93±8.75 years). We used the R factor in scintigraphy and performed semi-quantitative analysis with SUV in PET/CT. We calculated the R factor as the total count rate in the bone metastasis and the total count rate in contralateral area ratio. We evaluated the mean pixel and the total surface of lesion product in scintigraphy, TLG (Total Lesion Glycolysis) in 18F-FDG PET/CT and TLA (Total Lesion Activity) in 18F-FCH PET/CT.

Results: We found the mean SUVmax value significantly higher in patients who underwent 18F-FCH PET/CT than in 18F-FDG PET/CT (5.17±2.24, 3.71±1.56, $p<0.05$). The R factor differences in both groups (patients who underwent BS + 18F-FDG PET/CT, BS + 18F-FCH PET/CT) occurred as insignificant (1.92±0.87, 2.03±0.57, respectively, ns). There was no significant Pearsons' correlation coefficient (Rp) between the average R factor and the mean SUVmax within analyzed groups (Rp= 0.42; 0.31) and between the average R factor and the average SUVmean (Rp= 0.43; 0.28). We found high Rp between measured total surface in BS and volume in PET/CT of the bone lesions. In patients who underwent BS and 18F-FDG PET/CT or BS and 18F-FCH PET/CT, Rp was 0.95 and 0.70.

Conclusions: Three analysed methods provided comparable results in bone metastases detection in prostate cancer patients and effected with complementary conclusions.

2.2 The role of let-7d and miR-18a in the biology of the head and neck cancers: TCGA data analysis

Tomasz Kolenda[1], Kacper Guglas[2], Marcel Ryś[3], Anna Teresiak[4], Renata Bliźniak[5], Katarzyna Lamperska[6]
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Background: In our previous study, a correlation between expression of let-7d and miR-18a in HNSCC was observed and their expression increased and reduced jointly in the same cancer tissue (R2=0.52, p<0.0001). Let-7d is usually described as tumor suppressor and miR-18a is known as oncogene, but this classification is still controversial. The TCGA data analysis supposed to determine the questionable role of let-7d and miR-18a in HNSCC patients.

Methods: Gene expression levels and clinical data HNSCC samples from TCGA project were obtained from available data bases. Four groups i) let-7d and miR-18a high, ii) let-7d and miR-18a low, iii) let-7d high and miR-18a low, and vi) let-7d low and miR-18a high was divided using mean of let-7d and miR-18a expression in cancer tissue as cut off. The clinical parameters and expression of genes were analyzed between these groups.

Results: TCGA data analysis showed over-expression of let-7d and miR-18a in HNSCC compared to normal samples (fold change 1.387756, p=5.57919e-07; fold change 2.779943, p=3.21511e-17, respectively). Moreover, expression of let-7d and miR-18a was correlated only in cancer but not in normal tissue. No significant differences between expression levels of let-7d and miR-18a and personal gender, age or HPV status were observed. Only in the case of let-7d differences in expression levels between neoplasm histologic grade and regional lymph node N-stage were noticed. Analysis of let-7d and miR-18a expression groups showed significant longer disease free survival and longer overall survival between patients with let-7d and miR-18a high vs let-7d high and miR-18a low (median DFS 16.39 vs 29.93 months, p=0.0273; median OS 17.9 vs 26.86 months, p=0.0471). Gene expression analysis indicated differences in expression pattern of genes connected with many important cellular processes.

Conclusions: TCGA data analysis confirmed our previously observation. Let-7d and miR-18a are frequently up-regulated in HNSCC and their expression is correlated. The overexpression of let-7d and miR-18a creates unique cell phenotype, which influences on course of disease.

2.3 DHMEQ – an inhibitor of NF-KB pathway as a new drug improving response to platinum-based treatment in ovarian cancer

Michał Lach[1], , Marcin Michalak[2], Wiktoria M. Suchorska[3]

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Background: Ovarian cancer (OvCa) is one of the most lethal gynecological malignancies. It is diagnosed mostly in advanced stage of disease. Due to lack of appropriate early detection markers and non-ambiguous symptoms the 5-year survival rate of patients is significantly reduced. Besides primary good response to platinum-based therapy, approximately 70% of patients will develop chemoresistance. According to various studies NF-kB signaling pathway is involved in formation of resistant phenotype. It is responsible for increase the viability, cell cycle progression, inducing growth of cells (secretion of IL-6 and TNF-α) and migration potential of neoplasm cells. A few independents studies suggest the correlation between activation of NF-kB and poor outcome in OvCa patients. That is why development of inhibitors of NF-kB pathway is a new target of cancer therapies. One of the promising compounds is dehydroxymethylepoxyquinomicin (DHMEQ). Its antitumor effect was already shown in hepatoma, bladder cancer and lymphotic leukemia. The aim of this preliminary study was to indicate the application of DHMEQ in combination with platinum-based drugs as a new approach in OvCa therapy.

