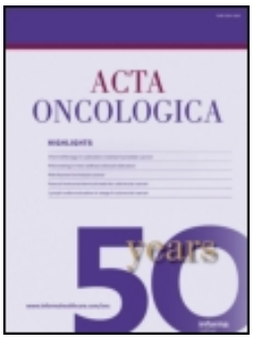

Acta Oncologica

ISSN: 0284-186X (Print) 1651-226X (Online) Journal homepage: informahealthcare.com/journals/ionc20

Biology-guided adaptive radiotherapy (BiGART) – more than a vision?

Cai Grau, Morten Høyer, Markus Alber, Jens Overgaard, Jacob Christian Lindegaard & Ludvig Paul Muren

To cite this article: Cai Grau, Morten Høyer, Markus Alber, Jens Overgaard, Jacob Christian Lindegaard & Ludvig Paul Muren (2013) Biology-guided adaptive radiotherapy (BiGART) – more than a vision?, Acta Oncologica, 52:7, 1243-1247, DOI: 10.3109/0284186X.2013.829245

To link to this article: https://doi.org/10.3109/0284186X.2013.829245

Published online: 29 Aug 2013.

Acta Oncologica, 2013; 52: 1243–1247

informa
healthcare

EDITORIAL

Biology-guided adaptive radiotherapy (BiGART) – more than a vision?

CAI GRAU[1], MORTEN HØYER[1], MARKUS ALBER[2], JENS OVERGAARD[3], JACOB CHRISTIAN LINDEGAARD[1] & LUDVIG PAUL MUREN[2]

[1]*Department of Oncology, Aarhus University Hospital, Aarhus, Denmark,* [2]*Department of Medical Physics, Aarhus University Hospital, Aarhus, Denmark and* [3]*Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark*

Acta Oncologica can this year celebrate its 50 years jubilee as the leading Scandinavian journal in oncology. As a part of this celebration the 11th Acta Oncologica Symposium was held in Aarhus, Denmark, on June 11–13, 2013. The symposium was dedicated to aspects of Biology-Guided Adaptive Radiotherapy (BiGART). The 172 participants of the meeting included physicians, physicists, radiobiologists and other scientists with an active interest in this specific area. The format included invited presentations, proffered papers and discussion rounds. More than 100 abstracts were submitted to the conference.

Acta Oncologica has sponsored scientific symposia since 1989. The aim of this activity has been to focus on oncological issues of emerging interest, preferably with a multi-disciplinary or multi-professional approach. The current series of Acta Oncologica meetings with focus on radiotherapy (RT) have encompassed stereotactic body RT (SBRT) [1], image-guided RT (IGRT) [2,3], adaptive RT (BiGART) [4] and particle RT [5]. Other topics have over the years included sentinel lymph node biopsy in breast cancer, prostate cancer, normal tissue morbidity, breast cancer, and rehabilitation.

The goal of BiGART is adaptation of RT in time and space based on biological and anatomical features, maximizing the therapeutic ratio for each individual patient. Key topics for the BiGART2013 conference included:

1. Biology of tumors and normal tissue to guide patient selection, target volumes and dose prescription in RT;
2. Functional imaging of tumors and normal tissues with functional imaging techniques based on magnetic resonance imaging (MRI) and positron emission tomography (PET), and the use of such images for dose painting and normal tissue avoidance in RT;
3. Treatment planning and delivery challenges in adaptation of radiotherapy based on changes in tumor and normal tissue biology, anatomy and/or function;
4. Clinical outcome of adaptive RT.

The current issue of Acta Oncologica contains a collection of peer-reviewed papers from the conference, and additional papers will be published in upcoming issues of the journal.

The most relevant biological features to explore and exploit within BiGART include hypoxia, proliferation, cell density and intrinsic radio-resistance. It is evident that the biological characterization of tumors has moved towards genetic profiling, and current radio-genomic research aims at establishing the full genetic signature associated with radiation response. Several studies suggest that it is possible to use gene profiles, e.g. to predict the benefit of post-operative RT in breast cancer, to identify tumors with, e.g. hypoxia in esophageal or prostate cancer [6,7] or to predict the benefit from hypoxic cell sensitization [8]. Such genetic signature will be of value in clinical decision-making, but more studies are needed since treatment adaptation requires more detailed information than currently available.

