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References

- [1] The international agency for research on cancer. *www.globocan.iarc.fr*. January 2016.
- [2] The Netherlands comprehensive cancer organisation. *www.cijfersoverkanker.nl*. January 2016.
- [3] FIGO Committee on Gynecologic Oncology. FIGO staging for carcinoma of the vulva, cervix, and corpus uteri. *Int. J. Gynecol. Obstet.* 2014;125:97–98.
- [4] Greco A, Mason P, Leung AWL, *et al.* Staging of carcinoma of the uterine cervix: MRI-surgical correlation. *Clin. Radiol.* 1989;40:401–405.
- [5] Burghardt E, Hofmann HMH, Ebner F, *et al.* Magnetic resonance imaging in cervical cancer: A basis for objective classification. *Gynecol. Oncol.* 1989;33:61–67.
- [6] de Boer P, Adam JA, Buist MR, *et al.* Role of MRI in detecting involvement of the uterine internal os in uterine cervical cancer: systematic review of diagnostic test accuracy. *Eur. J. Radiol.* 2013;82:e422–e428.
- [7] Bipat S, van den Berg RA, van der Velden J, *et al.* The role of magnetic resonance imaging in determining the proximal extension of early stage cervical cancer to the internal os. *Eur. J. Radiol.* 2011;78:60–64.
- [8] Bipat S, Glas AS, van der Velden J, *et al.* Computed tomography and magnetic resonance imaging in staging of uterine cervical carcinoma: a systematic review. *Gynecol. Oncol.* 2003;91:59–66.
- [9] Kaidar-Person O, Bortnyak-Abdah R, Amit A, *et al.* The role of imaging in the management of non-metastatic cervical cancer. *Med. Oncol.* 2012;29:3389–3393.
- [10] Gaffney DK, Erickson-Wittmann BA, Jhingran A, *et al.* ACR appropriateness criteria on advanced cervical cancer expert panel on radiation oncology-gynecology. *Int. J. Radiat. Oncol. Biol. Phys.* 2011;81:609–614.
- [11] Singh AK, Grigsby PW, Dehdashti F, *et al.* FDG-PET lymph node staging and survival of patients with FIGO stage IIIB cervical carcinoma. *Int. J. Radiat. Oncol. Biol. Phys.* 2003;56:489–493.
- [12] Gien LT, Covens A. Fertility-sparing options for early stage cervical cancer. *Gynecol. Oncol.* 2010;117:350–357.
- [13] Henderson MA, Burmeister BH, Ainslie J, *et al.* Adjuvant lymph-node field radiotherapy versus observation only in patients with melanoma at high risk of further lymph-node field relapse after lymphadenectomy (ANZMTG 01.02/TROG 02.01): 6-year follow-up of a phase 3, randomised controlled trial. *Lancet Oncol.* 2015;16:1049–1060.
- [14] Rose PG, Bundy BN, Watkins EB, *et al.* Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N. Engl. J. Med.* 1999;340:1144–1153.
- [15] Peters WA, Liu PY, Barrett RJ, *et al.* Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. *J. Clin. Oncol.* 2000;18:1606–1613.
- [16] Whitney CW, Sause W, Bundy BN, *et al.* Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. *J. Clin. Oncol.* 1999;17:1339–1348.
- [17] van der Zee J, González González D, van Rhoon GC, *et al.* Comparison of radiotherapy alone with radiotherapy plus hyperthermia in locally advanced pelvic tumours: a prospective, randomised, multicentre trial. *Lancet.* 2000;355:1119–1125.
- [18] Franckena M, Stalpers LJA, Koper PCM, *et al.* Long-term improvement in treatment outcome after radiotherapy and hyperthermia in locoregionally advanced cervix cancer: an update of the Dutch Deep Hyperthermia Trial. *Int. J. Radiat. Oncol. Biol. Phys.* 2008;70:1176–1182.
- [19] Lutgens L, van der Zee J, Pijls-Johannesma M, *et al.* Combined use of hyperthermia and radiation therapy for treating locally advanced cervical carcinoma. *Cochrane Libr. Syst. Rev.* 2010;1:CD006377.
- [20] Al-Mansour Z, Verschraegen C. Locally advanced cervical cancer: what is the standard of care? *Curr. Opin. Oncol.* 2010;22:503–512.
- [21] Hellebust TP, Kirisits C, Berger D, *et al.* Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group: Considerations and pitfalls in commissioning and applicator reconstruction in 3D image-based treatment planning of cervix cancer brachytherapy. *Radiother. Oncol.* 2010;96:153–160.

- [22] Wang X, Liu R, Ma B, *et al.* High dose rate versus low dose rate intracavity brachytherapy for locally advanced uterine cervix cancer. *Cochrane Database Syst. Rev.* 2010;7:CD007563.
- [23] Rath GK, Sharma DN, Julka PK, *et al.* Pulsed-dose-rate intracavitary brachytherapy for cervical carcinoma: the AIIMS experience. *Am. J. Clin. Oncol.* 2010;33:238–241.
- [24] Engelsman M, Schwarz M, Dong L. Physics controversies in proton therapy. *Semin. Radiat. Oncol.* 2013;23:88–96.
- [25] Siddiqui F, Shi C, Papanikolaou N, *et al.* Image-guidance protocol comparison: Supine and prone set-up accuracy for pelvic radiation therapy. *Acta Oncol.* 2008;47:1344–1350.
- [26] Wiesendanger-Wittmer EM, Sijtsema NM, Muijs CT, *et al.* Systematic review of the role of a belly board device in radiotherapy delivery in patients with pelvic malignancies. *Radiother. Oncol.* 2012;102:325–334.
- [27] Stromberger C, Kom Y, Kawgan-Kagan M, *et al.* Intensity-modulated radiotherapy in patients with cervical cancer. An intra-individual comparison of prone and supine positioning. *Radiat. Oncol.* 2010;5:63.
- [28] Martin J, Fitzpatrick K, Horan G, *et al.* Treatment with a belly-board device significantly reduces the volume of small bowel irradiated and results in low acute toxicity in adjuvant radiotherapy for gynecologic cancer: results of a prospective study. *Radiother. Oncol.* 2005;74:267–274.