Methods: A2780 and SKOV3 cell lines were used in this study. For estimation IC50 of DHMEQ, cisplatin (CDDP) and carboplatin (CBP) MTT assay was performed. Further cells were treated with DHMEQ combined

with CDDP or CBP for 72h or 96h. The effect of drugs was evaluated using flow cytometry (apoptosis and cell cycle), clonogenic assays. Additionally combination index (CI) with dose reduction index (DRI) was calculated using CompuSyn software.

Results: DHMEQ combined with CDDP or CBP enhance the apoptosis in A2780 cell line and cause stronger cell cycle arrest in G2/M phase SKOV3 cell line. DHMEQ combined with CDDP cause synergistic effect in SKOV3. In A2780 cell line the synergistic effect was observed in DHMEQ combined with CBP. The DRI indicate onto favourable reduction of CDDP or CBP doses when it combined with DHMEQ, what could decrease their side effects.

Conclusions: Combination of DHMEQ with CDDP or CBP could be a new approach in ovarian cancer treatment. However, in vivo analysis should be performed to establish appropriate dosage for clinical trials.

2.4 Surgical wound fluids from patients treated with intraoperative radiotherapy induce radiobiological response in breast cancer cells

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Background: Breast cancer is the most common cancer occurring in women. Currently the standard treatment involves breast-conserving surgery followed by whole breast radiotherapy. The fact that the majority of metastases occur within the scar initiated a series of research and clinical trials which aimed to evaluate the effectiveness of localized intraoperative radiotherapy (IORT) in inhibiting local recurrence formation. IORT was previously reported to modify the biological activity of surgical wound fluids [Belletti et. al, 2008]. Moreover it has been shown, that soluble factors secreted by irradiated cells can induce DNA damage and mutagenesis in unirradiated bystander cells. This radiation induced bystander effect (RIBE) is likely to contribute to the local tumor control after IORT treatment. The aims of this study were to determine whether the wound fluids collected from patients treated with IORT induce radiobiological response in breast cancer cells and to assess the role of RIBE in this process.

Methods: Wound fluids from patients which underwent IORT (RT-WF), as well as from control group without radiotherapy (WF), were collected 24 hours after the surgery. Conditioned medium (CM) was collected from breast cancer cell culture 24 hours after exposure to the dose of 10 Gy. Two human cancer cell lines with different molecular status (basal – MDA-MB-468, luminal – MCF-7) were incubated with wound fluids and conditioned medium (CM, WF, RT-WF, WF+CM) in culture medium without serum. We used flow cytometry to assess DNA damage and RT-qPCR to analyze the activity of DNA damage repair pathways.

Results: Our results showed that both wound fluids from patients who received IORT (RT-WF) and a combination of surgical wound fluids with conditioned medium (WF+CM) induced DNA damage and activated DNA damage repair pathways in breast cancer cells. This effect was not observed after stimulation with control group (WF).

Conclusions: Our results show that, unlike control group (WF), wound fluids collected from IORT-treated patients induce radiobiological response in breast cancer cells. We ascribe this phenomenon to the activity of soluble factors secreted by irradiated cells. Our findings demonstrate that IORT reduces the local recurrence rates not only through the cancer cell killing, but also by altering tumor's microenvironment.

2.5 hTERT promoter methylation status as a molecular marker of cancer progression in head and neck cancer patients

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Background: The head and neck squamous cell carcinoma (HNSCC) is the sixth leading cause of cancer worldwide, representing over half a million incidents every year. Cancer cells, including HNSCC, are characterized by an increased telomerase activity. This enzymatic complex is active in approximately 80-90% of all malignancies, and is regulated by many factors, i.e. methylation status of hTERT gene promoter. hTERT gene is also surmised to be differentially methylated in cancer patients than in controls. The aim of this study was to analyze the hTERT gene promoter methylation status in blood leukocytes of HNSCC patients.