Functional imaging modalities linked to BiGART include dynamic computed tomography (CT) with

Correspondence: C. Grau, Department of Oncology, Aarhus University Hospital, 44 Nørrebrogade, 8000 Aarhus C, Denmark. Tel: +45 78462553. Fax: +45 78462530. E-mail: caigrau@dadlnet.dk

(Received 18 July 2013; accepted 22 July 2013)

ISSN 0284-186X print/ISSN 1651-226X online
DOI: 10.3109/0284186X.2013.829245

contrast-enhancement, diffusion-weighted MRI, dynamic contrast-enhanced MRI, and PET with various tracers [9–13]. A number of studies have shown that functional imaging information on, e.g. hypoxia is prognostic for the outcome of RT. The main challenges in imaging for BiGART are resolution and dynamics. The radiobiological relevant hypoxia is likely to be distributed more heterogeneous on a microscopic level than what current imaging can pick up. If so, our current imaging and delivery techniques are probably too coarse to fully address the biological distribution. A promising novel technology that was discussed at the symposium is hyperpolarized MR which offers a considerably improved signal to noise ratio [14]. The dynamics of the biological features of interest determines how frequent the patient needs to be subjected to repetitive imaging during radiotherapy, and also this needs further studies.

The application of functional imaging on a larger clinical scale meets with a number of problems and also opens up new questions. The issues range from the mere technical, like deformable image registration for the combination of multiple images, to the very basic understanding of multi-modality functional imaging and inter-patient heterogeneity [15–17]. The development of solutions for deformable image registration is clearly moving towards specialization with respect to body site and image modalities to be combined, in order to achieve the accuracy required for treatment planning. The complementary approach is to extract more information from a single modality, or use it for multiple purposes. Due to its great versatility, MRI can play a much more dominant role in the future, and maybe also replace the obligatory CT scan for dose computation. Great efforts are being directed at the development of new imaging sequences and computer algorithms to produce an electron density map from MR images. Simultaneously, it becomes clear that the interpretation of both MR and PET images requires the support of models, algorithms and knowledge databases [18,19]. In the presence, the handling of functional images is still associated with large uncertainties and ambiguities in interpretation, which require a careful and cautious use of such means while more evidence needs to be collected.

The underlying rationale for the exploration of both biological endpoints and functional imaging parameters in adaptive RT settings is that they carry information connected to the dose-response of both tumors as well as normal tissues. Such information should therefore have considerable potential to improve the current (population-based) RT dose-response relationships – often referred to as tumor control probability (TCP) and normal tissue complication probability (NTCP) models. So far, imaging parameters associated with tumor cell density and oxygenation status has been explored in the TCP models, derived mostly from functional MRI and/or PET [18,20]. Imaging-based functional measures are being explored also for several key normal tissues in treatment of major tumor sites [12]. A number of studies has explored CT-based imaging techniques in the lung, where local density changes have been associated with local function [12,21–23], including also a study presented at this meeting [23]. However, there are a number of confounding factors that needs to be accounted for in such studies [24,25], including also challenges related to properly account for any 'physical' uncertainties influencing geometry and ultimately dose [26–28].

Functional imaging can influence treatment planning on many levels, from target volume delineation to image intensity-guided dose escalation [20,29,30]. The rationale for the more sophisticated usages is generally still very weak and associated with many uncertainties. For example, the achievable levels of image sensitivity place very strict limits on the possibility for dose de-escalation. Dose escalation, however, can give rise to complications with a higher frequency and severity. The first clinical trials show encouraging results and also often prove that focused dose escalation can be performed with low toxicity profiles if adequate care is invested into imaging and image interpretation. The primary sites for this seem to be intermediate- and high-risk prostate cancer, based on multi-modal MRI, and head-and-neck cancer, based on FDG or hypoxia PET, with dose escalation of up to 30% and without de-escalation. For other sites like uterine cervix, evidence is mounting that radiation insensitive tumor cores exist in a subpopulation of patients, which might be the next target for dose painting.

Adaptive RT also calls for advanced treatment delivery approaches. So far, photon-based intensity-modulated RT techniques have shown large promise in terms of dose shaping abilities [19,30,31]. Geometrical uncertainties are a challenge for all RT applications. Image-guided treatment strategies are therefore currently state of the art in RT, with tumor tracking showing large potential to remedy the residual uncertainties so far unaccounted for [32,33]; tracking has recently been studied together with dose painting plans [34]. However, the increased complexity in spatial dose prescription patterns might indeed call for RT with other modalities, first and foremost with protons, possibly also heavier ions. Particle beam therapy is in general receiving considerable attention currently, exemplified both by another recent Acta Oncologica symposium [17,35–38] as well as in another dedicated issue of

the present journal [5,39]. In the current issue, Combs, Debus and co-workers at the Heidelberg Ion Therapy Centre present promising results for brain and skull base tumors and provide a review of the currently available evidence for heavy ions [40,41]. Adaptive strategies may be even more important in particle radiotherapy because of the poor robustness of particles [39]. Much more attention has to been given to this research field.