- [29] Lim K, Small W, Portelance L, *et al.* Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy for the definitive treatment of cervix cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2011;79:348–355.
- [30] Fotina I, Winkler P, Künzler T, *et al.* Advanced kernel methods vs. Monte Carlo-based dose calculation for high energy photon beams. *Radiother. Oncol.* 2009;93:645–653.
- [31] Krieger T, Sauer OA. Monte Carlo- versus pencil-beam-/collapsed-cone- dose calculation in a heterogeneous multi-layer phantom. *Phys. Med. Biol.* 2005;50:859–868.
- [32] Cozzi L, Dinshaw KA, Shrivastava SK, *et al.* A treatment planning study comparing volumetric arc modulation with RapidArc and fixed field IMRT for cervix uteri radiotherapy. *Radiother. Oncol.* 2008;89:180–191.
- [33] Lomax A. Intensity modulation methods for proton radiotherapy. *Phys. Med. Biol.* 1999;44:185–205.
- [34] Johansson B, Ridderheim M, Glimelius B. The potential of proton beam radiation therapy in prostate cancer, other urological cancers and gynaecological cancers. *Acta Oncol.* 2005;44:890–895.
- [35] Georg D, Georg P, Hillbrand M, *et al.* Assessment of improved organ at risk sparing for advanced cervix carcinoma utilizing precision radiotherapy techniques. *Strahlenther. Onkol.* 2008;184:586–591.
- [36] van Herk M. Different styles of image-guided radiotherapy. *Semin. Radiat. Oncol.* 2007;17:258–267.
- [37] Dawson LA, Jaffray DA. Advances in image-guided radiation therapy. *J. Clin. Oncol.* 2007;25:938–946.
- [38] Mao W, Hsu A, Riaz N, *et al.* Image-guided radiotherapy in near real time with intensity-modulated radiotherapy megavoltage treatment beam imaging. *Int. J. Radiat. Oncol. Biol. Phys.* 2009;75:603–610.
- [39] Herman MG, Pisansky TM, Kruse JJ, *et al.* Technical aspects of daily online positioning of the prostate for three-dimensional conformal radiotherapy using an electronic portal imaging device. *Int. J. Radiat. Oncol. Biol. Phys.* 2003;57:1131–1140.
- [40] Dávila Fajardo R, Lekkerkerker SJ, van der Horst A, *et al.* EUS-guided fiducial markers placement with a 22-gauge needle for image-guided radiation therapy in pancreatic cancer. *Gastrointest. Endosc.* 2014;79:851–855.
- [41] Chai X, van Herk M, van de Kamer JB, *et al.* Behavior of lipiodol markers during image guided radiotherapy of bladder cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;77:309–314.
- [42] Machiels M, van Hooft J, Jin P, *et al.* Endoscopy/EUS-guided fiducial marker placement in patients with esophageal cancer: a comparative analysis of 3 types of markers. *Gastrointest. Endosc.* 2015;82:641–649.
- [43] Jin P, Hulshof MCCM, de Jong R, *et al.* Quantification of respiration-induced esophageal tumor motion using fiducial markers and four-dimensional computed tomography. *Radiother. Oncol.* 2016;118:492–497.
- [44] Kaatee RSJP, Olofsen MJJ, Verstraate MJB, *et al.* Detection of organ movement in cervix cancer patients using a fluoroscopic electronic portal imaging device and radiopaque markers. *Int. J. Radiat. Oncol. Biol. Phys.* 2002;54:576–583.
- [45] Hariopotornkul NH, Nath SK, Scanderbeg D, *et al.* Evaluation of intra- and inter-fraction movement of the cervix during intensity modulated radiation therapy. *Radiother. Oncol.* 2011;98:347–351.

- [46] Langerak T, Mens JW, Quint S, *et al.* Cervix motion in 50 cervical cancer patients assessed by daily cone beam computed tomographic imaging of a new type of marker. *Int. J. Radiat. Oncol. Biol. Phys.* 2015;93:532–539.
- [47] Yan D, Vicini F, Wong J, *et al.* Adaptive radiation therapy. *Phys. Med. Biol.* 1997;42:123–132.
- [48] Yan D, Ziaja E, Jaffray D, *et al.* The use of adaptive radiation therapy to reduce setup error: a prospective clinical study. *Int. J. Radiat. Oncol. Biol. Phys.* 1998;41:715–720.
- [49] Nuver TT, Hoogeman MS, Remeijer P, *et al.* An adaptive off-line procedure for radiotherapy of prostate cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2007;67:1559–1567.
- [50] de Boer HCJ, Heijmen BJM. A protocol for the reduction of systematic patient setup errors with minimal portal imaging workload. *Int. J. Radiat. Oncol. Biol. Phys.* 2001;50:1350–1365.
- [51] Bel A, van Herk M, Bartelink H, *et al.* A verification procedure to improve patient set-up accuracy using portal images. *Radiother. Oncol.* 1993;29:253–260.
- [52] Wright P, Muren LP, Høyer M, *et al.* Evaluation of adaptive radiotherapy of bladder cancer by image-based tumour control probability modelling. *Acta Oncol.* 2010;49:1045–1051.
- [53] Vestergaard A, Søndergaard J, Petersen JB, *et al.* A comparison of three different adaptive strategies in image-guided radiotherapy of bladder cancer. *Acta Oncol.* 2010;49:1069–1076.
- [54] Ahmad R, Bondar L, Voet P, *et al.* A margin-of-the-day online adaptive intensity-modulated radiotherapy strategy for cervical cancer provides superior treatment accuracy compared to clinically recommended margins: a dosimetric evaluation. *Acta Oncol.* 2013;52:1430–1436.
- [55] Søvik A, Rødal J, Skogmo HK, *et al.* Adaptive radiotherapy based on contrast enhanced cone beam CT imaging. *Acta Oncol.* 2010;49:972–977.
- [56] Stewart J, Lim K, Kelly V, *et al.* Automated weekly replanning for intensity-modulated radiotherapy of cervix cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;78:350–358.