Methods: DNA was extracted from PBMC (Peripheral Blood Mononuclear Cells) of 92 patients with histologically diagnosed HNSCC and 53 healthy volunteers. Methylation status of 19 CpG islands was estimated using bisulfide conversion technique followed by sequencing of PCR products.

Results: Close to the significant (p=0,0532) differences in the general frequency of hTERT CpG sites methylation was detected between patients and healthy controls. However, it was discovered that some of analyzed positions (CpG islands: 1 [p=0,0235], 5 [p=0,0462], 8 [p=0,0343]) are significantly more often methylated in HNSCC patients than in controls. The opposite finding was observed in case of CpG position 2 (p=0,0210). Furthermore, closer analysis of single CpG positions revealed differences in methylation status dependent on anatomical site and TNM classification.

Conclusions: Analysis of hTERT promoter methylation status (all or single CpG positions) may be used as a molecular markers of HNSCC progression.

Session 3 (physics) ***chair: Julian Malicki***

3. 1 Ferrofluid as a sonosensitizer for ultrasonic hyperthermia

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Background: Ultrasound hyperthermia is a medical procedure, which due to ultrasounds, heats the tumor tissue up to temperatures between 41-45°C. Achieved temperature increase, trigger several physiological reactions in the body. Due to this physiological changes anti-cancer therapies, such as radio or chemotherapy, are more effective. Effectiveness of ultrasound hyperthermia can be improved due to application of sonosensitizers - materials which increases wave attenuation and in consequence leads to higher temperatures during sonication. The purpose of my work is to investigate the influence of concentration of sonosensitizing material on the thermal effect of ultrasound hyperthermia.

Methods: Experimental research were conducted on tissue-mimicking agar phantoms. Two types of phantom were prepared for measurements: pure agar-gel sample without any scattering material and agar-gel samples with sonosensitizers. As a sonosensitizers - magnetic nanoparticles, coated with biocompatible layer of surfactant were used. Temperature increase in phantoms with different concentration of sonosensitizers, due to 1 MHz and 3.5 MHz ultrasound sonication were measured via digital thermometer with optical fiber. Moreover, acoustic properties (attenuation coefficient, ultrasonic wave, specific heat) of phantoms were calculated and measured by ultrasonic methods.

Results: Assumptions of supplementary heat occurrence due to sonosensitizers addition have been confirmed experimentally and theoretically. Temperature increase achieved during ultrasound hyperthermia for phantom with added sonosentizing material is higher than this achieved for pure agar phantoms.

Conclusions: Summarizing, magnetic nanoparticles are good candidates for sonosensitizers. Their presence in tissue phantoms improves thermal effect of ultrasonic hyperthermia. Due to improved effectiveness of hyperthermia, sonication time and ultrasound intensity during treatment can be reduced. It will consequently minimize the negative side effects of this therapy such as discomfort, pain, skin redness. Moreover, magnetic nanoparticles in the presence of alternating magnetic field also can produce heat. So they are also promising material for synergistic sono-magnetic hyperthermia. Combination of ultrasound and magnetic hyperthermia will lead to even better results which can be considered as a new cancer therapy.

3. 2 Evaluation of the Smart Deviceless4D 4DCT system

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Background: The aim of the study is to evaluate the Smart Deviceless4D system as a 4DCT imaging tool and compare it to the Advantage4D system.

Methods: The scanning and registration methods were tested on the cone-shape phantom, specially made for the purpose of presented study, as well as on radiotherapy patients scans. Delineations of structures “External”, “Lung” and “Target” and operations on the delineated structures were made using Oncentra MasterPlan (Nucletron, Columbia, USA). The analyses of the obtained values were made using the volume of structures and Dice similarity coefficient (DSC).

Results: During testing of the systems with Dynamic Phantom Model008A (CIRS, Norfolk, USA), it occurred that the Maximum Intensity Projection (MIP) volume of the Target in the soft tissue window

was 29,98cm3 for Advantage4D and 18,46cm3 for Deviceless4D. Deviceless4D was unable to properly create MIP reconstruction of the phantom. This led to the construction of the cone-shaped phantom. The minimum volume of the \"Lung\" and \"External\" structures were for Adwantage4D 320,78±0,03cm3 and 649,08±0,05cm3 respectively in the "50%" phase. As for Deviceless4D 321,18±0,20cm3 and 649,77±0,29cm3 respectively in the unusual "60%" phase. Knowledge of the maximum exhalation is necessary to determine the peak-exhale location of the tumor. This could be a potential source of errors. Reconstructed Target volume of Deviceless4D in each phase remains within the range of 0,39% to 13,04% difference from the known value while Advantage4D ranged from 0,06% up to 19,63% difference in the \"20%\" phase reconstruction. At the point where the enlargement occurred was a stitching point of two cine-scan blocks, in which images were merged in slightly different moments of the cycle. MIP images of patients reconstructed using both systems were compared among themselves. Mean values of DSC in patients were 0,952±0,02.