The clinical aspects of anatomy-based adaptive radiotherapy have been studied in a number of clinical studies in recent years [42–50]. A number of presentations at this meeting demonstrated that there is a potential for adaptation to anatomical changes during the course of radiotherapy based on the technology that we have available today. Previous studies on cone-beam CT scans in RT for lung cancer have revealed that changes in density of the lung and atelectasis that resolves may influence the dose distribution in the liver and lung [51]. A study presented at the symposium showed that anatomical changes frequently occurred during the course of radiotherapy, and a large proportion of the patients would benefit from re-planning [52]. Another study elegantly demonstrated that changes detected with portal dosimetry during the course of radiotherapy might reveal a resolved atelectasis and a need for treatment re-planning [53].

Daily adaptive online re-planning/optimization is an ambitious strategy that involves a chain of tools, e.g. auto-segmentation, dose reconstruction/accumulation and plan evaluation that are not readily available today. A number of technical obstacles in this chain must be overcome before this concept is feasible and ready for clinical use. However, adaptation by a daily plan selection strategy can be realised with the technology that we have today [54–56]. Preliminary clinical results were presented of a study on RT for bladder cancer where one of three plans was selected based on the size and shape of the bladder on the cone-beam CT scan [54,57], and where RT technologists selected the plans on a daily basis. It was shown that with a proper training program, this was feasible within a time frame of approximately two minutes.

In brachytherapy there are convincing data showing beneficial effects by image-guided and adaptive strategies [58–60], now also with results from the retro-EMBRACE database with almost 800 cervical cancer patients, as presented at the meeting. At three years after therapy, more than 90% of the tumors were locally controlled and even the most advanced tumors were controlled in more than 80% of the cases. Similar favorable results were demonstrated in a single institution retrospective case control study of image-guided adaptive brachytherapy of cervical cancer [61].

Early assessment of treatment response is a key player in the adaptive strategies, but currently there is only limited clinical experience with this strategy. Functional imaging of the tumor may reveal metabolic changes predicting the long-term response of the therapy. This may be used for selection of patients with radio-resistant tumors for more aggressive therapy [62,63]. In cervix and head-and-neck cancer, FDG-PET response might steer the aggressiveness of chemo-radiation and in rectal and esophageal cancer the response may potentially guide decision making about organ preservation [62].

In conclusion, the current issue of Acta Oncologica with papers from the BiGART2013 conference shows that there is still some way before individualized adaptive radiotherapy is a standard clinical approach. However, the significant advances especially within functional molecular imaging of tumors support that BiGART will mature to become more than just a vision for the future in radiotherapy.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

[1] Grau C, Hoyer M, Lindegaard J, Overgaard J. The emerging evidence for stereotactic body radiotherapy. Acta Oncol 2006;45:771–4.

[2] Grau C, Muren LP, Hoyer M, Lindegaard J, Overgaard J. Image-guided adaptive radiotherapy – integration of biology and technology to improve clinical outcome. Acta Oncol 2008;47:1182–5.

[3] Muren LP, Petersen JB, Hansen J, Hafslund R. Medical physics in the Nordic countries: The past, the present and the future. Acta Oncol 2009;48:165–8.

[4] Grau C, Olsen DR, Overgaard J, Hoyer M, Lindegaard JC, Muren LP. Biology-guided adaptive radiation therapy – presence or future? Acta Oncol 2010;49:884–7.

[5] Muren LP, Rossi C, Hug E, Lee A, Glimelius B. Establishing and expanding the indications for proton and particle therapy. Acta Oncol 2013;52:459–62.

[6] Winther M. Hypoxia-regulated gene expression and prognosis in loco-regional gastroesophageal cancer. Acta Oncol 2013;(this issue).

[7] Ishkanian AS, Zafarana G, Thoms J, Bristow RG. Array CGH as a potential predictor of radiocurability in intermediate risk prostate cancer. Acta Oncol 2010;49:888–94.