- [57] Thörnqvist S, Hysing LB, Zolnay AG, *et al.* Adaptive radiotherapy in locally advanced prostate cancer using a statistical deformable motion model. *Acta Oncol.* 2013;52:1423–1429.
- [58] Lutkenhaus LJ, Visser J, de Jong R, *et al.* Evaluation of delivered dose for a clinical daily adaptive plan selection strategy for bladder cancer radiotherapy. *Radiother. Oncol.* 2015;116:51–56.
- [59] Heijkoop ST, Langerak TR, Quint S, *et al.* Clinical implementation of an online adaptive plan-of-the-day protocol for nonrigid motion management in locally advanced cervical cancer IMRT. *Int. J. Radiat. Oncol. Biol. Phys.* 2014;90:673–679.
- [60] Meijer GJ, van der Toorn P-P, Bal M, *et al.* 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;105:174–179.
- [61] Vestergaard A, Kallehauge JF, Petersen JBB, *et al.* An adaptive radiotherapy planning strategy for bladder cancer using deformation vector fields. *Radiother. Oncol.* 2014;112:371–375.
- [62] Nijkamp J, Marijnen C, van Herk M, *et al.* Adaptive radiotherapy for long course neo-adjuvant treatment of rectal cancer. *Radiother. Oncol.* 2012;103:353–359.
- [63] Gill S, Pham D, Dang K, *et al.* Plan of the day selection for online image-guided adaptive post-prostatectomy radiotherapy. *Radiother. Oncol.* 2013;107:165–170.
- [64] Ahmad R, Hoogeman MS, Quint S, *et al.* Inter-fraction bladder filling variations and time trends for cervical cancer patients assessed with a portable 3-dimensional ultrasound bladder scanner. *Radiother. Oncol.* 2008;89:172–179.
- [65] Bondar L, Hoogeman M, Mens JW, *et al.* Toward an individualized target motion management for IMRT of cervical cancer based on model-predicted cervix-uterus shape and position. *Radiother. Oncol.* 2011;99:240–245.
- [66] Ahmad R, Hoogeman MS, Bondar M, *et al.* Increasing treatment accuracy for cervical cancer patients using correlations between bladder-filling change and cervix-uterus displacements: proof of principle. *Radiother. Oncol.* 2011;98:340–346.
- [67] Kerkhof EM, van der Put RW, Raaymakers BW, *et al.* Intrafraction motion in patients with cervical cancer: The benefit of soft tissue registration using MRI. *Radiother. Oncol.* 2009;93:115–121.

- [68] Kerkhof EM, Raaymakers BW, van der Heide UA, *et al.* Online MRI guidance for healthy tissue sparing in patients with cervical cancer: an IMRT planning study. *Radiother. Oncol.* 2008;88:241–249.
- [69] Marnitz S, Wlodarczyk W, Neumann O, *et al.* Which technique for radiation is most beneficial for patients with locally advanced cervical cancer? Intensity modulated proton therapy versus intensity modulated photon treatment, helical tomotherapy and volumetric arc therapy for primary radiation – an intraindividual comparison. *Radiat. Oncol.* 2015;10:91.
- [70] Milby AB, Both S, Ingram M, *et al.* Dosimetric comparison of combined intensity-modulated radiotherapy (IMRT) and proton therapy versus IMRT alone for pelvic and para-aortic radiotherapy in gynecologic malignancies. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;82:e477–e484.
- [71] Song WY, Huh SN, Liang Y, *et al.* Dosimetric comparison study between intensity modulated radiation therapy and threedimensional conformal proton therapy for pelvic bone marrow sparing in the treatment of cervical cancer. *J. Appl. Clin. Med. Phys.* 2010;11:3255.
- [72] Eifel PJ, Winter K, Morris M, *et al.* Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high-risk cervical cancer: an update of Radiation Therapy Oncology Group trial (RTOG) 90-01. *J. Clin. Oncol.* 2004;22:872–880.
- [73] Jadon R, Pembroke CA, Hanna CL, *et al.* A systematic review of organ motion and image-guided strategies in external beam radiotherapy for cervical cancer. *Clin. Oncol.* 2014;26:185–196.
- [74] Heijkoop ST, Langerak TR, Quint S, *et al.* Quantification of intra-fraction changes during radiotherapy of cervical cancer assessed with pre- and post-fraction Cone Beam CT scans. *Radiother. Oncol.* 2015;117:536–541.
- [75] van de Schoot AJAJ, Schooneveldt G, Wognum S, *et al.* Generic method for automatic bladder segmentation on cone beam CT using a patient-specific bladder shape model. *Med. Phys.* 2014;41:031707.
- [76] Bondar ML, Hoogeman M, Schillemans W, *et al.* Intra-patient semi-automated segmentation of the cervix-uterus in CT-images for adaptive radiotherapy of cervical cancer. *Phys. Med. Biol.* 2013;58:5317–5332.
- [77] van de Schoot AJAJ, de Boer P, Crama KF, *et al.* Dosimetric advantages of proton therapy compared with photon therapy using an adaptive strategy in cervical cancer. *Acta Oncol.* 2016; doi:10.3109/0284186X.2016.1139179.
- [78] Bondar L, Hoogeman MS, Vásquez Osorio EM, *et al.* A symmetric nonrigid registration method to handle large organ deformations in cervical cancer patients. *Med. Phys.* 2010;37:3760–3772.
- [79] Veiga C, McClelland J, Moinuddin S, *et al.* Toward adaptive radiotherapy for head and neck patients: Feasibility study on using CT-to-CBCT deformable registration for “dose of the day” calculations. *Med. Phys.* 2014;41:031703.
- [80] Stanley N, Glide-Hurst C, Kim J, *et al.* Using patient-specific phantoms to evaluate deformable image registration algorithms for adaptive radiation therapy. *J. Appl. Clin. Med. Phys.* 2013;14:4363.
- [81] Onozato Y, Kadoya N, Fujita Y, *et al.* Evaluation of on-board kV cone beam computed tomography based dose calculation with deformable image registration using hounsfield unit modifications. *Int. J. Radiat. Oncol. Biol. Phys.* 2014;89:416–423.