Conclusions: The innovative binning of the Deviceless4D requires new testing methods. Also a way to minimize the number of cine stitching points should be proposed, as they affect reconstructed images. Obtained results have shown that, despite the differences in reconstruction techniques, both of the studied systems allow for correct determination of the volumes of interests.

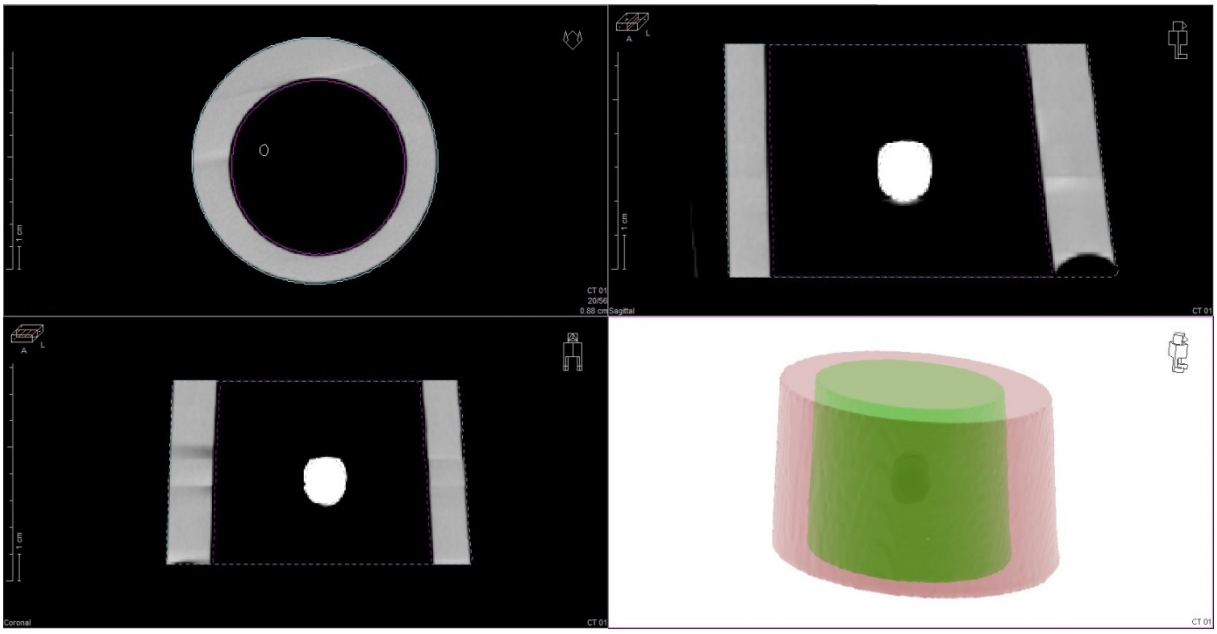

Figure 1. CT reconstruction of the cone-shaped phantoms body visualized in Oncentra Masterplan

3. 3 Comparison of imaging procedures and irradiation of patients in three oncology centres using ionizing radiation based on clinical audit

Aleksandra Misiura
Uniwersytet Medyczny im. Karola Marcinkowskiego w Poznaniu

Background: The aim of the study is to select appropriate quality control issues and to subsequently establish a compliance with these standards at medical facilities. The study included three centres which use ionizing radiation for medicinal purposes, at which didactic activities were carried for electrocardiography students. The purpose of each inspection is to provide feedback on the quality and effectiveness of the study.

Methods: A clinical audit is used as a tool for systematic review as well as a review of medical procedures and aims at improving the quality and outcomes of treatment through a review of practices. The study involved procedures for preparing patients for radiotherapy, quality control of data, and the role of the

electroradiologist during the process. In order to ensure full objectivity, the audit was conducted by means of a personal visit and through the gathering of all the necessary data into a pre-prepared questionnaire, based on the IAEA guidelines. Primarily, this was a descriptive study, where points for the final evaluation of the medical facilities were also awarded.

