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Commentary

Target Volumes, Image Fusion and Contouring in Modern Radiotherapy Treatment Planning

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Introduction

In modern radiotherapy using ultra-tight treatment margins to spare normal tissues, accurate target delineation is very important. Traditional 2-Dimensional (2D) simulators we used for decades [1] are now replaced by computed tomography (CT) and magnetic resonance imaging (MRI) [2]. Modern radiotherapy relies on 3D imaging data [3] that require contouring of the gross target volume (GTV), clinical target volume (CTV) and planning target volume (PTV). GTV includes the tumor imaged and all other pertinent information, CTV includes clinical at risk area of microscopic spread and lymph nodes at risk, internal target volume (ITV) includes CTVs from different respirator phases, and PTV includes the set up errors [1].This paper is part of a series discussing some of the challenges and solutions of modern radiotherapy planning. For specific cancer sites, this study primarily focused on important aspects related to treatment planning of head and neck, and breast cancers as specific cancer sties .

Observer variability in targeting and contouring

There are well-known inter-observer and intra-observer variations for contouring of target [4-7] and normal tissues [8,9]. For example, in one study, the median PTV and the ratio of the largest to smallest contoured volume were respectively 9.22 cm^3 (range, 7.17 – 14.3 cm^3) and 1.99 for pituitary adenoma [6], and 6.86 cm^3 (range 6.05 – 14.6 cm^3) and 2.41 for meningioma. Some plans used 1-2 mm PTV margin, some used 0 mm margin is this study [6]. When the contours superimposed onto the "ideal" plan, there is an excessive dose of 23.64 Gy (up to 268% of the default plan) in pituitary adenoma and 24.84 Gy (131% of the default plan) in meningioma to the optic nerve [6]. The optic tract dose was to be kept within 50 Gy (in equivalent dose of 2 Gy fractions). Overall, contouring variability and errors are the most important challenge to modern 3D and 4D radiotherapy treatment planning [7].

Image fusion and contouring variability because of imaging modalities

Understanding the strengths and limitations of various imaging modalities is important in modern radiotherapy treatment planning. PET/CT has been found to be very useful in contouring of GTVs in treatment planning. When a dedicated PET-CT is used, the target volume could be directly contoured on the PET-CT [10]. Otherwise the PET-CT needs to be fused to the treatment CT, by registering the CT of the PET-CT to the treatment CT in most cases [10]. The information from the registration is used to bring PET of the PET-CT to fuse with the treatment CT [10]. It has been found that using the 40-50% standardized uptake value (SUV) is the best in contouring based on phantom [11] and 20–40% in some clinical studies [12]. Part of the PET SUV blurring comes from respiratory motion [12]. In one study [13], 50% PET value and CT lung window and level of 1600 and -300 Hounsfield Units (HU) when the cancer is in the lung correlated best the pathologic size of the cancer. Mediastinal window and level of 600 HU and 40 HU were used when the tumor was close to the mediastinum [13]. The contouring on the fused PET image could facilitate contouring on the CT and MRI that are more commonly used imaging modalities in modern radiotherapy treatment planning [2,13,14]. Cone beam CT used for on-board imaging has poor tissue contrast making it more difficult to contour especially for pelvic tissues [15,16]. MRI (3D and 2D) data can better imaging the pelvic tissues [2,17-19] but would require more complex imaging during ra-

diotherapy.

Consensus and challenges in target and normal tissue contouring

The Radiation Therapy Oncology Group (RTOG) [7,20,21] and other US and international radiotherapy groups [7,22,23] have developed site specific contouring atlases since around 2009, when Intensity Modulated Radiotherapy (IMRT) and 3-Dimensional Radiotherapy (3D-CRT) became the standard of care. Blood vessels were found to be a good surrogate for lymph nodes and CTVs [24]. Contouring in 3D radiotherapy era is very time consuming, for example, the average time in contouring an oropharyngeal cancer case was about two hours [25]. It may be even more time consuming when 4D CT scan data are used [26]. Auto-contouring and semi-automatic programs have recently been developed to save the clinician time in contouring [27-32], including some specialize on using RTOG consensus atlases [33]. However, these auto-contouring programs still need to be validated before clinical use. Other than time consuming, 3D target and normal tissue contouring remain to have many challenges as discussed in this paper.