- [82] Oh S, Stewart J, Moseley J, *et al.* Hybrid adaptive radiotherapy with on-line MRI in cervix cancer IMRT. *Radiother. Oncol.* 2014;110:323–328.
- [83] Bondar ML, Hoogeman MS, Mens JW, *et al.* Individualized nonadaptive and online-adaptive intensity-modulated radiotherapy treatment strategies for cervical cancer patients based on pretreatment acquired variable bladder filling computed tomography scans. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;83:1617–1623.
- [84] van de Schoot AJAJ, de Boer P, Buist MR, *et al.* Quantification of delineation errors of the gross tumor volume on magnetic resonance imaging in uterine cervical cancer using pathology data and deformation correction. *Acta Oncol.* 2014;54:224–231.
- [85] Kontaxis C, Bol GH, Lagendijk JJW, *et al.* A new methodology for inter- and intrafraction plan adaptation for the MR-linac. *Phys. Med. Biol.* 2015;60:7485–7497.
- [86] Jaffray DA, Siewerdsen JH, Wong JW, *et al.* Flat-panel cone-beam computed tomography for image-guided radiation therapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2002;53:1337–1349.
- [87] Oelfke U, Tücking T, Nill S, *et al.* Linac-integrated kV-cone beam CT: technical features and first applications. *Med. Dosim.* 2006;31:62–70.

- [88] Muren LP, Smaaland R, Dahl O. Conformal radiotherapy of urinary bladder cancer. *Radiother. Oncol.* 2004;73:387–398.
- [89] Tyagi N, Lewis JH, Yashar CM, *et al.* Daily online cone beam computed tomography to assess interfractional motion in patients with intact cervical cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2011;80:273–280.
- [90] Peng C, Ahunbay E, Chen G, *et al.* Characterizing interfraction variations and their dosimetric effects in prostate cancer radiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2011;79:909–914.
- [91] Nijkamp J, de Jong R, Sonke J-J, *et al.* Target volume shape variation during irradiation of rectal cancer patients in supine position: comparison with prone position. *Radiother. Oncol.* 2009;93:285–292.
- [92] Taylor A, Powell MEB. An assessment of interfractional uterine and cervical motion: implications for radiotherapy target volume definition in gynaecological cancer. *Radiother. Oncol.* 2008;88:250–257.
- [93] Buchali A, Koswig S, Dinges S, *et al.* Impact of the filling status of the bladder and rectum on their integral dose distribution and the movement of the uterus in the treatment planning of gynaecological cancer. *Radiother. Oncol.* 1999;52:29–34.
- [94] Thongphiew D, Wu QJ, Lee WR, *et al.* Comparison of online IGRT techniques for prostate IMRT treatment: Adaptive vs repositioning correction. *Med. Phys.* 2009;36:1651.
- [95] Lim K, Kelly V, Stewart J, *et al.* Pelvic radiotherapy for cancer of the cervix: is what you plan actually what you deliver? *Int. J. Radiat. Oncol. Biol. Phys.* 2009;74:304–312.
- [96] Pos FJ, Hulshof M, Lebesque J, *et al.* Adaptive radiotherapy for invasive bladder cancer: a feasibility study. *Int. J. Radiat. Oncol. Biol. Phys.* 2006;64:862–868.
- [97] Li T, Thongphiew D, Zhu X, *et al.* Adaptive prostate IGRT combining online re-optimization and re-positioning: a feasibility study. *Phys. Med. Biol.* 2011;56:1243–1258.
- [98] Burrige N, Amer A, Marchant T, *et al.* Online adaptive radiotherapy of the bladder: small bowel irradiated-volume reduction. *Int. J. Radiat. Oncol. Biol. Phys.* 2006;66:892–897.
- [99] Foroudi F, Wong J, Kron T, *et al.* Online adaptive radiotherapy for muscle-invasive bladder cancer: results of a pilot study. *Int. J. Radiat. Oncol. Biol. Phys.* 2011;81:765–771.
- [100] Weiss E, Wu J, Sleeman W, *et al.* Clinical evaluation of soft tissue organ boundary visualization on cone-beam computed tomographic imaging. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;78:929–936.
- [101] Stippel G, van Rooijen DC, Crezee J, *et al.* Automatic delineation of body contours on cone-beam CT images using a delineation booster. *Phys. Med. Biol.* 2012;57:N225–N236.
- [102] Poulsen PR, Fledelius W, Keall PJ, *et al.* A method for robust segmentation of arbitrarily shaped radiopaque structures in cone-beam CT projections. *Med. Phys.* 2011;38:2151.
- [103] Fledelius W, Worm E, Elstrøm U V, *et al.* Robust automatic segmentation of multiple implanted cylindrical gold fiducial markers in cone-beam CT projections. *Med. Phys.* 2011;38:6351–6361.
- [104] Yan D, Jaffray DA, Wong JW. A model to accumulate fractionated dose in a deforming organ. *Int. J. Radiat. Oncol. Biol. Phys.* 1999;44:665–675.
- [105] Jaffray DA, Lindsay PE, Brock KK, *et al.* Accurate accumulation of dose for improved understanding of radiation effects in normal tissue. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;76:S135–S139.
- [106] Chai X, van Herk M, Betgen A, *et al.* Automatic bladder segmentation on CBCT for multiple plan ART of bladder cancer using a patient-specific bladder model. *Phys. Med. Biol.* 2012;57:3945–3962.
- [107] Chai X, van Herk M, Betgen A, *et al.* Semiautomatic bladder segmentation on CBCT using a population-based model for multiple-plan ART of bladder cancer. *Phys. Med. Biol.* 2012;57:N525–N541.
- [108] Taubin G. A signal processing approach to fair surface design. *Proc. 22nd Annu. Conf. Comput. Graph. Interact. Tech.* 1995:351–358.
- [109] Brechbühler C, Gerig G, Kübler O. Parametrization of closed surfaces for 3-D shape description. *Comput. Vis. Image Underst.* 1995;61:154–170.