Results: All the centres achieved a positive and desirable result, requiring only some minor corrective measures in some areas. The Wielkopolskie Centrum Onkologii had the highest evaluation score, with 85 of 89 possible points (95.5%). The following centres had similar results, namely Centre A with 76 points (85.4%) and Centre B with 75 points (84.3%).

Conclusions: A clinical audit is an excellent tool for examining and reviewing medical procedures. The clinical audit program can contribute to the quality of medical procedures, medical care as well as patient safety. The carrying out of a clinical audit is labour-intensive and time-consuming, but as a result, all institutions have benefited from identifying areas requiring corrective measures, which after implementation will improve the quality of treatment.

3. 4 Proton radiography for inline treatment planning and positioning verification of small animals

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Background: As proton/particle therapy is gaining increasing availability, the need for high-quality in vivo data for the assessment of the effects of particle irradiation upon tumor tissue and healthy tissue becomes of increasing importance. For instance, existing preclinical data suggest that the most widely used beam modalities (photon, proton, carbon ions) differ strongly in terms of relative biological effectiveness (RBE), whereas the underlying biological mechanisms remain obscure. Thus, there is a necessity to address these and related questions with experimental setups that allow for easily applicable, efficient application of image-guided, fractionated particle irradiation of small animals, the most widely used pre-clinical model.

Methods: In this work, a method is proposed to perform dual-energy proton radiography for inline positioning verification and treatment planning. Dual-energy proton radiography exploits the differential enhancement of object features in two successively measured two-dimensional (2D) dose distributions at two different proton energies. The two raw images show structures that are dominated by energy absorption (absorption mode) or scattering (scattering mode) of protons in the object, respectively. Data post-processing allowed for the separation of both signal contributions in the respective images. The images were evaluated regarding recognizable object details and feasibility of rigid registration to acquired planar X-ray scans.

Results: Robust, automated rigid registration of proton radiography and planar X-ray images in scattering mode could be reliably achieved with the animal's bedding unit used as registration landmark. Distinguishable external and internal features of the imaged mouse included the outer body contour, the skull with substructures, the lung, abdominal structures, and the hind legs. Image analysis based on the combined information of both imaging modes allowed image enhancement and calculation of 2D water-equivalent path length (WEPL) maps of the object along the beam direction.

Conclusions: Fractionated irradiation of exposed target volumes (e.g. subcutaneous tumor model or brain) can be realized with the suggested method being used for daily positioning and treatment planning. Robust registration of X-ray and proton radiography images allows for the irradiation of tumor entities that require conventional computed tomography (CT)-based planning, such as orthotopic lung or brain tumors, similar to conventional patient treatment.

3. 5 Enhanced Treatment Planning and Response Evaluation at Ultra-High-Magnetic Fields: Potentials and Limitations

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Background: Radiotherapy is a cornerstone in the treatment of glioblastoma and skull-base-meningioma. Currently, contrast-enhanced T1- and T2-weighted MRI-sequences at 3 Tesla represent the golden standard in target delineation and response assessment with its well-known limitations. Ultra-high-field-MRI is an emerging approach which yields increased spatial resolution and shows particularly promising results in sodium-imaging for tumor characterization and response evaluation. Here we present the first results of a prospective longitudinal study employing 7-Tesla-MRI during radiotherapy.

Methods: Four glioblastoma and four meningioma patients underwent imaging on a 7T-MRI-scanner (Siemens Healthineers, Erlangen, Germany) in addition to the standard 3T-MRI-protocol before, during and after definitive treatment. High-resolution T2-FLAIR-imaging was performed using a 24-channel head coil, employing a TSE- and a hyperecho-sequence (resolution: 0.57x0.57x5mm3). Sodium-MR-images were acquired with a double-resonant (1H/23Na) quadrature birdcage coil using a density-adapted 3D radial projection pulse sequence and an iterative 3D-DLCS reconstruction algorithm. 7T- and clinical 3T-MRI-images from different time points were co-registered manually using MITK. ROIs were delineated on clinical standard imaging by an experienced radiation oncologist: T1-weighted Gadolinium-contrast-enhancement (gdce) representing tumor tissue, T2-FLAIR hyperintensity representing edema and normal appearing white matter (nawm).

