OC-0445

Patterns of care and outcome analysis of SBRT for liver metastases - a DEGRO database initiative

N. Andratschke[1], H. Alheid[2], M. Allgäuer[3], G. Becker[4], O. Blanck[5], J. Boda-Hegemann[6], T. Brunner[7], S. Combs[8,9], M. Duma[8], S. Gerum[18], M. Guckenberger[1,10], G. Hildebrandt[11], C. Ostheimer[12], C. Panje[1], A. Papachristofilou[13], C. Petersen[14], T. Schneider[15], R. Semrau[16], S. Wachter[17], D. Habermehl[9]

[1]*University Hospital Zürich, Department of Radiation Oncology, Zurich, Switzerland*
[2]*Strahlentherapie Bautzen, Radiation Oncology, Bautzen, Germany*
[3]*Krankenhaus Barmherzige Brüder, Radiation Oncology, Regensburg, Germany*
[4]*RadioChirurgicum CyberKnife Südwest, Radiation Oncology, Göppingen, Germany*
[5]*Universitätsklinikum Schleswig-Holstein, Radiation Oncology, Kiel/Lübeck, Germany*
[6]*University Hospital Mannheim, Radiation Oncology, Mannheim, Germany*
[7]*University Hospital Freiburg, Radiation Oncology, Freiburg, Germany*
[8]*Klinikum rechts der Isar- Technische Universität München, Radiation Oncology, Munich, Germany*
[9]*University Hospital Heidelberg, Radiation Oncology, Heidelberg, Germany*
[10]*University Hospital Würzburg, Radiation Oncology, Würzburg, Germany*
[11]*University Hospital Rostock, Radiation Oncology, Rostock, Germany*
[12]*University Hospital Halle, Radiation Oncology, Halle, Germany*
[13]*University Hospital Basel, Radiation Oncology, Basel, Switzerland*
[14]*University Medical Center Hamburg-Eppendorf, Radiation Oncology, Hamburg, Germany*
[15]*Strahlenzentrum Hamburg, Radiation Oncology, Hamburg, Germany*
[16]*University Hospital of Cologne, Radiation Oncology, Cologne, Germany*
[17]*Klinikum Passau, Radiation Oncology, Passau, Germany*
[18]*University of Munich, Radiation Oncology, Munich, Germany*

Purpose or Objective: The intent of this pooled analysis as part of the German Society for Radiation Oncology (DEGRO) stereotactic body radiotherapy (SBRT) initiative was to analyse the pattern of care of SBRT for liver metastases in Germany and to derive factors influencing local control and overall survival in a large patient cohort.

Material and Methods: From 17 German and Swiss radiotherapy centers, data on all patients treated for liver metastases with SBRT since its introduction in 1997 was collected and entered into a centralised database as an effort of the SBRT task group of the DEGRO. In addition to patient and tumor characteristics, data on immobilization, image guidance and motion management as well as dose prescription and fractionation was gathered. Besides dose response and survival statistics, time trends of the aforementioned variables were investigated.

Results: In total, 442 patients with 586 liver metastases (median 1 lesion/patient; range 1-4) have been collected from 1997 until 2014. Predominant histologies were colorectal cancer (n=213), lung cancer (n=26) and breast cancer (n=57). All centers employed a SBRT-specific setup (including abdominal compression in 41%). Initially, stereotactic coordinates and CT simulation was used for treatment set-up (55%), but eventually replaced by CBCT guidance (28%) or more recently robotic tracking (17%). High variance in fraction (fx) number (median 1 fx; range 1-13) and dose per fraction (median: 18.5 Gy; range 3-37.5 Gy) was observed, although median BED remained consistently high after an initial learning curve. Median follow-up time was 13 months; median overall survival after SBRT was 24 months. 1 and 2 year local control rate of treated lesions was 77% and 64%; local control increased to 83% and 70%, respectively, if maximum isocenter biological equivalent dose (BED) was greater than 120 Gy EQD2Gy versus below that dose.