- [110] Söhn M, Birkner M, Yan D, *et al.* Modelling individual geometric variation based on dominant eigenmodes of organ deformation: implementation and evaluation. *Phys. Med. Biol.* 2005;50:5893–5908.

- [111] Nelder JA, Mead R. A simplex method for function minimization. *Comput. J.* 1965;7:308–13.
- [112] Lütgendorf-Caucig C, Fotina I, Stock M, *et al.* Feasibility of CBCT-based target and normal structure delineation in prostate cancer radiotherapy: multi-observer and image multi-modality study. *Radiother. Oncol.* 2011;98:154–161.
- [113] Foroudi F, Haworth A, Pangehel A, *et al.* Inter-observer variability of clinical target volume delineation for bladder cancer using CT and cone beam CT. *J. Med. Imaging Radiat. Oncol.* 2009;53:100–106.
- [114] de Crevoisier R, Melancon AD, Kuban D a, *et al.* Changes in the pelvic anatomy after an IMRT treatment fraction of prostate cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2007;68:1529–1536.
- [115] Wognum S, Bondar L, Zolnay AG, *et al.* Control over structure-specific flexibility improves anatomical accuracy for point-based deformable registration in bladder cancer radiotherapy. *Med. Phys.* 2013;40:021702.
- [116] Meijer GJ, Rasch CRN, Remeijer P, *et al.* Three-dimensional analysis of delineation errors, setup errors, and organ motion during radiotherapy of bladder cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2003;55:1277–1287.
- [117] Simmat I, Georg P, Georg D, *et al.* Assessment of accuracy and efficiency of atlas-based autosegmentation for prostate radiotherapy in a variety of clinical conditions. *Strahlenther. Onkol.* 2012;188:807–815.
- [118] Logsdon MD, Eifel PJ. Figo IIIB squamous cell carcinoma of the cervix: an analysis of prognostic factors emphasizing the balance between external beam and intracavitary radiation therapy. *Int. J. Radiat. Oncol. Biol. Phys.* 1999;43:763–775.
- [119] Portelance L, Chao KS, Grigsby PW, *et al.* Intensity-modulated radiation therapy (IMRT) reduces small bowel, rectum, and bladder doses in patients with cervical cancer receiving pelvic and para-aortic irradiation. *Int. J. Radiat. Oncol. Biol. Phys.* 2001;51:261–266.
- [120] van de Bunt L, van der Heide UA, Ketelaars M, *et al.* Conventional, conformal, and intensity-modulated radiation therapy treatment planning of external beam radiotherapy for cervical cancer: The impact of tumor regression. *Int. J. Radiat. Oncol. Biol. Phys.* 2006;64:189–196.
- [121] Vale CL, Tierney JF, Davidson SE, *et al.* Substantial improvement in UK cervical cancer survival with chemoradiotherapy: results of a Royal College of Radiologists' audit. *Clin. Oncol.* 2010;22:590–601.
- [122] Kraan AC, van de Water S, Teguh DN, *et al.* Dose uncertainties in IMPT for oropharyngeal cancer in the presence of anatomical, range, and setup errors. *Int. J. Radiat. Oncol. Biol. Phys.* 2013;87:888–896.
- [123] Georg D, Kirisits C, Hillbrand M, *et al.* Image-guided radiotherapy for cervix cancer: high-tech external beam therapy versus high-tech brachytherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2008;71:1272–1278.
- [124] Clivio A, Kluge A, Cozzi L, *et al.* Intensity modulated proton beam radiation for brachytherapy in patients with cervical carcinoma. *Int. J. Radiat. Oncol. Biol. Phys.* 2013;87:897–903.
- [125] Breedveld S, Storchi PRM, Voet PWJ, *et al.* iCycle: Integrated, multicriterial beam angle, and profile optimization for generation of coplanar and noncoplanar IMRT plans. *Med. Phys.* 2012;39:951–963.
- [126] Meedt G, Alber M, Nüsslin F. Non-coplanar beam direction optimization for intensity-modulated radiotherapy. *Phys. Med. Biol.* 2003;48:2999–3019.
- [127] Wang X, Zhang X, Dong L, *et al.* Effectiveness of noncoplanar IMRT planning using a parallelized multiresolution beam angle optimization method for paranasal sinus carcinoma. *Int. J. Radiat. Oncol. Biol. Phys.* 2005;63:594–601.
- [128] Ottosson RO, Engstrom PE, Sjöström D, *et al.* The feasibility of using Pareto fronts for comparison of treatment planning systems and delivery techniques. *Acta Oncol.* 2009;48:233–237.
- [129] Fredriksson A, Forsgren A, Hårdemark B. Minimax optimization for handling range and setup uncertainties in proton therapy. *Med. Phys.* 2011;38:1672–1684.
- [130] van Kesteren Z, Janssen TM, Damen E, *et al.* The dosimetric impact of leaf interdigitation and leaf width on VMAT treatment planning in Pinnacle: comparing Pareto fronts. *Phys. Med. Biol.* 2012;57:2943–2952.
- [131] Janssen T, van Kesteren Z, Franssen G, *et al.* Pareto fronts in clinical practice for pinnacle. *Int. J. Radiat. Oncol. Biol. Phys.* 2013;85:873–880.
- [132] Li H, Zhang X, Park P, *et al.* Robust optimization in intensity-modulated proton therapy to account for anatomy changes in lung cancer patients. *Radiother. Oncol.* 2015;114:367–372.

- [133] Ottosson RO, Karlsson A, Behrens CF. Pareto front analysis of 6 and 15 MV dynamic IMRT for lung cancer using pencil beam, AAA and Monte Carlo. *Phys. Med. Biol.* 2010;55:4521–4533.
- [134] Bosman PAN. The anticipated mean shift and cluster registration in mixture-based EDAs for multi-objective optimization. *Proc. 12th Annu. Conf. Genet. Evol. Comput.* 2010:351–358.
- [135] Bosman PAN. On gradients and hybrid evolutionary algorithms for real-valued multi-objective optimization. *IEEE Trans. Evol. Comput.* 2012;16:51–69.