Head and neck targeting and contouring

The IMRT for head and neck cancer is relative new, only about 10 years [1]. It produced equivalent clinical outcome compared to the large amount of clinical data accumulated in the 2D era [1], but with less toxicity mostly better salivary function [1]. Usually, elective head and neck radiation treatment is used when the nodal recurrence is about 15-20% [1,25]. The RTOG guidelines for head and neck contouring are limited to N0 disease. In this study [25], the contouring variability of a node positive (N+) head and neck patient was studied. It was found that, the target to treat in oropharynx has shown significant variability even for published head and neck IMRT experts [25]. Some investigators have chosen to treat ipsilateral neck only for advanced stage III tonsillar cancers[25], the doses were variable ranging from 66 Gy to 70 Gy in 2 Gy fractions [25].In this study [25], 8 out of 20 academic and community centers used one level of CTV dose level, twelve used two CTV dose levels(high-risk and low-risk CTVs). Five of these twelve centers used an expansion of GTV and used the same dose level as used for the GTV [25]. The mean target volume irradiated was 250 cc (range 37– 676 cc) [25]. All centers covered the levels II and III, 95% covered the retropharyngeal lymph nodes and 85% covered the ipsilateral level Ib nodes [25]. Average CTV to PTV expansion was 4.11 mm (0 – 15 mm) [25]. The average time clinicians contouring the target and at risk organs was about two and a half hours [25]. Some clinicians use concurrent chemotherapy [25], but significant number of centers did not. Thus treatment variability remains a challenge even for a typical oropharyngeal cancer. Most of the information on normal tissue tolerance has been collected with 3D conformal radiotherapy [34-36]. Only, recently head and neck normal tissue tolerance in the IMRT era has been published [37]. More normal tissue tolerance information is needed in the IMRT era.

Breast cancer targeting and contouring

Breast cancer surgery has become more conservative over the past few decades moving away from radical mastectomy [1]. Recently more breast cancer patients undergo immediate breast reconstruction that could present a challenge to post-mastectomy radiotherapy [38,39]. Breast reconstruction using tissue expanders is associated with capsular contraction and other complications after radiotherapy [40,41], autologous more vascularized transplant is more appropriate when radiotherapy is planned [42]. Irradiated flap could atrophize about 21% while 16% in non-irradiated refs over 6-10 months [42]. In a randomized trial RESTORE-2, tissue defect up to 150 ml are eligible for the surgical reconstruction [42]. Recently, DIEP (deep inferior epigastric perforator) flap has been used in additional to TRAM (transverse rectus abdominismyocutaneous flap) [42-44]. In one study, a higher rate of complication was observed in the minority of patients who received 10 Gy scar boost [45]. However, overall post mastectomy radiotherapy (PMRT) to the usual dose of about 50-50.4Gy in 1.8-2 Gy fractions can be safely used after immediate or delayed breast reconstruction [40-45]. For reconstructed breast lumpectomy cavity, and with surgical clips placed, the lumpectomy cavity is contoured as the GTV and CTV is the same as the GTV [46] as compared with traditional lumpectomy cavity contouring when seroma is contoured as a GTV, and GTV to CTV of about 1 cm is typically used [46]. MRI can better see the lumpectomy cavity because of the fluid intensity on T2 MRI [47].