Results: The comparison of gross tumor volumes derived from 3T- and 7T-FLAIR-images respectively shows divergent results for different field strengths. Concerning 7T-MRI sequences, there is a tendency towards larger volumes in the FLAIR-hyperecho sequence ($p>0.05$). There are considerable changes in sodium-mean signal-intensity in tumor- and edema-ROIs in all glioblastoma patients (Figure 1). Furthermore, the early signal trends point in different directions for the therapy responders and the non-responder. No clear changes can be observed in tumor and nawm in the meningioma patients. This stability of sodium-signals in non-infiltrative disease suggests indifference of sodium imaging towards possible radiotherapy-induced changes in unaffected white matter. Hence, the signal changes in the glioblastoma cohort might reflect treatment response of tumorous tissue.

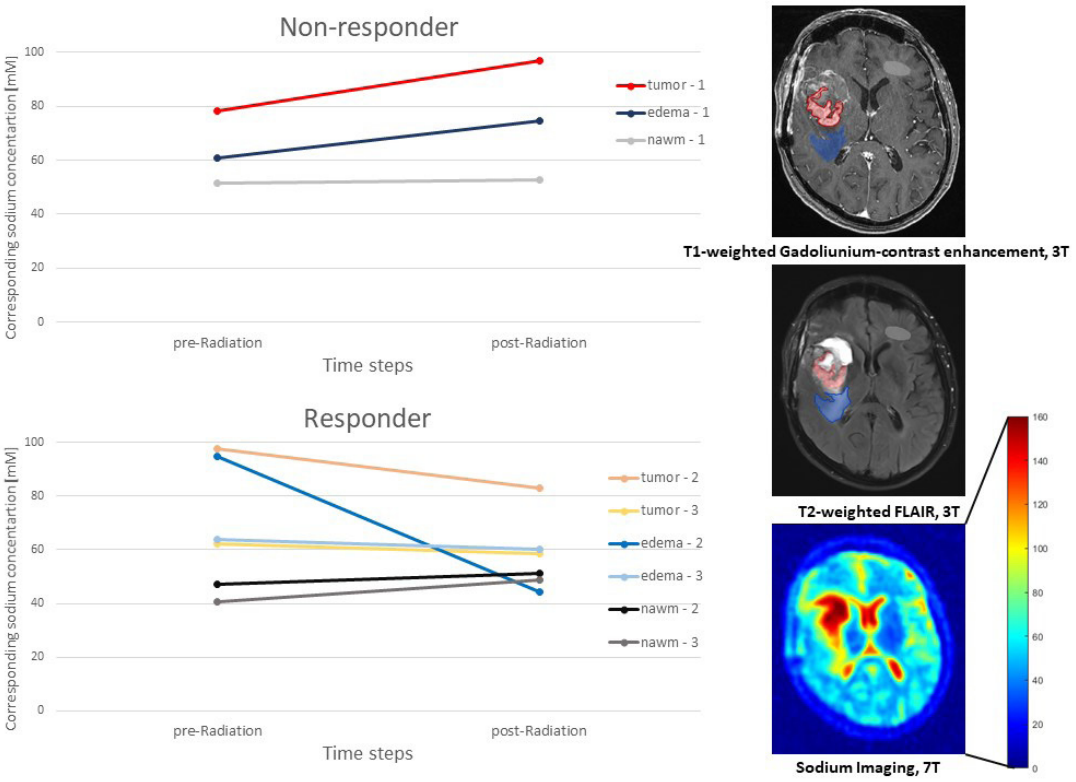

Figure 1. Left: Comprehensive development of mean sodium signal in one non-responsive and two responsive glioblastoma patients. Right: Exemplary definition of ROIs for patient 2. Red: tumor, blue: edema, grey: normal appearing white matter (nawm)

Conclusions: The differences of target volumes derived from different 3T- and 7T-MRI-FLAIR-sequences suggest that both magnetic field strength and imaging technique might have an impact on treatment plans. The striking changes of sodium signal in glioblastoma patients possibly yield essential information about treatment response and merit further investigation.