- [136] Paganetti H. Range uncertainties in proton therapy and the role of Monte Carlo simulations. *Phys. Med. Biol.* 2012;57:R99–R117.
- [137] Gay HA, Barthold HJ, O'Meara E, *et al.* Pelvic normal tissue contouring guidelines for radiation therapy: a Radiation Therapy Oncology Group consensus panel atlas. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;83:e353–e362.
- [138] van de Schoot AJAJ, Visser J, van Kesteren Z, *et al.* Beam configuration selection for robust intensity-modulated proton therapy in cervical cancer using Pareto front comparison. *Phys. Med. Biol.* 2016;61:1780–1794.
- [139] Paganetti H, Niemierko A, Ancukiewicz M, *et al.* Relative biological effectiveness (RBE) values for proton beam therapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2002;53:407–421.
- [140] Stenmark MH, Conlon ASC, Johnson S, *et al.* Dose to the inferior rectum is strongly associated with patient reported bowel quality of life after radiation therapy for prostate cancer. *Radiother. Oncol.* 2014;110:291–297.
- [141] Roeske JC, Bonta D, Mell LK, *et al.* A dosimetric analysis of acute gastrointestinal toxicity in women receiving intensity-modulated whole-pelvic radiation therapy. *Radiother. Oncol.* 2003;69:201–207.
- [142] Weistrand O, Svensson S. The ANACONDA algorithm for deformable image registration in radiotherapy. *Med. Phys.* 2015;42:40–53.
- [143] van Rooijen DC, van Wieringen N, Stippel G, *et al.* Dose-guided radiotherapy: potential benefit of online dose recalculation for stereotactic lung irradiation in patients with non-small-cell lung cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;83:e557–e562.
- [144] Wognum S, Heethuis SE, Rosario T, *et al.* Validation of deformable image registration algorithms on CT images of ex vivo porcine bladders with fiducial markers. *Med. Phys.* 2014;41:071916.
- [145] Haie-Meder C, Pötter R, Van Limbergen E, *et al.* Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiother. Oncol.* 2005;74:235–245.
- [146] Tanderup K, Georg D, Pötter R, *et al.* Adaptive management of cervical cancer radiotherapy. *Semin. Radiat. Oncol.* 2010;20:121–129.
- [147] van Herk M. Errors and margins in radiotherapy. *Semin. Radiat. Oncol.* 2004;14:52–64.
- [148] Mitchell DG, Snyder B, Coakley F, *et al.* Early invasive cervical cancer: tumor delineation by magnetic resonance imaging, computed tomography, and clinical examination, verified by pathologic results, in the ACRIN 6651/GOG 183 Intergroup Study. *J. Clin. Oncol.* 2006;24:5687–5694.
- [149] Subak LL, Hricak H, Powell CB, *et al.* Cervical carcinoma: computed tomography and magnetic resonance imaging for preoperative staging. *Obstet. Gynecol.* 1995;86:43–50.
- [150] Barillot I, Reynaud-Bougnoux A. The use of MRI in planning radiotherapy for gynaecological tumours. *Cancer Imaging.* 2006;6:100–106.
- [151] Park H, Piert MR, Khan A, *et al.* Registration methodology for histological sections and in vivo imaging of human prostate. *Acad. Radiol.* 2008;15:1027–1039.
- [152] Groenendaal G, Moman MR, Korporaal JG, *et al.* Validation of functional imaging with pathology for tumor delineation in the prostate. *Radiother. Oncol.* 2010;94:145–150.
- [153] Caldas-Magalhaes J, Kasperts N, Kooij N, *et al.* Validation of imaging with pathology in laryngeal cancer: accuracy of the registration methodology. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;82:e289–e298.
- [154] deSouza NM, Scoones D, Krausz T, *et al.* High-resolution MR imaging of stage I cervical neoplasia with a dedicated transvaginal coil: MR features and correlation of imaging and pathologic findings. *AJR. Am. J. Roentgenol.* 1996;166:553–559.

- [155] Zhang Y, Hu J, Li J, *et al.* Comparison of imaging-based gross tumor volume and pathological volume determined by whole-mount serial sections in primary cervical cancer. *Onco. Targets. Ther.* 2013;6:917–923.
- [156] Klein S, Staring M, Murphy K, *et al.* Elastix: a toolbox for intensity-based medical image registration. *IEEE Trans. Med. Imaging.* 2010;29:196–205.
- [157] Dimopoulos JCA, De Vos V, Berger D, *et al.* Inter-observer comparison of target delineation for MRI-assisted cervical cancer brachytherapy: application of the GYN GEC-ESTRO recommendations. *Radiother. Oncol.* 2009;91:166–172.
- [158] Mazaheri Y, Bokacheva L, Kroon D-J, *et al.* Semi-automatic deformable registration of prostate MR images to pathological slices. *J. Magn. Reson. imaging.* 2010;32:1149–1157.
- [159] Sala E, Rockall A, Rangarajan D, *et al.* The role of dynamic contrast-enhanced and diffusion weighted magnetic resonance imaging in the female pelvis. *Eur. J. Radiol.* 2010;76:367–385.
- [160] Wyatt RM, Beddoe AH, Dale RG. The effects of delays in radiotherapy treatment on tumour control. *Phys. Med. Biol.* 2003;48:139–155.
- [161] Pötter R, Georg P, Dimopoulos JCA, *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;100:116–123.
- [162] Castelnau-Marchand P, Chargari C, Maroun P, *et al.* Clinical outcomes of definitive chemoradiation followed by intracavitary pulsed-dose rate image-guided adaptive brachytherapy in locally advanced cervical cancer. *Gynecol. Oncol.* 2015;139:288–294.
- [163] Kavanagh BD, Pan CC, Dawson LA, *et al.* Radiation dose-volume effects in the stomach and small bowel. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;76:101–107.
- [164] Taylor A, Rockall AG, Reznick RH, *et al.* Mapping pelvic lymph nodes: guidelines for delineation in intensity-modulated radiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2005;63:1604–1612.