Conclusion: After a learning curve with regards to total cumulative doses, consistent biologically effective doses were employed, although with a significant variation in number of fraction, single fraction dose and prescription isodose. A clear dose response was observed with high local control after 1 and 2 years with higher BED. Nevertheless, local control is still inferior compared to lung metastases with a similar distribution of histologies. Therefore, further analysis needs to investigate the influence of image guidance and motion management as well as radiation sensitivity on local tumor control.

OC-0446

Extra-cranial SBRT in patients with oligometastatic disease: a dose-escalation study

F. Deodato[1], G. Macchia[1], S. Cilla[2], M. Nuzzo[1], L. Ronchi[3], A. Ianiro[2], R. Autorino[4], G. Mantini[4], R. Frakulli[3], S. Cammelli[3], G. Compagnone[5], A.L. Angelini[5], G. Frezza[6], L. Caravatta[7], A. Farioli[8], V. Valentini[4], A.G. Morganti[3]

[1]*Fondazione di Ricerca e Cura "Giovanni Paolo II"- Catholic University of Sacred Heart, Radiation Oncology Unit, Campobasso, Italy*
[2]*Fondazione di Ricerca e Cura "Giovanni Paolo II"- Catholic University of Sacred Heart, Medical Physics Unit, Campobasso, Italy*
[3]*S. Orsola-Malpighi Hospital- University of Bologna, Radiation Oncology Center- Department of Experimental- Diagnostic and Specialty Medicine – DIMES, Bologna, Italy*
[4]*Policlinico Universitario "A. Gemelli"- Catholic University of Sacred Heart, Radiation Oncology Center, Roma, Italy*
[5]*S. Orsola-Malpighi Hospital- University of Bologna, Department of Medical Physics, Bologna, Italy*
[6]*Bellaria Hospital, Radiotherapy Department, Bologna, Italy*
[7]*P.O. Businco, Radiotherapy Unit- Centro di Radioterapia e Medicina Nucleare, Cagliari, Italy*
[8]*S. Orsola-Malpighi Hospital- University of Bologna, Department of Medical and Surgical Sciences DIMEC, Bologna, Italy*

Purpose or Objective: To define maximum tolerated dose (MTD) of stereotactic treatment (SBRT) performed in different clinical settings.

Material and Methods: This analysis was based on a dose-escalation (Phase I) trial. Patients were enrolled in seven different arms depending on treatment site and previous treatment: 1) intraparenchymal lung tumors; 2) lung tumors near to chest wall or to mediastinum; 3) extra pulmonary tumors; 4) re-irradiation after radiotherapy (< 60 Gy); 5) re-irradiation after radiotherapy (> 60 Gy) or re-irradiation of pelvic and pancreatic tumors; 6) boost after a dose < 50Gy; 7) boost after a dose ≥ 50Gy. SBRT was delivered in 5 fractions. The dose was prescribed at isocenter with a 3D static technique using 4-5 non-coplanar beams or with VMAT technique. PTV was defined as the GTV + 5-15 mm. Considering study arms, the first group of patients received 20 Gy, while other cohorts of patients received doses up to 50 Gy. Grade 3 acute and late toxicities were considered as dose limiting toxicity (DLT). If 2/6 or 4/12 DLT were recorded in one cohort, that dose was considered as MTD.

		1	2	3	4	5	6	7
Level	n° pts	Lung Target	Lung Target with inclusion of mediastinum or chest wall	Extra thoracic target (neck, abdomen, pelvis)	Retreatment		SBRT-boost	SBRT-boost
					Previous Dose ≤ 60Gy (pancreas and pelvis); Previous Dose>60Gy)	Previous Dose≤60Gy	(Post ERT 45-50 Gy)	(Post ERT >50Gy)
A	6 §	25 Gy	25 Gy	25 Gy	20 Gy	25 Gy	25 Gy	20 Gy
B	6 §	37.5 Gy	30 Gy	30 Gy	25 Gy	30 Gy	30 Gy	25 Gy
C	6 §	45 Gy	35 Gy	35 Gy	30 Gy*	35 Gy	35 Gy*	30 Gy
D	6 §	50 Gy	40 Gy	40 Gy	35 Gy	40 Gy		
E	6 §		45 Gy	45 Gy	40 Gy	45 Gy		
F	6 §		50 Gy	50 Gy	45 Gy	50 Gy		