Poster presentations ***chair: Bartosz Urbański***

P. 1 Radiation Therapist workflow after 2 months extended scope of practice

Justyna Michalewska
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Background: As a radiation therapist (electroradiologist), involved in a trial program, my daily practice is based on cooperation between patient and Radiation Oncologist (RO) directly on the radiotherapy department/unit. The scope of practice is different from the standard RTT practice and overlook working on medical linac. Background: Analysis of two months' workflow as a radiation therapist working strictly on the ward, evaluate the possibility of participation in the treatment planning process, preparing a patient to radiotherapy. The purpose of the study is presenting problems encountered by the RTT who started his practice just after graduation the university.

Methods: Two months' workflow included 48 patients with different tumor sites in age 31-85 years preparing for radiotherapy treatment from September to October. The results show the learning curve. The effectiveness of the study was assessed on the basis of the amount of time devoted to the individual processes involved in the preparation of the patient for the treatment process.

Results: In the analyzed group, the following results occurred in observation process. On 12 patients iCT (initial CT for planning) scans was performed. An average time for one patient in the first month of work was 15 min. and 10 min in second moths respectively. For 14 patients in the first month and 10 in second Avg. time for CT with a virtual simulation was 16 minutes. The average time needed for conventional simulations (Acuity) in September was 13min 20s, and in October 13min 30s. The average time needed for simulations in September was 13min 20s, and 13min 30s in October. Due to the small number of patients on the simulation, the results are presented in the form of a general average, without a monthly report. The time spent on making individual thermoplastic masks was In September, for the 3-point mask - 17min, the 5-point - 20min. In October 5-point immobilization took an average of 16min 20s. Contouring organs at risk (OAR) depend on the localization and range from 120 minutes to 60 minutes.

Conclusions: The time spent on computed tomography with a virtual isocentre is similar, because of the low number of patients. Splitting palliative and radical treatment are necessary for future analyses. Time for contouring depends on localization and its take comparable to advance practitioners amount of time. The most time consuming was abdominal and head and neck (H&N) OAR. Difficulties encountered after starting trial program apply: too low experience in preparing the patient for treatment, lack of knowledge about software used for treatment (Simulation, CT,) and low experience engagement with contouring. The remaining time can be used to implement other procedures like coordination of patient path for radiotherapy treatment.

P. 2 Forced differentiation process in vitro leads to stress-induced activation of DNA damage response

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Background: We investigated the mechanisms of DNA damage response (DDR) activated in chondrocyte-like cells differentiated from human induced pluripotent stem cells (ChiPS) after ionizing radiation (IR) treatment. Importantly, irradiated ChiPS reveal the extremely high level of DNA repair mechanisms. Such high level of DDR mechanisms is considerably associated with the forced chondrogenic differentiation in vitro, that constitutes a meaningful stress for cells. The aims of the study were: a) to investigate gene expression profile of the obtained ChiPS, b) to compare expression of genes involved in DDR process between ChiPS with hiPSCs and mature chondrocytes c) to evaluate the level of activated stress in hiPSCs undergoing differentiation in vitro.

Methods: • Chondrogenic differentiation of hiPSCs (Suchorska et al., 2017) was conducted. • Global gene expression microarray was performed and analyzed using GeneAtlasTMWT Expression Kit Assay and AffymetrixGeneAtlasTM Operating Software. The Bioconductor and statistical programming language R were used. • The validation of microarrays was performed by RT-qPCR.

Results: The cut-off criteria were based on differences in the gene expression fold change higher than abs. 2 and adjusted p value ≤ 0.05. All differentially genes engaged in specific biological processes were visualized using gene ontology (GO) plot library. Our latest results indicate that ChiPS possess induced DDR mechanisms acquired during differentiation. In ChiPS, the increased expression of genes classified to the

inter alia following GO terms: is “cell cycle arrest”, “cell cycle checkpoint”, “DNA damage response”, “signal transduction in response to DNA damage” and “cellular response to stress” is observed. Moreover, based on the Kyoto Encyclopedia of Genes and Genomes the one of superior pathway regulated during chondrogenic differentiation in vitro is p53. The expression of selected genes involved in DDR mechanisms and particularly in p53 signaling pathway was verified with RT-qPCR analysis. We assume that a noticeable activation of DDR is particularly enhanced during treatment with genotoxic agents like IR.

Conclusions: We found that hiPSCs differentiated toward ChiPS undergo a stress that leads to activation of DDR mechanisms. The differentiated cells are very prone to exposure to genotoxic agents. Thus, they demonstrate extremely high level of members taking part in DNA damage and repair during IR treatment.

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