- [165] van de Bunt L, Jürgenliemk-Schulz IM, de Kort GAP, *et al.* Motion and deformation of the target volumes during IMRT for cervical cancer: what margins do we need? *Radiother. Oncol.* 2008;88:233–240.
- [166] Collen C, Engels B, Duchateau M, *et al.* Volumetric imaging by megavoltage computed tomography for assessment of internal organ motion during radiotherapy for cervical cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;77:1590–1595.
- [167] de Boer P, Bleeker MCG, Spijkerboer AM, *et al.* Craniocaudal tumour extension in uterine cervical cancer on MRI compared to histopathology. *Eur. J. Radiol. Open.* 2015;2:111–117.
- [168] Pötter R, Haie-Meder C, van Limbergen E, *et al.* Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy — 3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. *Radiother. Oncol.* 2006;78:67–77.
- [169] International commission on radiation units and measurements. *ICRU report 83: prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy (IMRT)*. Vol. 10. Oxford, UK: Oxford University Press; 2010.
- [170] Feuvret L, Noël G, Mazeron J-J, *et al.* Conformity index: a review. *Int. J. Radiat. Oncol. Biol. Phys.* 2006;64:333–342.
- [171] Marks LB, Yorke ED, Jackson A, *et al.* Use of normal tissue complication probability models in the clinic. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;76:S10–S19.
- [172] Langendijk JA, Lambin P, de Ruyscher D, *et al.* Selection of patients for radiotherapy with protons aiming at reduction of side effects: The model-based approach. *Radiother. Oncol.* 2013;107:267–273.
- [173] Höckel M, Horn L-C, Fritsch H. Association between the mesenchymal compartment of uterovaginal organogenesis and local tumour spread in stage IB–IIB cervical carcinoma: a prospective study. *Lancet Oncol.* 2005;6:751–756.
- [174] Kim H, Kim W, Lee M, *et al.* Tumor volume and uterine body invasion assessed by MRI for prediction of outcome in cervical carcinoma treated with concurrent chemotherapy and radiotherapy. *Jpn. J. Clin. Oncol.* 2007;37:858–866.

- [175] Plante M, Gregoire J, Renaud M-C, *et al.* The vaginal radical trachelectomy: An update of a series of 125 cases and 106 pregnancies. *Gynecol. Oncol.* 2011;121:290–297.
- [176] Nishio H, Fujii T, Kameyama K, *et al.* Abdominal radical trachelectomy as a fertility-sparing procedure in women with early-stage cervical cancer in a series of 61 women. *Gynecol. Oncol.* 2009;115:51–55.
- [177] Diaz JP, Sonoda Y, Leitao MM, *et al.* Oncologic outcome of fertility-sparing radical trachelectomy versus radical hysterectomy for stage IB1 cervical carcinoma. *Gynecol. Oncol.* 2008;111:255–260.
- [178] Georg P, Pötter R, Georg D, *et al.* Dose effect relationship for late side effects of the rectum and urinary bladder in magnetic resonance image-guided adaptive cervix cancer brachytherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;82:653–657.
- [179] Mazon R, Petit C, Rivin E, *et al.* 45 or 50 Gy, which is the optimal radiotherapy pelvic dose in locally advanced cervical cancer in the perspective of reaching magnetic resonance image-guided adaptive brachytherapy planning aims? *Clin. Oncol.* 2016;28:171–177.
- [180] Lu C, Chelikani S, Papademetris X, *et al.* An integrated approach to segmentation and nonrigid registration for application in image-guided pelvic radiotherapy. *Med. Image Anal.* 2011;15:772–785.
- [181] Lu C, Chelikani S, Jaffray D a, *et al.* Simultaneous nonrigid registration, segmentation, and tumor detection in MRI guided cervical cancer radiation therapy. *IEEE Trans. Med. Imaging.* 2012;31:1213–1227.
- [182] Fledelius W, Worm E, Høyer M, *et al.* Real-time segmentation of multiple implanted cylindrical liver markers in kilovoltage and megavoltage x-ray images. *Phys. Med. Biol.* 2014;59:2787–2800.
- [183] de Kerf G, van Gestel D, Mommaerts L, *et al.* Evaluation of the optimal combinations of modulation factor and pitch for Helical TomoTherapy plans made with TomoEdge using Pareto optimal fronts. *Radiat. Oncol.* 2015;10:191.
- [184] Lechner W, Kragl G, Georg D. Evaluation of treatment plan quality of IMRT and VMAT with and without flattening filter using Pareto optimal fronts. *Radiother. Oncol.* 2013;109:437–441.
- [185] Wala J, Craft D, Paly J, *et al.* Maximizing dosimetric benefits of IMRT in the treatment of localized prostate cancer through multicriteria optimization planning. *Med. Dosim.* 2013;38:298–303.
- [186] Djajaputra D, Wu Q, Wu Y, *et al.* Algorithm and performance of a clinical IMRT beam-angle optimization system. *Phys. Med. Biol.* 2003;48:3191–3212.
- [187] Tang S, Deville C, Tochner Z, *et al.* Impact of intrafraction and residual interfraction effect on prostate proton pencil beam scanning. *Int. J. Radiat. Oncol. Biol. Phys.* 2014;90:1186–1194.
- [188] Zhu X, Espana S, Daartz J, *et al.* Monitoring proton radiation therapy with in-room PET imaging. *Phys. Med. Biol.* 2011;56:4041–4057.
- [189] Mori S, Zenklusen S, Knopf AC. Current status and future prospects of multi-dimensional image-guided particle therapy. *Radiol. Phys. Technol.* 2013;6:249–272.
- [190] Cheung JP, Park PC, Court LE, *et al.* A novel dose-based positioning method for CT image-guided proton therapy. *Med. Phys.* 2013;40:051714.
- [191] Mendenhall NP, Hoppe BS, Nichols RC, *et al.* Five-year outcomes from 3 prospective trials of image-guided proton therapy for prostate cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2014;88:596–602.
- [192] van Dijk IWEM, Oldenburger F, Cardous-Ubbink MC, *et al.* Evaluation of late adverse events in long-term wilms' tumor survivor. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;78:370–378.