On-going dose level is underlined; *: 1 DLT; ERT: external beam radiotherapy

Results: 213 patients were enrolled (M/F: 125/88), median age was 69 years (35-90) and 281 lesions were treated (102 primary tumors or local recurrences, 96 nodal and 83 distant metastases); they were mainly lung cancer (31%), gynaecologic cancer (24%), gastrointestinal neoplasms (22%),

urologic tumour (12%), in the following sites: 150 in neck or chest, 70 in abdomen and 61 in pelvis. With a median follow-up of 17 months (3-131) the overall response rate was 82% (Complete Response: 58%; Partial Response: 24%), with only 3% of patients developing disease progression. DLT was recorded only in two patients, both treated with 50 Gy. Two-year and 4-year local control were 71% and 62%, respectively. Two-year and 4-year metastases free survival were 46% and 39%, respectively.

Conclusion: SBRT in five fractions up to a dose of 50 Gy is well tolerated in different clinical settings.

OC-0447

Stereotactic Body Radiotherapy (SBRT) in oligometastatic prostate cancer patients

C.L. Chaw[1], D. Henderson[1], V. Khoo[1], A. Tree[1], R. Eeles[1], N. Van As[1]

[1]*Institute of Cancer Research, Royal Marsden Hospital-Academic Uro-Oncology Department, London, United Kingdom*

Purpose or Objective: Oligometastatic prostate cancer is a state of limited metastatic disease≤(3 sites) that may be amenable to aggressive local therapy to achieve long term survival. The use of SBRT in this clinical setting has been reported to confer local control rate in excess of 90%, and encouraging progression free survival rate with no significant treatment –related toxicities1-4. One of the goals with this approach is to delay initiation of palliative systemic treatment, which can potentially impact negatively on quality of life. This study evaluated the outcomes of SBRT in our cohort.

Material and Methods: Forty five patients diagnosed with oligometastatic prostate cancer (defined as a rising PSA and positive CT/PET choline scan) after definitive local therapy were treated with 1-2 courses of SBRT between July 2011 and July 2015. Over 90% of metastases were situated in lymph nodes or bone. Median dose was 30 Gy in 3 fractions, prescribed to the highest isodose covering the PTV. Retrospective data collection and analysis were performed for these patients. Kaplan-Meier was utilised to estimate progression free survival and overall survival and time to initiation of systemic treatment. Nineteen of the 35 patients with castration sensitive disease were treated with SBRT alone for their oligometastatic disease, 16 patients received SBRT and Androgen Deprivation Therapy (ADT) with median duration of 5 months. 10 patients who were castration resistant at the diagnosis of oligometastases were treated with SBRT with ongoing systemic treatment.

Results: The median follow-up was 29 months (range 6-60 months). Local control rate of lesions following SBRT treatment was 90%, overall progression free survival (PFS) was 38%, overall survival (OS) of 89% at 29 months. A reduction of pre-treatment PSA value of 48% and 75%, respectively was seen in castration sensitive patients who received SBRT alone and SBRT with ADT, and a 25% PSA reduction in castration resistant patients treated with SBRT and ADT. Median time to clinical progression was longer in castration sensitive patients treated with SBRT and ADT compared to SBRT alone (13 months vs 25 months). The median ADT-free survival for castration sensitive patients was 16 months. Median time to initiation of next line therapy in castration resistant patients following SBRT treatment was 6 months. No grade 3 or 4 treatment related toxicities reported.