[8] Toustrup K, Sorensen BS, Lassen P, Wiuf C, Alsner J, Overgaard J, et al. Gene expression classifier predicts for hypoxic modification of radiotherapy with nimorazole in squamous cell carcinomas of the head and neck. Radiother Oncol 2012;102:122–9.

[9] Busk M. PET imaging of tumor hypoxia using 18F labeled pimonidazole. Acta Oncol 2013;(this issue).

[10] Malinen E. Functional imaging to monitor vascular and metabolic response in canine head and neck tumors during fractionated radiotherapy. Acta Oncol 2013;(this issue).

[11] Nielsen T. Ultra-high field ^{1}H magnetic resonance imaging approaches for acute hypoxia. Acta Oncol 2013;(this issue).

[12] Partridge M, Yamamoto T, Grau C, Hoyer M, Muren LP. Imaging of normal lung, liver and parotid gland function for radiotherapy. Acta Oncol 2010;49:997–1011.
[13] Mortensen LS, Johansen J, Kallehauge J, Primdahl H, Busk M, Lassen P, et al. FAZA PET/CT hypoxia imaging in patients with squamous cell carcinoma of the head and neck treated with radiotherapy: Results from the DAHANCA 24 trial. Radiother Oncol 2012;105:14–20.
[14] Ardenkjaer-Larsen JH. Magnetic resonance imaging of tumor oxygenation and metabolic profile. Acta Oncol 2013;(this issue).
[15] Thor M, Petersen JB, Bentzen L, Hoyer M, Muren LP. Deformable image registration for contour propagation from CT to cone-beam CT scans in radiotherapy of prostate cancer. Acta Oncol 2011;50:918–25.
[16] Malinen E, Rodal J, Knudtsen IS, Sovik A, Skogmo HK. Spatiotemporal analysis of tumor uptake patterns in dynamic (18)FDG-PET and dynamic contrast enhanced CT. Acta Oncol 2011;50:873–82.
[17] Munck Af Rosenschold P, Engelholm S, Ohlhues L, Law I, Vogelius I, Engelholm SA. Photon and proton therapy planning comparison for malignant glioma based on CT, FDG-PET, DTI-MRI and fiber tracking. Acta Oncol 2011;50:777–83.
[18] Andersen EKF, Kristensen GB, Lyng HD, Malinen E. Pharmacokinetic analysis and k-means clustering of DCEMR images for radiotherapy outcome prediction of advanced cervical cancers. Acta Oncol 2011;50:859–65.
[19] Maggio A, Fiorino C, Mangili P, Cozzarini C, de Cobelli F, Cattaneo GM, et al. Feasibility of safe ultra-high (EQD(2)>100 Gy) dose escalation on dominant intra-prostatic lesions (DILs) by helical tomotherapy. Acta Oncol 2011;50: 25–34.
[20] Toma-Dasu I, Uhrdin J, Antonovic L, Dasu A, Nuyts S, Dirix P, et al. Dose prescription and treatment planning based on FMISO-PET hypoxia. Acta Oncol 2012;51:222–30.
[21] Nyeng TB, Kallehauge JF, Hoyer M, Petersen JB, Poulsen PR, Muren LP. Clinical validation of a 4D-CT based method for lung ventilation measurement in phantoms and patients. Acta Oncol 2011;50:897–907.
[22] Palma DA, de Koste JRV, Verbakel W, Senan S. A new approach to quantifying lung damage after stereotactic body radiation therapy. Acta Oncol 2011;50:509–17.
[23] De Ruysscher DSH, Defraene G, Kerns SL, Christiaens M, De Ruyck K. Quantification of radiation-induced lung damage with CT scans: The possible benefit for radiogenomics Acta Oncol 2013;(this issue).
[24] Huang EX, Hope AJ, Lindsay PE, Trovo M, El Naqa I, Deasy JO, et al. Heart irradiation as a risk factor for radiation pneumonitis. Acta Oncol 2011;50:51–60.
[25] Vogelius IR, Westerly DC, Aznar MC, Cannon GM, Korreman SS, Mackie TR, et al. Estimated radiation pneumonitis risk after photon versus proton therapy alone or combined with chemotherapy for lung cancer. Acta Oncol 2011;50:772–6.
[26] Knudtsen IS, Rodal J, Brustugun OT, Helland A, Skretting A, Malinen E. Dynamic respiratory gated (18)FDG-PET of lung tumors – a feasibility study. Acta Oncol 2011;50: 889–96.
[27] Andersen ES, Muren LP, Sorensen TS, Noe KO, Thor M, Petersen JB, et al. Bladder dose accumulation based on a biomechanical deformable image registration algorithm in volumetric modulated arc therapy for prostate cancer. Phys Med Biol 2012;57:7089–100.