- [193] van Dijk IWEM, Cardous-Ubbink MC, van der Pal HJH, *et al.* Dose-effect relationships for adverse events after cranial radiation therapy in long-term childhood cancer survivors. *Int. J. Radiat. Oncol. Biol. Phys.* 2013;85:768–775.
- [194] Hall EJ. Intensity-modulated radiation therapy, protons, and the risk of second cancers. *Int. J. Radiat. Oncol. Biol. Phys.* 2006;65:1–7.
- [195] Mizumoto M, Tsuboi K, Igaki H, *et al.* Phase I/II trial of hyperfractionated concomitant boost proton radiotherapy for supratentorial glioblastoma multiforme. *Int. J. Radiat. Oncol. Biol. Phys.* 2010;77:98–105.
- [196] Higginson DS, Morris DE, Jones EL, *et al.* Stereotactic body radiotherapy (SBRT): Technological innovation and application in gynecologic oncology. *Gynecol. Oncol.* 2011;120:404–412.

- [197] Taylor A, Rockall AG, Powell MEB. An atlas of the pelvic lymph node regions to aid radiotherapy target volume definition. *Clin. Oncol.* 2007;19:542–550.
- [198] Groenendaal G, Borren A, Moman MR, *et al.* Pathologic validation of a model based on diffusion-weighted imaging and dynamic contrast-enhanced magnetic resonance imaging for tumor delineation in the prostate peripheral zone. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;82:e537–e544.
- [199] Gladwish AP, Han K, Foltz WD. Variation in apparent diffusion coefficient measurements among women with locally advanced cervical cancer. *Radiother. Oncol.* 2015;117:532–535.
- [200] McVeigh PZ, Syed AM, Milosevic M, *et al.* Diffusion-weighted MRI in cervical cancer. *Eur. J. Radiol.* 2008;18:1058–1064.
- [201] Lund KV, Simonsen TG, Hompland T, *et al.* Short-term pretreatment DCE-MRI in prediction of outcome in locally advanced cervical cancer. *Radiother. Oncol.* 2015;115:379–385.
- [202] Kallehauge JF, Tanderup K, Duan C, *et al.* Tracer kinetic model selection for dynamic contrast-enhanced magnetic resonance imaging of locally advanced cervical cancer. *Acta Oncol.* 2014;53:1064–1072.
- [203] Fu Z-Z, Peng Y, Cao L-Y, *et al.* Value of apparent diffusion coefficient (ADC) in assessing radiotherapy and chemotherapy success in cervical cancer. *Magn. Reson. Imaging.* 2015;33:516–524.
- [204] Hameeduddin A, Sahdev A. Diffusion-weighted imaging and dynamic contrast-enhanced MRI in assessing response and recurrent disease in gynaecological malignancies. *Cancer Imaging.* 2015;15:3.
- [205] Lee YK, Bollet M, Charles-Edwards G, *et al.* Radiotherapy treatment planning of prostate cancer using magnetic resonance imaging alone. *Radiother. Oncol.* 2003;66:203–216.
- [206] Siversson C, Nordström F, Nilsson T, *et al.* MRI only prostate radiotherapy planning using the statistical decomposition algorithm. *Med. Phys.* 2015;42:6090–6097.
- [207] Mutic S, Dempsey JF. The ViewRay system: magnetic resonance-guided and controlled radiotherapy. *Semin. Radiat. Oncol.* 2014;24:196–199.
- [208] Raaymakers BW, Lagendijk JJW, Overweg J, *et al.* Integrating a 1.5 T MRI scanner with a 6 MV accelerator: proof of concept. *Phys. Med. Biol.* 2009;54:N229–N237.
- [209] Ali I, Ahmad S, Alsbou N, *et al.* Correction of image artifacts from treatment couch in cone-beam CT from kV on-board imaging. *J. Xray. Sci. Technol.* 2011;19:321–332.
- [210] Han X, Pearson E, Pelizzari C, *et al.* Algorithm-enabled exploration of image-quality potential of cone-beam CT in image-guided radiation therapy. *Phys. Med. Biol.* 2015;60:4601–4633.
- [211] Yan H, Cervino L, Jia X, *et al.* A comprehensive study on the relationship between the image quality and imaging dose in low-dose cone beam CT. *Phys. Med. Biol.* 2012;57:2063–2080.
- [212] Tian Z, Jia X, Yuan K, *et al.* Low-dose CT reconstruction via edge-preserving total variation regularization. *Phys. Med. Biol.* 2011;56:5949–5967.
- [213] Li X, Quan EM, Li Y, *et al.* A fully automated method for CT-on-rails-guided online adaptive planning for prostate cancer intensity modulated radiation therapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2013;86:835–841.
- [214] Wooten HO, Green O, Yang M, *et al.* Quality of intensity modulated radiation therapy treatment plans using a ⁶⁰Co magnetic resonance image guidance radiation therapy system. *Int. J. Radiat. Oncol. Biol. Phys.* 2015;92:771–778.
- [215] Lagendijk JJW, Raaymakers BW, van Vulpen M. The magnetic resonance imaging-linac system. *Semin. Radiat. Oncol.* 2014;24:207–209.
- [216] Bol GH, Lagendijk JJW, Raaymakers BW. Virtual couch shift (VCS): accounting for patient translation and rotation by online IMRT re-optimization. *Phys. Med. Biol.* 2013;58:2989–3000.
- [217] Raaymakers BW, Raaijmakers AJE, Lagendijk JJW. Feasibility of MRI guided proton therapy: magnetic field dose effects. *Phys. Med. Biol.* 2008;53:5615–5622.
- [218] Crijns SPM, Raaymakers BW, Lagendijk JJW. Real-time correction of magnetic field inhomogeneity-induced image distortions for MRI-guided conventional and proton radiotherapy. *Phys. Med. Biol.* 2011;56:289–297.
- [219] Hartman J, Kontaxis C, Bol GH, *et al.* Dosimetric feasibility of intensity modulated proton therapy in a transverse magnetic field of 1.5 T. *Phys. Med. Biol.* 2015;60:5955–5969.