Conclusion: SBRT can provide a substantial delay to the next initiation of systemic therapy in castration sensitive patients whilst for castration resistant patients, there is a modest prolongation before initiation of subsequent therapy. Phase III data is lacking but will shortly be addressed in the SABR-COMET and CORE trials.

OC-0448

Give me five: extreme hypofractionated IG-IMRT for organ confined prostate cancer

B.A. Jereczek-Fossa[1,2], D. Ciardo[1], S.P. Colangione[3], C. Fodor[1], D. Zerini[1], A. Cecconi[1], A. Surgo[1], M.A. Gerardi[1], M. Muto[1], G. Timon[1], S. Comi[4], F. Pansini[4], A. Bazani[4], D. Maestri[4], M. Garioni[4], V. Scroffi[1], F. Cattani[4], R. Cambria[4], O. De Cobelli[2,5], R. Orecchia[1,2]

[1]*European Institute of Oncology, Department of Radiation Oncology, Milan, Italy*

[2]*University of Milan, Department of Oncology and Hemato-oncology, Milan, Italy*

[3]*European Institute of Oncology, Department of Radiation Oncology affiliation at the time of the study, Milan, Italy*

[4]*European Institute of Oncology, Unit of Medical Physics, Milan, Italy*

[5]*European Institute of Oncology, Department of Urology, Milan, Italy*

Purpose or Objective: Radiobiological findings suggest an improvement in the therapeutic ratio for prostate cancer (PCa) treated with hypofractionation, compared with conventional fractionation. On this basis, in 2012 we activated a prospective study on extreme hypofractionated image-guided intensity modulated radiation therapy (IG-IMRT) in organ-confined PCa. The aim of this study is the assessment of the feasibility of the proposed protocol – Give me five, in terms of acute and late toxicity and biochemical efficacy.

Material and Methods: The study was performed within the Institutional Ethics Committee notification regarding hypofractionated IGRT for PCa. Inclusion criteria were: low to intermediate-risk (according to NCCN risk categories) histologically confirmed PCa; personalized indication for high-risk patients; prostate volume <100cm3; N0 and cM0; age >18 years; specific informed consent. In 10% of patients, multiparametric MRI was used for an improved definition of the patient anatomy, in addition to CT imaging. The nominal prescription dose was 32.5 or 35 Gy scheduled in 5 fractions on alternate days (therefore the name of protocol, “Give me five”), namely 6.5-7 Gy/fraction respectively, corresponding to a normalized total dose delivered at 2-Gy/fraction of 74.3 or 85 Gy, respectively, estimating an α/ß ratio of 1.5 Gy. Dose delivery was performed with VERO®-BrainLab-Mitsubishi or RapidArc®-Varian. No fiducial markers were implanted and set-up verification was performed daily by means of CBCT imaging. Toxicity was evaluated according RTOG/EORTC scales. The study was founded by Associazione Italiana per la Ricerca sul Cancro - AIRC, grant no. 13218.

Results: Between April 2012 and May 2015, 166 patients were eligible. All patients completed the treatment. Median follow-up was 12.5 months (range 6-32.7 months). Fifty-eitght, 83, 24 and 1 patients out of 166 were at low, intermediate, high and unknown risk, respectively. Median age was 74.3 years, median Gleason score was 6. Considering acute toxicity, 89.8%, 7.8%, 2.4% of patients had gastro-intestinal G0, G1, G2 toxicity, respectively; 54.2%, 35.5%, 9.6%, 0.6% of patients had genito-urinary G0, G1, G2, G4 toxicity, respectively. Late toxicity and outcome were assessed in 129 patients (6 months minimum follow-up). Considering late toxicity, 3.1% and 0.8% of patients had gastro-intestinal G1 and G2 toxicity; 12.4%, 6.2% and 0.8% of patients had genito-urinary G1, G2, G3 toxicity, respectively. Clinical and biochemical progression prostate disease was observed in 2/129 of patients; currently, no evidence of prostate disease in 127/129 patients.