[28] Thor M, Bentzen L, Hysing LB, Ekanger C, Helle SI, Karlsdottir A, et al. Prediction of rectum and bladder morbidity following radiotherapy of prostate cancer based on motion-inclusive dose distributions. Radiother Oncol 2013; 107:147–52.
[29] Fellin F, Azzeroni R, Maggio A, Lorentini S, Cozzarini C, Di Muzio N, et al. Helical tomotherapy and intensity modulated proton therapy in the treatment of dominant intraprostatic lesion: A treatment planning comparison. Radiother Oncol 2013;107:207–12.
[30] Moller DS, Khalil AA, Knap MM, Muren LP, Hoffmann L. A planning study of radiotherapy dose escalation of PET-active tumour volumes in non-small cell lung cancer patients. Acta Oncol 2011;50:883–8.
[31] Maggiulli E, Fiorino C, Passoni P, Broggi S, Gianolini S, Salvetti C, et al. Characterisation of rectal motion during neo-adjuvant radiochemotherapy for rectal cancer with image-guided tomotherapy: Implications for adaptive dose escalation strategies. Acta Oncol 2012;51:318–24.
[32] Fledelius W, Keall PJ, Cho BC, Yang XH, Morf D, Scheib S, et al. Tracking latency in image-based dynamic MLC tracking with direct image access. Acta Oncol 2011;50:952–9.
[33] Ravkilde T, Keall PJ, Hojbjerre K, Fledelius W, Worm E, Poulsen PR. Geometric accuracy of dynamic MLC tracking with an implantable wired electromagnetic transponder. Acta Oncol 2011;50:944–51.
[34] Skyt PS, Petersen JBB, Yates ES, Poulsen PR, Ravkilde TL, Balling P, Muren LP, et al. Dosimetric verification 1 of complex radiotherapy with a 3D optically based dosimetry system: Dose painting and target tracking. Acta Oncol 2013;(this issue).
[35] Nystrom H, Blomqvist E, Hoyer M, Montelius A, Muren LP, Nilsson P, et al. Particle therapy – a next logical step in the improvement of radiotherapy. Acta Oncol 2011;50:741–4.
[36] Schippers JM, Lomax AJ. Emerging technologies in proton therapy. Acta Oncol 2011;50:838–50.
[37] Liao Z, Lin SH, Cox JD. Status of particle therapy for lung cancer. Acta Oncol 2011;50:745–56.
[38] Mendenhall NP, Malyapa RS, Su Z, Yeung D, Mendenhall WM, Li ZF. Proton therapy for head and neck cancer: Rationale, potential indications, practical considerations, and current clinical evidence. Acta Oncol 2011; 50:763–71.
[39] Thornqvist S, Muren LP, Bentzen L, Hysing LB, Hoyer M, Grau C, et al. Degradation of target coverage due to interfraction motion during intensity-modulated proton therapy of prostate and elective targets. Acta Oncol 2013;52:521–7.
[40] Combs S. Proton and carbon ion radiotherapy for primary brain tumors and tumors of the skull base. Acta Oncol 2013;(this issue).
[41] Combs S. Treatment with heavy charged particles: Systematic review of results of clinical data and current clinical (comparative) trials. Acta Oncol 2013;(this issue).
[42] Schwartz DL, Garden AS, Shah SJ, Chronowski G, Sejpal S, Rosenthal DI, et al. Adaptive radiotherapy for head and neck cancer – Dosimetric results from a prospective clinical trial. Radiother Oncol 2013;106:80–4.
[43] Meijer GJ, van der Toorn PP, Bal M, Schuring D, Weterings J, de Wildt M. High precision bladder cancer irradiation by integrating a library planning procedure of 6 prospectively generated SIB IMRT plans with image guidance using lipiodol markers. Radiother Oncol 2012;105:174–9.
[44] Nijkamp J, Marijnen C, van Herk M, van Triest B, Sonke JJ. Adaptive radiotherapy for long course neo-adjuvant treatment of rectal cancer. Radiother Oncol 2012;103: 353–9.
[45] Madani I, Duprez F, Boterberg T, Van de Wiele C, Bonte K, Deron P, et al. Maximum tolerated dose in a phase I trial on adaptive dose painting by numbers for head and neck cancer. Radiother Oncol 2011;101:351–5.