In modern era, the side effects of post-operative breast cancer radiotherapy include cardiac toxicity, arm lymphedema, pneumonitis, neuropathy, skin changes [48]. Trastuzumab is associated with cardiac toxicity (1-4%), unlike anthracyclin-related cardiomyopathy, it is not dose dependent, rarely causes death, and reversible when treated or when the drug is discontinued [48]. Trastuzumab is not used concurrently with anthracyclin because of cardiac toxicity [48]. Breast cancer radiotherapy after 1990 using modern techniques showed similar advantages for left sided versus right sided breast cancer patients [1,48]. Pericarditis and related pericardial effusion have decreased from 20% to 2.5% using modern 3D techniques [48]. Local regional radiotherapy is related to 4.1% of radiation pneumonitis, and 0.9% for local radiotherapy [48], 3.9% when treated with chemotherapy and 1.4% without chemotherapy [48]. Using supraclavicular and axillary fields has a 9-58% of arm lymphedema, the rate is negligible when these fields are not used [48]. Skin thickening and fibrosis occur in 1/3 of patients and in 5% for severe fibrosis [48]. Arm lymphedema occur in 13% of patients after lymph node dissection versus 1-3% using sentinel lymph node dissection [48]. Thus sparing the car-

diac and other normal tissues, by following the recommended organ at risk (OAR) guidelines, has become an important area of investigation over the past 2-3 decades and remains to be very important [36].

For hypofractionated whole breast radiotherapy, 40 Gy in 2.67 Gy fractions is usually used, 9 Gy in 3 fractions is used to boost the tumor bed [49]. In one study [49], patient is immobilized by a wing board and other personalized immobilization device [49]. CTV includes the whole breast tissue, and is expanded 5 mm to get the PTV [49]. Heart and lungs are contoured as OARs [49]. The median breast volume was 760.64 cc (range 44.77 – 1892.1 cc) [49]. The median boost volume was 143.33 cc (23.07–230.02 cc) [49]. Median time to first skin reaction was 12 days (5 –40 days) [49]. Other dose fractionations have also been used in whole breast hypofractionated radiotherapy and have similar outcome and cosmesis when compared with standard fractionation [49,50]. American Society of Therapeutical Radiation Oncology (ASTRO) recommended patients older than 50 years old, T1-T2N0, without chemotherapy, and dose homogeneity less than <7% are appropriate for hypofractionated whole breast radiotherapy [49]. The use of boost was associated with acute and late skin toxicities [49].

Conclusion

Over the last couple of decades, much has been learned about targeting the correct treatment volumes, the use of multi-modal image fusion to aid contouring and using advanced simulation (e.g. 4D), and image guided radiotherapy. However, as discussed above, this will be a continuous process along the progress in radiotherapy.

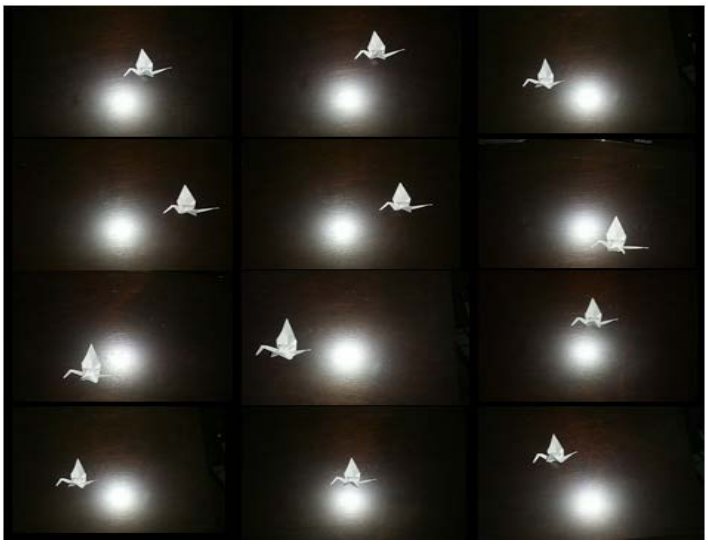

Figure Legend
Post-thoughts:
Cranes to Moons: Cranes present good wishes, happiness, and legend has it that each crane lives a thousand years. May each origami crane represent 100 best wishes for each of our patients.

References

1. Cox JD, Ang KK. Radiation Oncology: Rationale, Technique, Results, 9th Edition. 2009.

2. Krishnatry R, Patel FD, Singh P, Sharma SC, Oinam AS et al. CT or MRI for image-based brachytherapy in cervical cancer. Jpn J Clin Oncol. 2012, 42(4): 309-313.

3. Qiu H, Wild AT, Wang H, Fishman EK, Hruban RH et al. Comparison of conventional and 3-dimensional computed tomography against histopathologic examination in determining pancreatic adenocarcinoma tumor size: implications for radiation therapy planning. Radiother Oncol. 2012, 104(2): 167-172.

4. Mok H, Crane CH, Palmer MB, Briere TM, Beddar S et al. Intensity modulated radiation therapy (IMRT): differences in target volumes and improvement in clinically relevant doses to small bowel in rectal carcinoma. Radiat Oncol. 2011, 6: 63.

5. Perna L, Cozzarini C, Maggiulli E, Fellin G, Rancati T et al. Inter-observer variability in contouring the penile bulb on CT images for prostate cancer treatment planning. Radiat Onco. 2011, 6: 123.

6. Yamazaki H, Shiomi H, Tsubokura T, Kodani N, Nishimura T et al. Quantitative assessment of inter-observer variability in target volume delineation on stereotactic radiotherapy treatment for pituitary adenoma and meningioma near optic tract. Radiat Oncol. 2011, 6: 10.

7. Fuller CD, Nijkamp J, Duppen JC, Rasch CR, Thomas CR Jr et al. Prospective randomized double-blind pilot study of site-specific consensus atlas implementation for rectal cancer target volume delineation in the cooperative group setting. Int J Radiat Oncol Biol Phys. 2011, 79(2): 481-489.

8. Feng M, Demiroz C, Vineberg KA, Eisbruch A, Balter JM. Normal tissue anatomy for oropharyngeal cancer: contouring variability and its impact on optimization. Int J Radiat Oncol Biol Phys. 2012, 84(2): e245-249.

9. Gay HA, Barthold HJ, O'Meara E, Bosch WR, El Naqa I 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(3): e353-362.

10. Caballero Perea B, Villegas AC, Rodriguez JM, Velloso MJ, Vicente AM et al. Recommendations of the Spanish Societies of Radiation Oncology (SEOR), Nuclear Medicine & Molecular Imaging (SEMNiM), and Medical Physics (SEFM) on (18)F-FDG PET-CT for radiotherapy treatment planning. Rep Pract Oncol Radiother. 2012, 17(6): 298-318.

11. Uto F, Shiba E, Onoue S, Yoshimura H, Takada M et al. Phantom study on radiotherapy planning using PET/CT--delineation of GTV by evaluating SUV. J Radiat Res. 2010, 51(2): 157-164.

12. Lamb JM, Robinson C, Bradley J, Laforest R, Dehdashti F et al. Generating lung tumor internal target volumes from 4D-PET maximum intensity projections. Med Phys. 2011, 38: 5732-5737.

13. Wu K, Ung YC, Hwang D, Tsao SM, Darling G et al. Autocontouring and Manual Contouring: Which Is the Better Method for Target Delineation Using 18F-FDG PET/CT in Non–Small Cell Lung Cancer? J Nucl Med. 2010, 51(10): 1517-1523.

14. Metcalfe P, Liney GP, Holloway L, Walker A, Barton M et al. The potential for an enhanced role for MRI in radiation-therapy treatment planning. Technol Cancer Res Treat. 2013, 12(5): 429-446.

15. Weiss E, Wu J, Sleeman W, Bryant J, Mitra P et al. Clinical evaluation of soft tissue organ boundary visualization on cone-beam computed tomographic imaging. Int J Radiat Oncol Biol Phys. 2010, 78(3): 929-936.

16. Nishioka K, Shimizu S, Kinoshita R, Inoue T, Onodera S et al. Evaluation of inter-observer variability of bladder boundary delineation on cone-beam CT. Radiat Oncol. 2013, 8: 185.

17. Petric P, Hudej R, Rogelj P, Blas M, Segedin B et al. Comparison of 3D MRI with high sampling efficiency and 2D multiplanar MRI for contouring in cervix cancer brachytherapy. Radiol Oncol. 2012, 46(3): 242-251.

18. Rischke HC, Nestle U, Fechter T, Doll C, Volegova-Neher N et al. 3 Tesla multiparametric MRI for GTV-definition of Dominant Intraprostatic Lesions in patients with Prostate Cancer--an interobserver variability study. Radiat Oncol. 2013, 8: 183.