[46] Castadot P, Geets X, Lee JA, Gregoire V. Adaptive functional image-guided IMRT in pharyngo-laryngeal squamous cell carcinoma: Is the gain in dose distribution worth the effort? Radiother Oncol 2011;101:343–50.
[47] Simone CB, 2nd, Ly D, Dan TD, Ondos J, Ning H, Belard A, et al. Comparison of intensity-modulated radiotherapy, adaptive radiotherapy, proton radiotherapy, and adaptive proton radiotherapy for treatment of locally advanced head and neck cancer. Radiother Oncol 2011;101:376–82.
[48] Tuomikoski L, Collan J, Keyrilainen J, Visapaa H, Saarilahti K, Tenhunen M. Adaptive radiotherapy in muscle invasive urinary bladder cancer – An effective method to reduce the irradiated bowel volume. Radiother Oncol 2011;99:61–6.
[49] Murthy V, Master Z, Adurkar P, Mallick I, Mahantshetty U, Bakshi G, et al. 'Plan of the day' adaptive radiotherapy for bladder cancer using helical tomotherapy. Radiother Oncol 2011;99:55–60.
[50] Elstrom UV, Wysocka BA, Muren LP, Petersen JB, Grau C. Daily kV cone-beam CT and deformable image registration as a method for studying dosimetric consequences of anatomic changes in adaptive IMRT of head and neck cancer. Acta Oncol 2010;49:1101–8.
[51] Bertelsen A, Schytte T, Bentzen SM, Hansen O, Nielsen M, Brink C. Radiation dose response of normal lung assessed by cone beam CT – A potential tool for biologically adaptive radiation therapy. Radiother Oncol 2011;100:351–5.
[52] Lykkegaard Schmidt M. Dosimetric impact of respiratory motion, interfraction baseline shifts, and anatomical changes in radiotherapy of non-small cell lung cancer. Acta Oncol 2013;(this issue).
[53] Verhaegen F. First clinical results of adaptive radiotherapy based on 3D portal dosimetry for lung cancer patients with atelectasis treated with volumetric modulated arc therapy (VMAT). Acta Oncol 2013;(this issue).
[54] Vestergaard A, Sondergaard J, Petersen JB, Hoyer M, Muren LP. A comparison of three different adaptive strategies in image-guided radiotherapy of bladder cancer. Acta Oncol 2010;49:1069–76.
[55] Hoogeman M. A margin-of-the-day online-adaptive IMRT strategy for cervical cancer provides superior treatment accuracy compared to clinically recommended margins: A dosimetric evaluation. Acta Oncol 2013;(this issue).
[56] Tuomikoski L. Implementation of adaptive radiation therapy for urinary bladder carcinoma: Imaging, planning and image guidance. Acta Oncol 2013;(this issue).
[57] Wright P, Redpath AT, Hoyer M, Muren LP. A method to individualize adaptive planning target volumes for deformable targets. Phys Med Biol 2009;54:7121–33.
[58] Potter R, Georg P, Dimopoulos JCA, Grimm M, Berger D, Nesvacil N, et al. Clinical outcome of protocol based image (MRI) guided adaptive brachytherapy combined with 3D conformal radiotherapy with or without chemotherapy in patients with locally advanced cervical cancer. Radiother Oncol 2011;100:116–23.
[59] Tanderup K, Georg D, Potter R, Kirisits C, Grau C, Lindegaard JC. Adaptive management of cervical cancer radiotherapy. Semin Radiat Oncol 2010;20:121–9.
[60] Dimopoulos JCA, Petrow P, Tanderup K, Petric P, Berger D, Kirisits C, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (IV): Basic principles and parameters for MR imaging within the frame of image based adaptive cervix cancer brachytherapy. Radiother Oncol 2012;103:113–22.
[61] Lindegaard J. MRI-guided adaptive radiotherapy in locally advanced cervical cancer from a Nordic perspective. Acta Oncol 2013;(this issue).
[62] Hoeben B. Molecular PET imaging for biology-guided adaptive radiotherapy of head and neck cancer. Acta Oncol 2013;(this issue).
[63] Carvalho S. Prognostic value of metabolic metrics extracted from baseline PET images in NSCLC. Acta Oncol 2013;(this issue).

Participants at BIGART, Biology-Guided Adaptive Radiotherapy, 11th Acta Oncologica Symposium, Aarhus, June 11–13, 2013