19. McLaughlin PW, Narayana V, Meirovitz A, Troyer S, Roberson PL et al. Vessel-sparing prostate radiotherapy: dose limitation to critical erectile vascular structures (internal pudendal artery and corpus cavernosum) defined by MRI. Int J Radiat Oncol Biol Phys. 2005, 61(1): 20-31.

20. Lawton CA, Michalski J, El-Naqa I, Buyyounouski MK, Lee WR et al. RTOG GU Radiation oncology specialists reach consensus on pelvic lymph node volumes for high-risk prostate cancer. Int J Radiat Oncol Biol Phys. 2009, 74(2): 383-387.

21. Myerson RJ, Garofalo MC, El Naqa I, Abrams RA, Apte A et al. Elective clinical target volumes for conformal therapy in anorectal cancer: a radiation therapy oncology group consensus panel contouring atlas. Int J Radiat Oncol Biol Phys. 2009, 74(3): 824-830.

22. Toita T, Ohno T, Kaneyasu Y, Uno T, Yoshimura R et al. A consensus-based guideline defining the clinical target volume for pelvic lymph nodes in external beam radiotherapy for uterine cervical cancer. Jpn J Clin Oncol. 2010, 40: 456-463.

23. Toita T, Ohno T, Kaneyasu Y, Kato T, Uno T et al. A consensus-based guideline defining clinical target volume for primary disease in external beam radiotherapy for intact uterine cervical cancer. Jpn J Clin Oncol. 2011, 41(9): 1119-1126.

24. Uno T, Isobe K, Ueno N, Kobayashi H, Sanayama Y et al. Vessel-contouring-based pelvic radiotherapy in patients with uterine cervical cancer. Jpn J Clin Oncol. 2009, 39(6): 376-380.

25. Hong TS, Tome WA, Harari PM. Heterogeneity in head and neck IMRT target design and clinical practice. Radiother Oncol. 2012, 103(1): 92-98.

26. Liu J, Wang JZ, Zhao JD, Xu ZY, Jiang GL. Use of combined maximum and minimum intensity projections to determine internal target volume in 4-dimensional CT scans for hepatic malignancies. Radiat Oncol. 2012, 7: 11.

27. Sharma N, Aggarwal LM. Automated medical image segmentation techniques. J Med Phys. 2010, 35(1): 3-14.

28. Multi-Institutional Target Delineation in Oncology Group. Human-computer interaction in radiotherapy target volume delineation: a prospective, multi-institutional comparison of user input devices. J Digit Imaging. 2011, 24(5): 794-803.

29. Kalpathy-Cramer J, Bedrick SD, Boccia K, Fuller CD. A pilot prospective feasibility study of organ-at-risk definition using Target Contour Testing/Instructional Computer Software (TaCTICS), a training and evaluation platform for radiotherapy target delineation. AMIA Annu Symp Proc. 2011: 654-663.

30. Kurugol S, Bas E, Erdogmus D, Dy JG, Sharp GC et al. Centerline extraction with principal curve tracing to improve 3D level set esophagus segmentation in CT images. Conf Proc IEEE Eng Med Biol Soc. 2011: 3403-3406.

31. Mahdavi SS, Chng N, Spadinger I, Morris WJ, Salcudean SE. Semi-automatic segmentation for prostate interventions. Med Image Anal. 2011, 15(2): 226-237.

32. Sharp G, Fritscher KD, Pekar V, Peroni M, Shusharina N et al. Vision 20/20: perspectives on automated image segmentation for radiotherapy. Med Phys. 2014, 41(5): 050902.

33. Velker VM, Rodrigues GB, Dinniwell R, Hwee J, Louie AV. Creation of RTOG compliant patient CT-atlases for automated

atlas based contouring of local regional breast and high-risk prostate cancers. Radiat Oncol. 2013, 8: 188.

34. Cheung MR, Tucker SL, Dong L, de Crevoisier R, Lee AK et al. Investigation of bladder dose and volume factors influencing late urinary toxicity after external beam radiotherapy for prostate cancer. Int J Radiat Oncol Biol Phys. 2007, 67(4): 1059-1065.

35. Tucker SL, Dong L, Bosch WR, Michalski J, Winter K et al. Late rectal toxicity on RTOG 94-06: analysis using a mixture Lyman model. Int J Radiat Oncol Biol Phys. 2010, 78(4): 1253-1260.

36. Marks LB, Yorke ED, Jackson A, Ten Haken RK, Constine LS et al. Use of normal tissue complication probability models in the clinic. Int J Radiat Oncol Biol Phys. 2010, 76(3 suppl): S10-19.

37. Studer G, Linsenmeier C, Riesterer O, Najafi Y, Brown M et al. Late term tolerance in head neck cancer patients irradiated in the IMRT era. Radiat Oncol. 2013, 8: 259.

38. Jackson WB, Goldson AL, Staud C. Postoperative irradiation following immediate breast reconstruction using a temporary tissue expander. J Natl Med Assoc. 1994, 86(7): 538-542.

39. Damast S, Beal K, Ballangrud A, Losasso TJ, Cordeiro PG et al. Do metallic ports in tissue expanders affect postmastectomy radiation delivery? Int J Radiat Oncol Biol Phys. 2006, 66(1): 305-310.

40. Russo JK, Armeson KE, Rhome R, Spanos M, Harper JL. Dose to level I and II axillary lymph nodes and lung by tangential field radiation in patients undergoing postmastectomy radiation with tissue expander reconstruction. Radiat Oncol. 2011, 6: 179.

41. Goh SC, Thorne AL, Williams G, Laws SA, Rainsbury RM. Breast reconstruction using permanent Becker expander implants: an 18 year experience. Breast. 2012, 21(6): 764-768.

42. Yoshimoto H, Hamuy R. Breast Reconstruction After Radiotherapy. Adv Wound Care (New Rochelle). 2012, 3(1): 12-15.

43. Clarke-Pearson EM, Chadha M, Dayan E, Dayan JH, Samson W et al. Comparison of irradiated versus nonirradiated DIEP flaps in patients undergoing immediate bilateral DIEP reconstruction with unilateral postmastectomy radiation therapy (PMRT). Ann Plast Surg. 2013, 71(3): 250-254.

44. Hirsch EM, Seth AK, Dumanian GA, Kim JY, Mustoe TA et al. Outcomes of immediate tissue expander breast reconstruction followed by reconstruction of choice in the setting of postmastectomy radiation therapy. Ann Plast Surg 72(3): 274-278.

45. Anderson PR, Hanlon AL, Fowble BL, McNeeley SW, Freedman GM. Low complication rates are achievable after postmastectomy breast reconstruction and radiation therapy. Int J Radiat Oncol Biol Phys. 2004, 59(4): 1080-1087.

46. Dzhugashvili M, Tournay E, Pichenot C, Dunant A, Pessoa E et al. 3D-conformal accelerated partial breast irradiation treatment planning: the value of surgical clips in the delineation of the lumpectomy cavity. Radiat Oncol. 2009, 4: 70.

47. Lee YS, Kim KJ, Ahn SD, Choi EK, Kim JH et al. The application of PET-CT to post-mastectomy regional radiation therapy using a deformable image registration. Radiat Oncol. 2013, 8: 104.

48. Agrawal S. Late effects of cancer treatment in breast cancer survivors. South Asian J Cancer. 2014, 3(2): 112–115.

49. Ciammella P, Podgornii A, Galeandro M, Micera R, Ramundo D et al. Toxicity and cosmetic outcome of hypofractionated whole-breast radiotherapy: predictive clinical and dosimetric factors. Radiat Oncol. 2014, 9: 97.

50. Scorsetti M, Alongi F, Fogliata A, Pentimalli S, Navarria P et al. Phase I-II study of hypofractionated simultaneous integrated boost using volumetric modulated arc therapy for adjuvant radiation therapy in breast cancer patients: a report of feasibility and early toxicity results in the first 50 treatments. Radiat Oncol. 2012, 7: 145.